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Serum Zonulin Level in Hashimoto Thyroditis Patients

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Abstract

Background: *Human zonulin is a protein that regulates the intercellular tight junctions in various tissues and organs of the human body. Hashimoto's thyroiditis (HT) is one of the most common endocrine autoimmune disorder, but the role in Hashimoto thyroiditis is unclear.*

Aim: *This study aimed to assess serum zonulin titre in Hashimoto thyroiditis patients.*

Patients and methods: *This cross sectional comparative analytic study was conducted on 44 patients who diagnosed as Hashimoto Thyroditis who were selected as healthy volunteer have the same age, sex and BMI.*

Results: *In the current study, this study included 44 female participants: 44 patients with Hashimoto thyroiditis. Patients had mean age of 34.43±7.99 years, all were female with mean body mass index of 31.1±3.8 (kg/m2). Thirty-four of patients (77.3%) had a goiter and were on medications. Hashimoto patients had median serum Zonulin of 37.1 ng/ml with IQR of 27.5 to 42.3 ng/ml. The There were insignificant correlations between serum Zonulin and age, BMI and thyroid profile.*

Conclusion: *There is no correlation between zonulin and thyroid hormones or autoantibodies in Hashimoto thyroiditis patients. Further research could be conducted in a larger cohort study is needed to elucidate a possible role of zonulin in the pathogenesis of Hashimoto thyroiditis.*

Key words: *Hashimoto Thyroditis, Serum Zonulin Level.*

Introduction

Hashimoto thyroiditis (HT), an autoimmune disease, is one of the most common ailments worldwide and affects certain organs. The characteristics of hypothyroidism include circulating autoantibodies against thyroid peroxidase (anti-TPO) and thyroglobulin (anti-Tg), tertiary lymphoid follicle development, and chronic inflammation. Thyroid parenchyma is replaced by lymphocyte infiltration, which results in organ enlargement, gland fibrosis, and destruction (1)(2)(3).

Zonulin plays akey role in IIP, when up regulated (4). Increased zonulin levels were reported to be correlated with IIP in vivo and changes in claudin-1, claudin-2, and myosin IXB gene expression (5). Increased serum zonulin levels were detected in human subjects during the pre-diabetic stage and preceded the onset of type 1 diabetes. In a rat model, zonulin-dependent IIP was shown to precede the onset of type 1 diabetes by 2-3 weeks. Moreover, oral administration of the zonulin inhibitor (AT-1001) to these rats blocked autoantibody formation, zonulin-mediated IIP, and finally reduced the incidence of diabetes. AT-1001 competitively blocks the apical zonulin receptor and prevents the opening of the TJ (6)(4)(5).

Aim of the study

This study aimed to assess serum zonulin titre in Hashimoto thyroiditis patients.

Patients and Methods

The endocrinology outpatient clinic at Suez Canal University Hospital served as the site of this descriptive cross-sectional investigation. In total, 44 patients between the ages of 18 and 45 who were diagnosed with Hashimoto Thyroditis at the endocrinology outpatient clinic were included in the study. The patients had decreased free thyroxine levels (FT4) <11 pmol/L, diffuse thyroid enlargement, elevated anti-TPO antibodies >35 IU/mL or positive anti-TPO antibodies, elevated anti-TG antibodies >20 IU/mL or positive anti-TG antibodies, increased TSH >5 IU/Ml, and elevated anti-TG antibodies >20 IU/mL or positive anti-TG antibodies.

Exclusions from the study included patients with type 1 or type 2 diabetes mellitus (diagnosed by fasting blood sugar and HbA1C), autoimmune disease (SLE, Rheumatoid Arthiritis), chronic or severe gastrointestinal disorders, on antibiotic therapy currently or within the last two weeks, taking probiotic agents currently or within the last three months, or taking fortified foods such as milk and dairy products with added vitamin D, patients on chemotherapy or suffering tumours, patients on laxative for chronic constipation, and patients with multiple sclerosis and non-alcoholic fatty liver were excluded from the study.

Patients were selected by simple random sampling from a list of patients with Hashimoto Thyroditis who were fulfilling the inclusion criteria attending endocrinology clinic in Suez Canal University Hospital (period: from July/2022 to July/2023).

