Süleyman Demirel Üniversitesi
Sağlık Bilimleri Dergisi
Cilt 13, Sayı 1, 30- 39, 2022

Suleyman Demirel University
Journal of Health Sciences
Volume 13, Issue 1, 30- 39, 2022

Periodontal Health Status of Adolescents with Hashimoto Thyroiditis

Hashimoto Tiroiditi Olan Adölesanlarda Periodontal Sağlık Durumu

Zuhal YETKİN AY [1*], Ayşegül TEKNECİ [2], Aykut TAN [1], Ayşe Rabia IŞIK [1], Özgür PİRGON [2]

[1] Süleyman Demirel University, Faculty of Dentistry, Department of Periodontology, Isparta, Turkey.
[2] Süleyman Demirel University, Faculty of Medicine, Department of Pediatric Endocrinology, Isparta, Turkey.

ABSTRACT

Objective: Possible mechanisms regarding the relationship between Hashimoto' thyroiditis (HT) and periodontal disease were suggested to be the autoimmune mechanisms. The aim is to report the oral and periodontal health status of a sample of adolescents with HT; and to investigate the correlations between the clinical periodontal and metabolic parameters of the adolescents with/without HT.

Material- Method: Sixty adolescent girls aged between 12-18 years (mean±SD: 15.03±2.05 years) have participated. The study population was comprised of HT (n = 30) and control (C, n = 30) groups. In addition to the endocrinologic evaluations (metabolic parameters) and intra- and extra-oral examinations, periodontal examination including the recording of percentage of bleeding on probing (BOP %), gingival index (GI), plaque index (PI), and pocket depth (PD) was made.

Results: Except the significantly higher anti-thyroid peroxidase (Anti-TPO) values in HT group than the C group (P = 0.001), none of the metabolic parameters have shown significant differences (P > 0.05). All of the subjects had gingivitis. The periodontal parameters were found not significantly different (P > 0.05). Salivary flow rate (SFR) has negative significant correlation with Anti-TPO (r = -0.367, P = 0.046), and cortisol has negative significant correlation with pocket depth (PD) (r = -0.378, P = 0.040).

Conclusions: Significant correlations between gingival index (GI) and fT4, and PD and fT4 have led us to consider that the periodontal inflammation might relate to HT. The adolescence period should also kept in mind; which results in exaggerated host response to the dental plaque, and projected with the presence of gingivitis in the whole study population.

Keywords: Hashimoto thyroiditis, gingivitis, salivary flow rate, children, autoimmune thyroiditis

Alınış / Received: 26.11.2021 Kabul / Accepted: 30.01.2022 Online Yayınlanma / Published Online: 15.04.2022

DOI: 10.22312/sdusbed.1028196
ARAŞTIRMA MAKALESİ

*Corresponding author: zuhalay@sdu.edu.tr

ÖZET

Amaç: Hashimoto tiroiditi (HT) ile periodontal hastalık arasındaki ilişkiye ilişkin olası mekanizmaların otoimmün mekanizmalar olduğu öne sürülmüştür. Amaç, HT' li bir adölesan örnekleminin ağız ve diş sağlığı durumunu bildirmek; ve HT'li olan ve olmayan adölesanların klinik periodontal ve metabolik parametreleri arasındaki korelasyonları incelemektir.

Materyal-metot: Çalışma popülasyonunu 12-18 yaş arası (ortalama±SS: 15.03±2.05 yıl) HT (n = 30) ve kontrol (C, n = 30) gruplarından oluşan toplam 60 kız adölesan oluşturdu. Metabolik parametrelerin incelendiği endokrinolojik incelemelerin yanı sıra hastaların ağız dışı ve periodontal muayeneyi içeren (sondlamada kanama yüzdesi (SK%), gingival indeks (GI), plak indeksi (Pİ) ve cep derinliği (CD)) ağız içi muayeneleri de yapılarak kaydedildi.

Bulgular: HT grubunda C grubuna göre anlamlı olarak daha yüksek anti-tiroid peroksidaz (Anti-TPO) değerleri (P = 0.001) dışında, metabolik parametrelerin hiçbiri anlamlı farklılık göstermedi (P > 0,05). Deneklerin tamamında gingivitis vardı. Periodontal parametreler istatistiksel açıdan anlamlı farklı bulunmadı (P > 0,05). Tükürük akış hızı (SFR) Anti-TPO ile negatif anlamlı (r = -0.367, P = 0,046) ve kortizol düzeyi cep derinliği (CD) ile negatif anlamlı korelasyona sahipti (r = -0.378, P = 0,040).

