Association of hypothyroidism with periodontal disease complexity

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Abstract

Aim: Hypothyroidism (HT) is an endocrine disorder characterized by insufficient production of thyroid hormones and is associated with alterations in the gastrointestinal microbiome. Periodontitis is characterized by loss of attachment secondary to dysbiotic plaque biofilm. The objective of this retrospective study was to assess the potential association of hypothyroidism and periodontitis. We hypothesized that patients diagnosed with HT would exhibit a greater percentage of teeth with elevated periodontal probing depths.

Materials and methods: Following IRB approval, 1,093 dental records initially were reviewed to obtain 832 patients ≥ 35 years-old (1996-2015). After excluding potentially confounding conditions, 538 records were further assessed. Significance was determined using independent sample t-tests adjusted for equality of variances, and chi-square tests of independence.

Results: HT patients exhibited 61.4% of teeth with ≥ 5 mm probing depths, while 48.1% of non-HT patients had probing depths ≥ 5 mm (CI[95%]7.9%-18.8%; P<.001). Similarly, the percentage of teeth with ≥ 6 mm probing depths was 36.2% for HT patients, compared to 28.2% of teeth for patients non-HT (CI[95%]3.1%–12.9%; P<.001], approximately 28% greater among patients with HT.

Conclusion: A greater proportion of probing depths ≥ 5 mm and ≥ 6 mm was associated with HT patients, suggesting more complex periodontitis. Dentists and endocrinologists might consider screening for HT and periodontitis, respectively, when appropriate.

Keywords: Periodontitis; pocket, periodontal; endocrine diseases; periodontal medicine; thyroid.

Introduction

Hypothyroidism (HT) is an endocrine disorder characterized by insufficient production of triiodothyronine (T3) and thyroxine (T4) (Chaker *et al*., 2017). In the United States, the prevalence of clinical and subclinical HT is 4.6% (Hollowell *et al*., 2002), with clinical HT reported at 2.4% (2.7% in females, 2% males; Jain, 2015). HT is more common among women, those > 65 years old (Chaker *et al*., 2017), and in patients from specific geographic regions, such as western New York, where the prevalence of HT has been reported to be as high as 15.0%, and as much as 22.6% among women (Yerke *et al*., 2020). HT occurs with variable severity, and often is associated with decreased metabolic rate, weight gain, hair loss, cold intolerance, and myxedema coma, a rare but life-threatening complication that includes difficulty with breathing and extreme fatigue (Chaker *et al*., 2017).

Periodontitis is a chronic, inflammatory condition associated with dysbiotic plaque biofilm that results in progressive attachment loss around teeth (Papapanou *et al*., 2018). In the past few decades, research has sought to elucidate the mechanisms through which systemic diseases influence the pathogenesis of periodontitis. Systemic conditions positively associated

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with periodontitis include cardiovascular disease (Sanz *et al.*, 2020), diabetes (Casanova *et al*., 2014), osteoporosis, obesity, and rheumatoid arthritis (Albandar *et al*., 2018). However, the potential relationship between HT and periodontitis has not received similar consideration and therefore has not been adequately explored (Zahid *et al*., 2011).

There are a number of reports that attempt to analyze the relationship between HT and periodontitis, but few have used appropriate criteria to characterize both conditions, as discussed in a recent review (Aldulaijan *et al*., 2020). Many of those studies have been compromised due to their reliance solely on gingival indices to identify periodontitis, or examined adolescents prior to the typical age of onset of either HT or periodontitis (Aldulaijan *et al*., 2020). Additional limitations of those previous studies included failure to exclude hyperthyroidism or thyroid disease secondary to cancer, missing or unsuitable control groups, or excessive reliance on case reports (Aldulaijan *et al*., 2020). As a result, there currently is minimal high-quality evidence to support or refute a relationship between HT and periodontitis. The purpose of this study was to retrospectively reassess that association among periodontitis patients in a faculty specialty practice who were appropriately screened for HT. We hypothesized that patients diagnosed with HT would exhibit a greater percentage of teeth with elevated periodontal probing depths, compared to patients without a previous HT diagnosis.

Materials and methods

This study was reviewed and approved by the University at Buffalo Health Sciences Institutional Review Board (STUDY#00001811), which did not require individual informed consent for this retrospective records analysis. The manuscript was prepared according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (von Elm *et al*., 2014). All dental records of patients from a university-based periodontal specialty practice presenting for their primary periodontal examination from 1996-2015 (n = 1,093), were initially available for this study. From that population, individuals ≥ 35 years old were included for subsequent analysis (n = 832) to ensure that the minimal age requirement for initial HT screening by the American Thyroid Association was met (Garber *et al*., 2012). The records of those patients were reviewed and retrospectively assigned a periodontal diagnosis based on the 2017 World Workshop (Tonetti *et al*., 2018) using radiographic data, as well as clinical findings (e.g., periodontal probing depths, attachment levels, furcation involvement, presence of bleeding upon probing, mobility, and patient age and history) for each patient. Patients with generalized periodontitis stage III or IV, grade B or C, subsequently were included in the study.