Methods:

All participants were subjected to complete history taking, thyroid examination and complete physical examination. Biochemical Samples included (Anti- thyroid peroxidase (Anti-TPO) anti-TPO were detected by Atellica IM Anti-Thyroid Peroxidase assay (SIEMENS Healthineers, Erlangen, Germany) using reference ranges for TPO-Ab > 30 IU/mL and (Anti –TG) anti- thyroglobulin antibodies. Thyroid-stimulating hormone (TSH), free thyroxine (FT4), free triiodothyronine (FT3) with reference

ranges for TSH 0.4–5 IU/mL; FT4 11–22 pmol/L; and FT3 2–5 pmol/L. Zonulin Serum Quantification by Sandwich-ELISA using the Human Zonulin ELISA Kit (Elabscience, Bethesda, MD, USA, catalog No:E-EL-H5560). The standard curve was constructed, and the zonulin concentrations was calculated by converting the obtained optical density in ng/ml which analytic detection range for serum zonulin 0.78-50 ng/ml (7).

Neck Ultrasound: A high-resolution ultrasound machine (Hitachi, Japan; EUB 7000) with a high frequency of MHz was used to do the thyroid USG. A linear transducer is advised if the frequency is less than 7.5 MHz. For a comprehensive thyroid examination, all measures were taken by a single operator. Transverse and longitudinal thyroid US pictures were acquired, along with colour Doppler images in every instance.

Data management:

All data was analyzed using SPSS version 26.0. Description of quantitative variables in the form of mean and standard variation. Description of qualitative variables in the form of frequency and percentages.

Results

This study included 44 female participants: 44 patients with Hashimoto thyroiditis. Patients had mean age of 34.43±7.99 years, all were female with mean body mass index of 31.1±3.8 (kg/m2). Thirty-four of patients (77.3%) had a goiter and were on medications as in table 1.

Table 1: Distribution of demographic and general characteristics of patients (n=44).

	Hashimoto Thyroiditis (*n*= 44)
Age(years)	
Mean± SD	
18–25	**9(20.5%)**
26–35	**17(38.6%)**
36–45	**18(40.9%)**
Sex	
Female	**44(100.0%)**
Residence	
Urban	**27(61.4%)**
Rural	**17(38.6%)**
Occupation	
Housewife	**25(56.8%)**
Employee	**16(36.4%)**

Student	**3(6.8%)**
BMI(kg/m^2)	
Mean± SD	**31.1±3.8**
Normal	**1(2.3%)**
Overweight	**17(38.6%)**
Obese	**26(59.1%)**
Hypertension	**3(6.8%)**
Goiter	**34(77.3%)**
On Medications	**34(77.3%)**

Figure 1 shows the distribution of the detailed thyroid profile of the 44 participants diagnosed with Hashimoto Thyroiditis. More than two thirds of the patients had a high Thyroid Stimulating Hormone (TSH), Thyroglobulin Antibodies (TgAb), and Thyroid Peroxidase Antibodies (TPOAb).

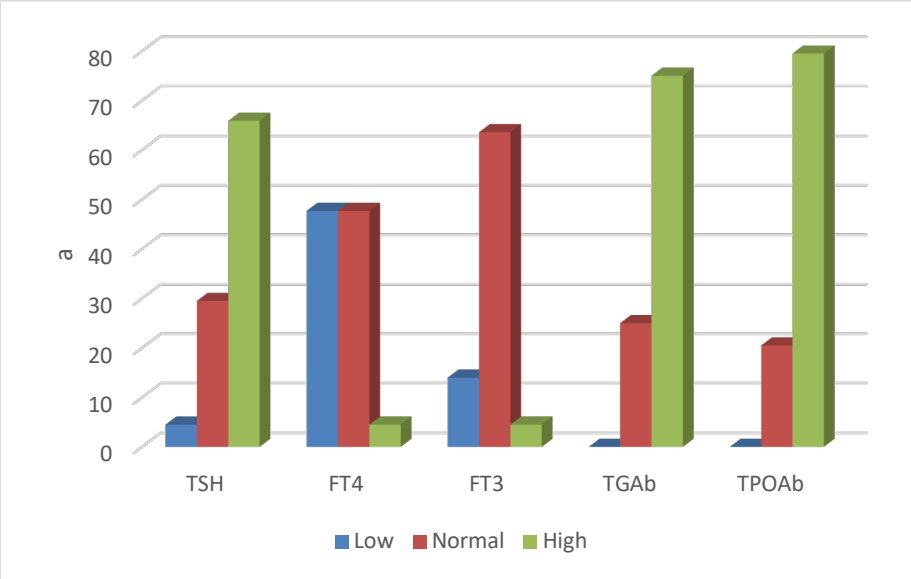

Figure 1: Thyroid profile of Hashimoto's Thyroiditis patients(n=44)

Table 2: Distribution of serum Zonulin among the patients.

	HashimotoThyroiditis (*n*= 44)
SerumZonulin (ng/ml)	**37.1(27.5–42.3)**

IQR:Interquartilerange

Table3 showed that the Hashimoto patients had median serum Zonulin of 37.1 ng/ml with IQR of 27.5 to 42.3 ng/ml.