Sonuç: Gingival indeks (GI) ve fT4 ile PD ve fT4 arasındaki önemli korelasyonlar, periodontal inflamasyonun HT ile ilişkili olabileceğini düşünmemize yol açmıştır. Çalışma popülasyonunun tamamında görülen gingivitis varlığının ergenlik döneminde dental plağa karşı oluşan aşırı konak yanıtı ile ilgili olabileceği de akılda tutulmalıdır.

Anahtar Kelimeler: Hashimoto tiroiditi, diş eti iltihabı, tükürük akış hızı, çocuk, otoimmün tiroidit

1. Introduction

The existence of relationships between periodontal disease and systemic diseases and the studies on the possible mechanisms have attracted interest in recent years. Diabetes mellitus, cardiovascular disease, low birth weight, obesity and respiratory system diseases regarding their association with periodontal diseases have been intensively studied [1]. Possible mechanisms between periodontal diseases and systemic diseases can be summarized as transition of periodontopathogens through the bacteremia to the outside of the mouth; and systemic inflammatory burden related to periodontal disease which may cause increased systemic inflammatory markers (CRP, IL-6, etc.) to exacerbate the existing systemic disease [1-7].

Hashimoto's thyroiditis [HT] causes most of the thyroid disease in children and adolescents [8]. The immune cells and autoantibodies in the thyroid tissue results in thyroid failure and destruction besides the apoptosis of the epithelial cells, and formation of goiter [9]. Possible mechanisms regarding the relationship between HT and periodontal disease were suggested to be the autoimmune mechanisms (antinuclear antibodies (ANA), anti-neutrophil cytoplasmic antibodies (ANCAs), apoptosis, super-antigens) [10].

Genetic and environmental factors have predisposed the effect of microbial activated or T cell independent superantigens, which favors the auto reactivity of T and B cells, production of multiple auto antibodies and ANA; the production of ANA results in thyrocyte apoptosis and delayed neutrophil apopthosis, causing the release of cytokines and reactive oxygen species and proteolytic enzymes [11]. These mechanism could be the explanation of the relationship between HT and periodontitis. The induction of autoantibodies, ANA, might be the result of the triggering effect of myeloperoxidase produced by neutrophils, periodontopathogens could trigger ANCA by TNF-α; the periodontopathogens

gain the ability to act as a super-antigen activate the B lymphocytes in a T cell-independent manner resulting in ANCA production [12].

The disturbed apoptosis and disturbed removal of apoptotic cells due to the microbial super-antigens result in the increase of cellular fragments and induced the production of ANA and ANCA [13]. It has been suggested that HT cause a difference in the microcircular structure of the interdental papilla, which decreases numerically, and more tortuous vascular loops were observed [11]. The precipitation of autoantibodies and immunocomplexes as a result of the damage to the endothelium were also suggested as a mechanism of the relationship between HT and periodontal disease [14]. This situation might result in the compromise of the defense with the increased pro-inflammatory cytokines which have role in periodontitis pathogenesis, such as prostaglandin E (PGE), interleukin (IL)-1, IL-6 and tumor necrosis factor (TNF)-α [10]. The endothelial disfunction result in impaired nitric oxide availibility, increased oxidative stress and increased serum prostanoids and cytokines and matrixmetalloproteinases. Another mechanistic role of stress was also suggested; due to the altered microcirculation inflammatory trafficking of defence cells are complicated [10].

Some oral findings related to HT are altered salivary glands and taste perception (decreased secretion, dysgeusia), development of roots (delaye), temporomandibular joint disorders (osteoarthritis), and in addition macroglossia, poor periodontal health and wound healing [15-17].

The oral and periodontal health status of adolescents with HT were not reported previously in our country as far as we know according to our literature search. Thus, the first aim of this study is to report the oral and periodontal health status of a sample of adolescents with Hashimoto' thyroiditis living in the south-western part of our country called the Mediterranean Region.

The null hypothesis of this study was that there is not any difference between the adolescents with and without HT in terms of clinical periodontal parameters. The alternative hypothesis is that the clinical periodontal parameters would present a statistically significant difference between the girls with HT and girls without HT (C). So, the second aim is to test this alternative-hypothesis and to determine the correlation between the clinical periodontal parameters and the metabolic parameters and salivary flow rate (SFR) in adolescent girls with or without HT.

2. Material and Method

The Clinical Research Ethics Committee of the Faculty of Medicine of the Suleyman Demirel University (SDU) has approved the present study (05/04/2017, decision number. 67), and this study was conducted according to the Declaration of Helsinki.

Study Population

Sixty adolescent girls aged between 12 to 18 years (mean age: 15.03±2.05 years) have participated. The study population was comprised of HT and control (C) groups; the present study based on voluntariness; all of the patients' parent/guardian signed the informed consent forms.

Endocrinologic Evaluations

Thirty consecutive non-obese adolescent girls with HT (aged 12 to 18 years, mean age: 15.01±2.03 years, mean body mass index (BMI): 23.40 ± 4.90), were participated to the study, evaluated by A.Tekneci and Ö.P. at SDU Faculty of Medicine's Department of Pediatric Endocrinology between January 2017 and January 2018. High Anti-TPO levels confirmed HT diagnosis with presence of heterogeneity in ultrasound. Thyroid ultrasound was performed with Toshiba Xario 200 device with a 3-5 MHz probe. When the signal obtained from thyroid was equal or below the neck muscles, the thyroid was determined as hypoechogenic.

The healthy girls with normal lifestyles and taking no medication apply to the hospital for minor illness such as common cold or conjunctivitis has have constituted the control group (C, 30 non-obese adolescent girls, mean age: 14.51 ± 2.32 years, mean BMI: 21.18± 4.17). At baseline, all girls in this population were identified as Tanner stage 5 by one observer (A.Tekneci) before any laboratory results were obtained [18]. The menstrual history of the participants were questioned. The girls screened to be below the 85th percentile of their BMI and within normal limits for BMI-standardized BMI (SDS) were

included. Weight and height were measured to calculate BMI. Non-obese healthy and non-obese with HT participants were defined as BMI of < 85th percentile according to BMI reference curves for Turkish girls [19]. Regular menstrual cycle, age between 12 and 18 years, and no use of medications or oral contraceptives were determined as inclusion criteria. The exclusion criteria were determined as follows: primary gonadal or adrenal diseases, congenital adrenal hyperplasia, bone dysplasia, chronic disease, endocrinological abnormalities (etc. insulin resistance), organic brain disease.

Blood Sampling Procedure

Fasting blood samples (at 8:30 AM) were obtained from 08:00 to 10:00 h to measure anti-thyroid peroxidase (Anti-TPO), adrenocorticotropic hormone (ACTH), thyroid stimulating hormone (TSH), free Thyroxin 4 (fT4), cortisol, alanine aminotransferase (ALT), and calcium (Ca). The blood samples were collected by venipuncture, centrifuged (3000 × g for 10 minutes) and portioned before being storaged at -80°C.

Biochemical Analysis

Anti-TPO, fT4 and TSH levels were evaluated using Beckman Coulter DxI 800 (Brea, CA, USA) with chem-illuminescence immune analysis (CLIA) method. Serum ALT and calcium levels were analyzed with spectrophotometric method using Beckman Coulter AU 5800 biochemical autoanalyser (Brea, CA, USA). Serum ACTH and cortisol levels were determined with electro CLIA method using Roche Cobas e411 hormone autoanalyser (Mannheim, Germany).

Oral Examination

In addition to the routine intra- and extra-oral examinations (including the tongue, cheeks, palate, tonsils, floor of the mouth, maxillary sinus, lymph nodes related to the oral tissues etc.), the number of the present deciduous and permanent teeth (NT), and the sum of decayed, missing and filled teeth (DMFT) in the permanent teeth was assessed by a single examiner (ARI) [19]. The Molar Incisor Hypomineralization (MIH) was also diagnosed according to the criteria defined by Weerheijm et al (2001) [20].

Periodontal Examination

The periodontal examination was conducted by a single calibrated examiner (A.Tan, intra-examiner weighted kappa > 0.85). In this examination, percentage of bleeding on probing (% BOP) [21]; plaque index (PI) [22]; gingival index (GI) [23]; and periodontal pocket depth (PD) and clinical attachment level (CAL) were measured and recorded. BOP, CAL, and PD were recorded for the six sites (mesio-buccal, mid-buccal, disto-buccal, mesio-lingual, mid-lingual, disto-lingual) of the present teeth with a Williams periodontal probe (Hu-Friedy, Chicago, IL).