Table 3: Correlations between serum Zonulin with patients age, BMI and thyroid profile.

Serum Zonulin(ng/ml)

	n	*r*	*p*-value
Age	44	0.043	**0.827**
BMI	44	0.148	**0.345**
TSH	44	-0.061	**0.699**
FT4	44	-0.072	**0.647**
FT3	44	0.175	**0.262**
TG Ab	44	0.214	**0.168**
TPOAb	**44**	**-0.149**	**0.339**

*. Statistically significant at p <0.05.r: Spearman's Correlation Coefficient

Table 3 presents the bivariate correlations between serum Zonulin and age, BMI and thyroid profile. There were insignificant correlations between serum Zonulin and age, BMI and thyroid profile.

Discussion

Hashimoto Thyroditis is characterized by chronic inflammation and is accompanied by tertiary lymphoid follicle development and increased circulating autoantibody concentrations against thyroid peroxidase and thyroglobulin (8,9). It is hypothesized that gut microbiota might play an important role in triggering HT (10).

So, this study aimed to assess serum zonulin titre in HT patients. This cross sectional comparative analytic study was conducted on 44 patients who diagnosed as Hashimoto Thyroditis. In the current study, all patients were female with mean age of 34.43±7.99 years old.

This is in agreement with literature which reported that, hashimoto's thyroiditis (HT) is an organ-specific autoimmune disease with an incidence of 0.3% to 1.5%, and the incidence in female is 4 to 10 times that of male [111].

Nine (14.4%) and 53 (85.5%) of the 62 participants in the other research had confirmed cases of Hashimoto's thyroiditis (12).

In the current study, Hashimoto group had high median serum and these results were observed by Özışık (13).

The potential role of zonulin in the pathogenesis of Hashimoto's thyroiditis was observed by Özışık (13). They found that serum zonulin levels in the patient group were significantly higher compared to control groups. However, they failed to determine a significant correlation between serum TSH, anti-TPO and anti-TG concentrations and zonulin levels in the patient group.

Similarly, a recent study, although no correlation was found between TSH and anti- TG levels and zonulin, instead a correlation was observed between anti-TPO levels and zonulin (14).

Moreover, another studies reported that decreased fecal zonulin levels were associated with gut microbiota overgrowth in stool samples (15,16).

In agreement with our results, Tomov et al. found that correlation analyses showed a negative correlation of zonulin with gender (r=-0.291, p=0.027) but positive one with age (r=0.217, p=0.05). A significant positive correlation was found between serum zonulin levels and weight and BMI (r=0.351, p= 0.008 and r=0.236, p=0.05, respectively). Overweight and obese patients had higher serum zonulin levels (p<0.05) (12).

The current study results are in agreement with other autoimmune diseases, as plasma zonulin concentrations elevated in celiac disease, T1DM, and inflammatory bowel disease such as Crohn's disease and ulcerative colitis (17,18).

In agreement with a pilot cross-sectional study investigates serum zonulin concentration in adults with Hashimoto's thyroiditis and assesses the relationship between zonulin levels, clinical hormonal and immunological characteristics. A group of 62 adults with HT participated in this study and were divided into three groups: hypothyroid (n=33) euthyroid (n=25) and hyperthyroid (n=4). Age, gender and BMI were different between groups (hypothyroid and euthyroid ones). Serum zonulin values ranged from 2.6 to 198.0 ng/mL in participants. A direct positive correlation was found between serum zonulin levels and weight and BMI ($r = 0.351$, $p = 0.008$ and $r = 0.236$, $p = 0.05$, respectively) (12).

Azad et al. reported that children and adolescents with HT had increased levels of zonulin compared to individuals with congenital hypothyroidism and concluded that all of these data suggested IIP in these patients (19).

In a study in patients with type 1 diabetes mellitus, Sapone et al. showed that patients with type 1 diabetes had elevated serum zonulin levels, which were correlated with IIP (20).

Conclusion

There is no correlation between zonulin and thyroid hormones or autoantibodies in Hashimoto thyroiditis patients. Further research could be conducted in a larger cohort study is needed to elucidate a possible role of zonulin in the pathogenesis of Hashimoto thyroiditis.

References:

[1] Burg MD. Poisoning & Drug Overdose. 4th ed: Kent R. Olson, MD. New York: Lange Medical Books/McGraw-Hill, 2004, 718 pages, $50.00 (softcover). Acad Emerg Med [Internet]. 2005;12(2):180–1. Available from: http://dx.doi.org/10.1197/j.aem.2004.09.005

[2] Caturegli P, De Remigis A, Rose NR. Hashimoto thyroiditis: Clinical and diagnostic criteria. Autoimmun Rev. 2014;13(4–5):391–7.