The periodontal diagnosis of the patients was made in accordance with the 2017 International Workshop for the Classification of Periodontal and Peri-implant Disease and Conditions [24]. All of the patients in the HT and C groups were diagnosed as generalized gingivitis case in intact periodontium [24].

Saliva Samples

Unstimulated whole saliva was collected from all patients according to the method established by Navazesh and Kumar (2008) [25]. Instructions were given to the patients/parents/guardians regarding the eating and drinking routines and daily oral hygiene habits (they were asked not to eat and drink before sampling procedure, and not to perform before salivary sampling). The SFR was calculated according to the method established by Navazesh and Kumar (2008) in ml/minute [25]. After collection, samples were placed on ice and aliquoted before being storaged at -80°C.

Statistical Analysis

The descriptive statistics consisted of mean and standard deviations (SD). After the analysis, the normal distribution of data has led to the use of the parametric paired t test to compare the variables between the groups. The Pearson correlation coefficient (r) and Spearman's rank correlation coefficient (rho)

were used to analyze the correlations. A probability value of $p < 0.05$ was considered significant. Commercial statistical software (SPSS 20, IBM Armonk, NY, USA) was used for all statistical analyses. The post hoc power analysis was also applied. The power of the study was 95% for Anti-TPO (α=0.05, β=0.05).

3. Results

The groups were not found significantly different regarding age and BMI ($p>0.05$, Table 1). Except the statistically significantly higher Anti-TPO and TSH values in HT group than the C group ($p<0.05$, Table 1), none of the metabolic parameters have shown significant differences between the two groups ($p>0.05$, Table 1).

Table 1: The metabolic characteristics of the study population

Parameters/Groups	HT (Mean±SD)	Controls (Mean±SD)	p value
Age	15.01±2.03	14.51±2.32	0.358
BMI (kg/m$^{2)}$	23.40±4.90	21.18±4.17	0.064
Anti-TPO (IU/ mL)	535.74±348.95	1.67±1.21	0.001*
fT4 (ng/dL)	0.93±0.39	0.83±0.11	0.210
TSH (uIU/ mL)	4.01±5.04	1.63±0.75	0.016*
Cortisol (µg/dL)	9.14±4.52	8.46±4.44	0.558
ACTH (pg/mL)	16.06±7.47	16.52±9.80	0.839
ALT (U/L)	17.53±12.37	13.53±3.77	0.098
Ca (mg/dL)	10.02±0.44	9.90±0.44	0.319
ACTH: adrenocorticotropic hormone, ALT: alanine aminotransferase, Anti-TPO: anti-thyroid peroxidase, Ca: calcium, BMI: body mass index , Ft4: free Thyroxin 4, TSH: thyroid stimulating hormone, *statistically significant difference, P < 0.05			

The dental and periodontal parameters' values were shown in Figure 1A and Figure 1B. None of the patients had shown attachment loss (CAL=0), because their periodontal diagnosis was gingivitis case with intact periodontium. The periodontal parameters were found not significantly different between the groups (GI, p=0.96; PI, p=0.94; PPD, p = 0.45; Figure 1A). None of the subjects had periodontitis, all of the subjects in both of the groups had gingivitis. The mean (± SD) BOP percentages were 78 (± 22) in the HT group and 67(± 30) in the C group; were not found significantly different between the groups (p=0.10). The DMFT, MIH and SFR have also not presented significant differences between the groups (p=0.89, p=0.22, p=0.79, respectively; Figure 1B).

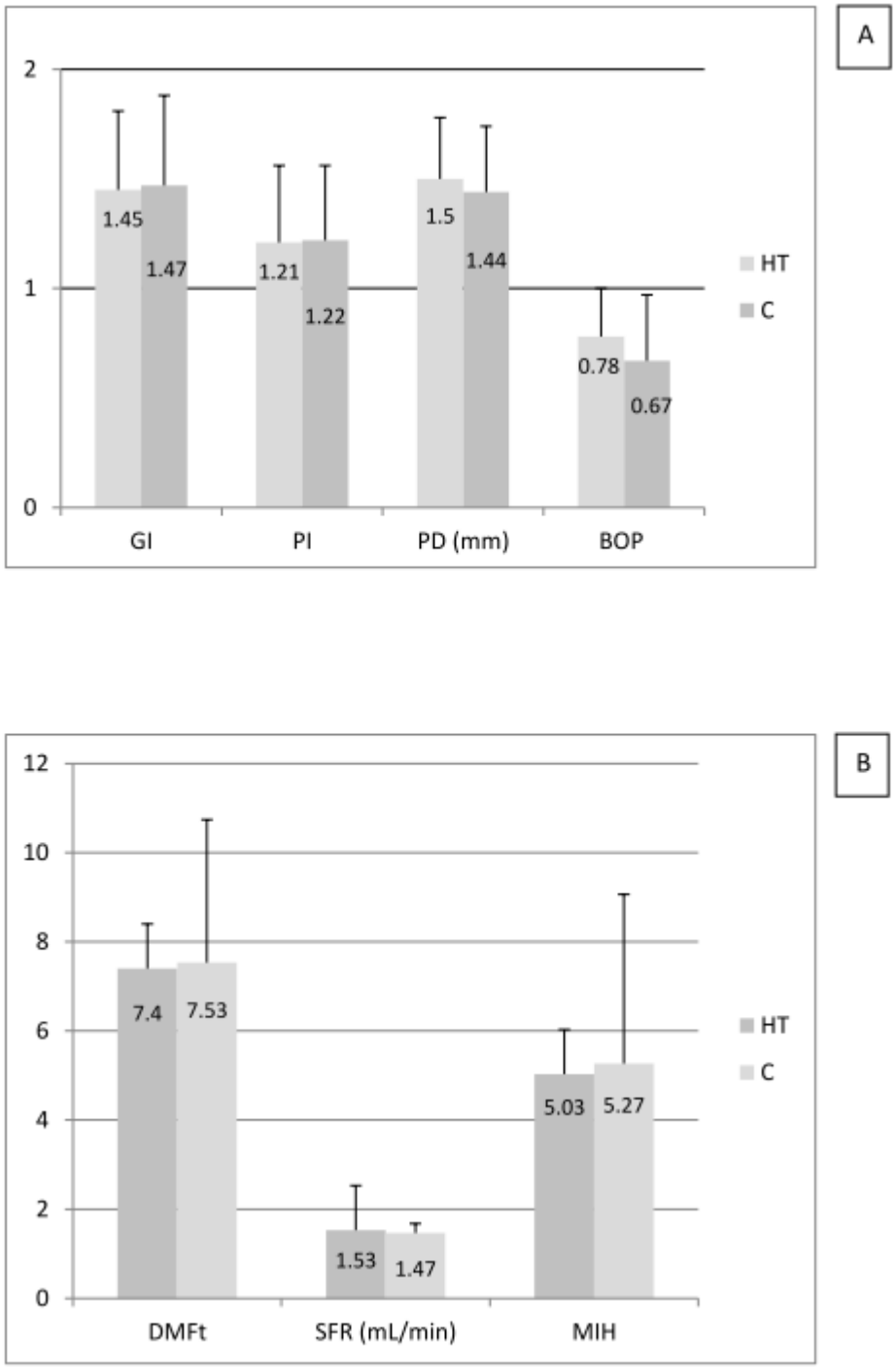

Figure 1: The periodontal parameters' values (mean±SD). Figure 1A. GI: gingival index, PD: probing depth, PI: plaque index. Figure 1B. DMFt: decayed/missed/filled teeth, MIH: molar incisor hypomineralization, SFR: salivary flow rate.

The significant correlations between investigated parameters were shown in Table 2. GI and PD have shown significant positive correlations with fT4 (Table 2). The periodontal parameters have not shown any significant correlations with DMFT, MIH and SFR ($p>0.05$). However, SFR has shown significant negative correlation with Anti-TPO ($r=-0.367$, $p=0.046$), and cortisol has shown significant negative correlation with PD ($r=-0.378$, $p=0.040$, Table 2). The periodontal parameters have shown significant correlations between each other ($p<0.05$, Table 2).