[3] Fröhlich E, Wahl R. Thyroid Autoimmunity: Role of Anti-thyroid Antibodies in Thyroid and Extra-Thyroidal Diseases. Front Immunol. 2017 May; 8:521.

[4] Wang W, Uzzau S, Goldblum SE, Fasano A. Human zonulin, a potential modulator of intestinal tight junctions. J Cell Sci. 2000;113(24):4435–40.

[5] Watts T, Berti I, Sapone A, Gerarduzzi T, Not T, Zielke R, et al. Role of the intestinal tight junction modulator zonulin in the pathogenesis of type I diabetes in BB diabetic-prone rats. Proc Natl Acad Sci U S A. 2005/02/14. 2005 Feb;102(8):2916–21.

[6] Arrieta MC, Bistritz L, Meddings JB. Alterations in intestinal permeability. Gut. 2006 Oct;55(10):1512–20.

[7] Küçükemre Aydın B, Yıldız M, Akgün A, Topal N, Adal E, Önal H. Children with Hashimoto's Thyroiditis Have Increased Intestinal Permeability: Results of a Pilot Study. J Clin Res Pediatr Endocrinol. 2020/01/28. 2020 Sep;12(3):303–7.

[8] Fenneman AC, Rampanelli E, Yin YS, Ames J, Blaser MJ, Fliers E, et al. Gut microbiota and metabolites in the pathogenesis of endocrine disease. Biochem Soc Trans. 2020;48(3):915–31.

[9] Zhang X, Li Y, Yang P, Liu X, Lu L, Chen Y, et al. Trimethylamine-N-oxide promotes vascular calcification through activation of NLRP3 (nucleotide-binding domain, leucine-rich-containing family, pyrin domain-containing-3) inflammasome and NF-κB (nuclear factor κB) signals. Arterioscler Thromb Vasc Biol. 2020;40(3):751–65.

[10] Ajjan RA, Weetman AP. The Pathogenesis of Hashimoto's Thyroiditis: Further Developments in our Understanding. Horm Metab Res. 2015;47(10):702–10.

[11] Ragusa F, Fallahi P, Elia G, Gonnella D, Paparo SR, Giusti C, et al. Hashimotos' thyroiditis: Epidemiology, pathogenesis, clinic and therapy. Best Pract Res Clin Endocrinol Metab. 2019;33(6):101367.

[12] Tomov DG, Levterova BA, Mihaylova VN, Troev DM, Miteva MZ, Orbetzova MM. SERUM ZONULIN LEVELS IN HYPOTHYROID AND EUTHYROID PATIENTS WITH HASHIMOTO'S THYROIDITIS - A PILOT STUDY. Acta Endocrinol (Bucharest, Rom 2005). 2021;17(4):449–54.

[13] Özışık G. İntestinal permeabilite düzenleyicisi zonulin'in hashimoto hastalığı patogenezindeki potansiyel rolü.

[14] İşleyen ZS, Yıldırım S, Gündoğan E, Sarı H, Küçük SH, Atay AE. Serum Zonulin Levels in Patients with Hashimoto's Thyroiditis. Med J Bakirkoy. 2022;18(4).

[15] Banga JP, Schott M. Autoimmune Thyroid Diseases. Horm Metab Res. 2018;50(12):837–9.

[16] Veres-Székely A, Szász C, Pap D, Szebeni B, Bokrossy P, Vannay Á. Zonulin as a Potential Therapeutic Target in Microbiota-Gut-Brain Axis Disorders: Encouraging Results and Emerging Questions. Int J Mol Sci. 2023;24(8):7548.

[17] Caviglia GP, Dughera F, Ribaldone DG, Rosso C, Abate ML, Pellicano R, et al. Serum zonulin in patients with inflammatory bowel disease: a pilot study. Minerva Med. 2019;110(2).

[18] Drago S, El Asmar R, Di Pierro M, Grazia Clemente M, Sapone ATA, Thakar M, et al. Gliadin, zonulin and gut permeability: Effects on celiac and non-celiac intestinal mucosa and intestinal cell lines. Scand J Gastroenterol. 2006;41(4):408–19.

[19] Azad MAK, Sarker M, Wan D. Immunomodulatory Effects of Probiotics on Cytokine Profiles. Biomed Res Int. 2018 Oct; 2018:8063647.

[20] Sapone A, de Magistris L, Pietzak M, Clemente MG, Tripathi A, Cucca F, et al. Zonulin Upregulation Is Associated with Increased Gut Permeability in Subjects with Type 1 Diabetes and Their Relatives. Diabetes. 2006;55(5):1443–9.