Table 2: The statistically significant correlations between the metabolic, periodontal, salivary parameters

Parameters	r	p
SFR-Anti-TPO	-0.367	0.046*
BOP- TSH	-0.421	0.020*
GI- fT4	0.408	0.025*
PD-fT4	0.386	0.035*
PD- Cortisol	-0.378	0.040*
PD-GI	0.508	0.004**
PD-PI	0.420	0.021*
PD-BOP	0.437	0.016*
GI-PI	0.746	< 0.001**
GI-BOP	0.737	< 0.001**
PI-BOP	0.409	0.025*
Anti-TPO: anti-thyroid peroxidase, BOP: bleeding on probing, GI: gingival index, PI, plaque index, PD: probing depth, fT4: free thyroxin, SFR: salivary flow rate. *P < 0.05, **: P < 0.01		

4. Discussion and Conclusion

The oral and periodontal health status of a sample of children/adults with Hashimoto' thyroiditis living in the south-western part of our country called the Mediterranean Region was investigated in the present study. Another aim of the study is to determine the correlation between the clinical periodontal parameters and the metabolic parameters and salivary flow rate (SFR) in adolescent girls with or without HT.

Adolescents constitute an age group that requires special attention for dentists with increased risk of caries, traumatic injuries and periodontal diseases, poor eating habits, increased aesthetic expectations and awareness, dental phobia, social and psychological needs [26,27]. The addition of a chronic disease to this situation should suggest that preventive measures should developed as well as complicated treatment approaches for dentists. In both preventive and therapeutic approaches, the etiology and size of the problem should be determined and a strategy based on it should develop. Although there are publications on the periodontal findings of individuals with HT in the literature, these are case reports [28] and review [29 and there is no clinical study as far as we know in the literature regarding adolescents. For this purpose, the present study was conducted and no statistically significant difference was observed between the HT and C groups in terms of periodontal parameters. The adolescent population in the present study has diagnosed as generalized gingivitis with intact periodontium, higher BOP was observed in both of the groups, and none of them had periodontitis.

However, when the whole study group (n = 60) was examined in terms of correlations between metabolic and periodontal clinical parameters, the negative correlation of Anti-TPO with SFR was significant. Although SFR did not differ significantly between groups, SFR has presented significant negative correlation with Anti-TPO. Interestingly, our clinical observation was that SFR was less in adolescents with HT, this significant correlation has confirmed with our clinical observation. This situation regarding xerostomia in HT was also reported in the literature [30].

When correlations are examined, the positive correlations found between fT4 (used in the diagnosis of HT) and GI (which contains bleeding component, and is the indicator of gingival inflammation), and PD were also observed. Although the differences regarding periodontal parameters were not found statistically significant between the groups, the significant correlations between GI and fT4, and between PD and fT4 have led us to consider that the periodontal inflammation might be related to HT. However, to clarify this situation further studies evaluating the levels of inflammatory markers in gingival crevicular fluid, saliva and gingiva are needed. In the present study, the gingival and periodontal health status were aimed to be determined in adolescents with HT. The inflammatory response in the gingiva might also relate to age-specific hormonal differences of the study group [31,32].

Hypomineralization observed in individuals with thyroid dysfunction was also evaluated in our study group [33]. Mineralization differences / irregularities / disorders seen on the tooth surface may play a role as predisposing factor for periodontal diseases by making plaque control difficult. It may also affect plaque accumulation according to the degree of hypomineralization. Molar Incisor Hypomineralization (MIH) values used for evaluation did not differ between groups. In the study of Venkatesh Babu and Patel [34], enamel defects of the groups were evaluated with developmental defects of enamel (DDE) and statistically significantly higher DDE values were found in children with HT. The present study groups have similar MIH values, which also explain the similar DMFT values.

The present study has some limitations. First, its cross-sectional design could not allow us to perform an analysis of the dental and periodontal variables in HT pathogenesis. However, to the best of our knowledge, this is the first study evaluated the dental and periodontal characteristics in adolescent HT patients. There are very few studies on the relationship and mechanisms between periodontal disease and HT in the literature, and there are no publications on periodontal health status in adolescents with HT. This creates difficulties in comparing and interpreting our findings.

Nevertheless, our results are important to develop oral, dental and periodontal health strategies in this particular patient population to provide oral health related quality of life in their whole life beginning with their young ages. The further longitudinal studies would provide us the opportunity to make clearer explanations.

Conclusion

Although the results of our study seem to have affirmed the null hypothesis, that there is not any difference between the HT and C groups regarding the periodontal clinical parameters, the low power of the present study necessiates the further studies with larger sample size (regarding the TSH data, 45% power was determined, requires 70 subjects in each group, although the power was found 95% for Anti-TPO).

However, given the possibility of and oral and dental infections that may affect the course of HT, an autoimmune disease, it is clear that this group should undergo a good dental and periodontal examination. The early beginning of destruction of supporting periodontal tissues should be kept in mind for this particular group. From this point of view, the fact that gingivitis has always been prior to periodontitis cases and the diagnosis of gingivitis in our entire study group emphasizes the importance of dentists' cooperation with doctors / endocrinologists of adolescents with HT.

Acknowledgment

This study was supported by Süleyman Demirel Univesity Scientific Research Projects Coordination Unit with the Project number TTU-2018-6815.

Declaration of Ethical Code

In this study, we undertake that all the rules required to be followed within the scope of the "Higher Education Institutions Scientific Research and Publication Ethics Directive" are complied with, and that none of the actions stated under the heading "Actions Against Scientific Research and Publication Ethics" are not carried out.

References

[1] Hegde, R., Awan, K.H. 2019. Effects of periodontal disease on systemic health. Disease-a-month: DM, 65[6],185-92.

[2] Jin, L., Chiu, G., Corbet, E. 2003. Are periodontal diseases risk factors for certain systemic disorders-What matters to medical practitioners? Hong Kong Medical Journal, 9[1]:31-7.

[3] Nylund, K.M., Meurman, J.H., Heikkinen, A.M., Honkanen, E., Vesterinen, M., Furuholm, J.O. 2015. Periodontal inflammatory burden and salivary matrix metalloproteinase-8 concentration among patients with chronic kidney disease at the predialysis stage. Journal of Periodontology, 86[11],1212-20.

[4] Srinivasa, T., Agrawal, P., Goyal, P., Farista, S., Sowmya, N., Deonani, S. 2015. Comparative clinical evaluation of glycosylated haemoglobin level in healthy and chronic periodontitis patients: A chairside diagnostic method. Indian Journal of Dental Research, 26[5], 504-7.

[5] Araújo, M.V., Hong, B.Y., Fava, P.L., Khan, S., Burleson, J.A., Fares, G. 2015. End stage renal disease as a modifier of the periodontal microbiome. BioMed Central Nephrology, 16, 80.

[6] Zhou, X., Han, J., Liu, Z., Song, Y., Wang, Z., Sun, Z. 2014. Effects of periodontal treatment on lung function and exacerbation frequency in patients with chronic obstructive pulmonary disease and chronic periodontitis: A 2-year pilot randomized controlled trial. Journal of Clinical Periodontology, 41[6], 564-72.

[7] Jindal, A., Parihar, A.S., Sood, M., Singh, P., Singh, N. 2015. Relationship between severity of periodontal disease and control of diabetes (glycated hemoglobin) in patients with type 1 diabetes mellitus. Journal of International Oral Health, 7[suppl 2], 17–20.

[8] Jenkins, R.C.W.A. 2002. Disease associations with autoimmune thyroid disease. Thyroid, 12[11], 977-88.

[9] Ohye, H., Nishihara, E., Sasaki, I., Kubota, S., Fukata, S., Amino, N. 2006. Four cases of Graves' disease which developed after painful Hashimoto's thyroiditis. Internal Medicine, 45[6], 385-9.

[10] Patil, B.S.P.S., Gururaj, T.R. 2011. Probable autoimmune causal relationship between periodontitis and Hashimotos thyroidits: a systemic review. Nigerian Journal of Clinical Practice, 14[3], 253-61. [11] Scardina, G.A., Messina, P., 2007. Microvascular periodontal alterations: a possible relationship between periodontitis and rheumatoid arthritis. Clinical Hemorheology and Microcirculation, 37[3], 229–35.

[12] Yard, B.A., Wille, A.I,. Haak, M., van der Woude, F.J., 2002. Human proteinase 3 can inhibit LPS-mediated TNF-alpha production through CD14 degradation: Lack of influence of antineutrophil cytoplasmic antibodies. Clinical Experimental Immunology,128 [3], 444-52.

[13] Zadeh, H.H., Kreutzer, D.L. 1996. Evidence for involvement of superantigens in human periodontal diseases: Skewed expression of T cell receptor variable regions by gingival T cells. Oral Microbiology and Immunology, 11[2], 88-95.

[14] Taddei, S., Caraccio, N., Virdis, A., Dardano, A., Versari, D., Ghiadoni, L., Ferrannini, E., Solvetti, A., Monzani, F., 2006. Low-grade systemic inflammation causes endothelial dysfunction in patients with Hashimoto's thyroiditis. Journal of Clinical Endocrinology and Metabolism, 91[12], 5076–82.

[15] Burman, K.D. M.-G.L. 2006. Dermatologic aspects of thyroid disease. Clinical Dermatology, 24[4], 247-55.

[16] Pizzorni, C.S.A., Craviotto, C., Tuccio, M., Seriolo, B., Cutolo, M. 2003. Diagnostic perspectives in the rheumatological vasculitis: The role of the videocapillaroscopy. Reumatismo, 54[2], 99-104.

[17] Chang, C.P., Shiau, Y.C., Wang, J.J., Ho, S.T., Kao, C.H. 2003. Decreased salivary gland function in patients with autoimmune thyroiditis. Head and Neck, 25[2], 132-7.

[18] Pinyerd, B., Zipf, W.B. 2005. Puberty—timing is everything! Journal of Pediatric Nursery, 20[2], 75-82.

[19] Ozturk, A., Mazicioglu, M.M., Hatipoglu, N., Budak, N., Keskin, G., Yazlak, Z. 2008. Reference body mass index curves for Turkish children 6 to 18 years of age. Journal of Pediatric Endocrinology & Metabolism, 21[9],827–36.

[20] Weerheijm, K.L.J.B., Alaluusua, S. 2001. Molar incisor hypomineralization. Caries Research, 35[5],390-1.

[21] Lobene, R.R., Weatherford, T., Ross, N.M., Lamm, R.A., Menaker, L. 1986. A modified gingival index for use in clinical trials. Clinical Preventive Dentistry, 8[1], 3-6.

[22] Löe, H. 1967. The gingival index, the plaque index and the retention index systems. Journal of Periodontology, 38[6], 610-6.

[23] Löe, H., Silness, J. 1963. Periodontal disease in pregnancy I. Prevalence and severity. Acta Odontologica Scandnavica, 21, 533-51.

[24] Trombelli, L., Farina, R., Silva, C.O., Tatakis, D.N. 2018. Plaque-induced gingivitis: Case definition and diagnostic considerations. Journal of Periodontology, 89[Suppl 1], S46–S73.

[25] Navazesh, M., Kumar, S.K.S. 2008. Measuring salivary flow challenges and opportunities. Journal of American Dental Association, 139, 35S-40S.

[26] Baker, S.R., Mat, A., Robinson, P.G. 2010. What psychosocial factors influence adolescents' oral health? Journal of Dental Research, 89[11], 1230-5.

[27 Yu, S.M., Bellamy, H.A., Schwalberg, R.H., Drum, M.A. 2001. Factors associated with use of preventive dental and health services among U.S. adolescents. Journal of Adolescent Health, 29[6], 395-405.

[28] Patil, B.S., Giri, G.R. 2012. A clinical case report of Hashimoto's thyroiditis and its impact on the treatment of chronic periodontitis. Nigerian Journal of Clinical Practice, 15[1], 112-4.

[29] Patil, B.S., Patil, S., Gururaj, T.R. 2011. Probable autoimmune causal relationship between periodontitis and Hashimotos thyroidits: A systemic review. Nigerian Journal of Clinical Practice, 14[3], 253-61.

[30 Agha-Hosseini F, Shirzad N, Moosavi MS. 2016. Evaluation of Xerostomia and salivary flow rate in Hashimoto's Thyroiditis. Medicina Oral, Patología Oral y Cirurgía Bucal, 21[1], e1-e5.

[31] Delaney, J.E., Ratzan, S.K., Kornman, K.S. 1986. Subgingival microbiata associated with puberty: studies of pre-, circum-, postpubertal human females. Pediatric Dentistry, 8[4], 268–75.

[32] Mombelli, A., Gusterbi, F.A., van Osten, M.A.C., Lang, N.P. 1989. Gingival health and gingivitis development during puberty. A 4-year longitudinal study. Journal of Clinical Periodontology, 16[7], 451–6.

[33] Hall, R.K. 1989. The prevalence of developmental defects of tooth enamel [DDE] in a paediatric hospital department of dentistry population (part I). Advanced Dental Research, 3[2], 114-9.

[34] Venkatesh Babu, N.S., Patel, P.B. 2016. Oral health status of children suffering from thyroid disorders. Journal of Indian Society of Pedodontics and Preventive Dentistry, 34[2], 139-44.