The presence of HT was assessed by reviewing the medical history to confirm an existing physician diagnosis of HT, as well as concurrent supplementation with levothyroxine or liothyronine medications. Patients with HT secondary to thyroid removal or cancer, or with hyperthyroidism, were excluded. Demographic information, including date of birth and gender, as well as smoking status, current medication use, and the presence of systemic disease, was obtained. Due to the number of potential confounders, the potential for error nevertheless existed even if the data were adjusted using multivariate analyses. Moreover, the uncertain effect of some conditions on periodontal outcome has the potential to introduce additional uncertainty. Since the sample size in the current study was relatively large, we therefore chose to exclude diabetes patients, smokers, patients using systemic steroids or hormone replacement therapy, or patients with non-thyroid autoimmune disorders such as rheumatoid arthritis or lupus erythematosus, yielding 538 records for analysis (Figure 1 and Table 3).

The same examiner (RC) recorded the whole mouth plaque index (Silness & Löe, 1964), as well as pocket depth measurements using Michigan "O" probes with standardized Williams markings measuring from the free gingival margin to the base of the pocket at 6 sites per tooth (the mesiobuccal, mid-buccal, and distobuccal aspects), as well as the corresponding lingual aspects, of all teeth, excluding third molars. As a result, inter-examiner error or bias was not considered to be a confounding factor in this cross-sectional study in accordance with STROBE guidelines. To differentiate moderate-to-severe periodontal disease from mild disease, the periodontal probing depth threshold criteria from the Centers for Disease Control and American Academy of Periodontology case definitions for periodontitis were used (Page & Eke, 2007). For this study, the percentage of teeth having at least 1 probing depth of ≥ 5 mm and ≥ 6 mm for each individual was separately calculated and used as a measure of periodontitis severity. Differences in the mean proportion of teeth with ≥ 5 mm and ≥ 6 mm periodontal probing depths subsequently were calculated for patients with and without HT, and were assessed using independent sample t-tests adjusted for equal or unequal variance as appropriate. Statistical significance was set at alpha = .05, and 95% confidence intervals were calculated using IBM SPSS v.26 (Armonk, NY, United States). Discontinuous plaque scores (Silness & Löe, 1964) were transformed to either low (PI ≤ 1.5) or high plaque (PI > 1.5) categories for both HT and non-HT groups, with group differences analyzed using 2 x 2 chi-square tests of independence.

Figure 1. Study population characteristics at a faculty periodontal specialty practice.

Results

Among the 832 patients ≥ 35 years old with generalized periodontitis stage III to IV, grade B to C, 87 patients presented with HT, as determined by prior physician diagnosis and history of current thyroid hormone supplementation, for an HT prevalence of 10.46%. The mean age of patients with HT was 59.3 years vs. 56.7 years in individuals with normal thyroid function, which was not statistically significant ($P > .05$). There also was no statistically significant difference in plaque scores between individuals with or without HT ($P > .05$) (Table 1). Females and males were disproportionately distributed in the hypothyroid and normal thyroid function groups (Table 2; X^2 (1, 538) = 16.47, $P < 0.001$). As noted in Table 3, the mean percentage of teeth having at least one site with ≥ 5 mm probing depths was 61.4% in patients with HT, vs. 48.1% among patients without HT. Therefore, this percentage was 27.7% greater for patients with HT, compared to patients without HT (mean difference 13.3%; $P < .001$). Similarly, the percentage of teeth with ≥ 6 mm probing depths was 36.2% among HT patients, compared to 28.2% of teeth for patients without HT, which was 28.2% greater for HT patients (mean difference 8.0%; $P < .001$).

Table 1. Plaque control in individuals with or without hypothyroidism.*

	Normal Thyroid Function	Hypothyroidism
High Plaque Index > 1.5**	198	33
Low Plaque Index ≤ 1.5**	279	28

* Pearson Chi-Square value (1, 538) = 3.498, P = 0.061).
** High or Low plaque categories were derived from discontinuous plaque scores (Silness & Löe, 1964).

Table 2. Gender distribution.

	Females	Males
Normal Thyroid Function	261	216
Hypothyroidism	50	11

Table 3. Percentage of elevated probing depths in individuals with or without hypothyroidism.

	Percent of teeth with pocket depths ≥ 5 mm	Percent of teeth with pocket depths ≥ 6 mm
Hypothyroidism*	61.4% (n = 61)	36.2% (n = 61)
Normal Thyroid Function*	48.1% (n = 477)	28.2% (n = 477)
Mean Difference (Thyroid vs No Thyroid Disease)	13.3%; 27.7% increase	8.0%; 28.4% increase
95% Confidence Interval	7.9% - 18.8%	3.1% - 12.9%
P-value	< .001	< .002

*Plaque differences not statistically significant between hypothyroid and non-hypothyroid groups (P > .05).

Discussion

The results indicate that a greater proportion of ≥ 5 mm or ≥ 6 mm probing depths occurs at teeth from patients diagnosed with HT, and imply that more complex periodontal disease might be associated with HT in patients old enough to have developed both conditions. This finding also is consistent with a cross-sectional study (Rahangdale & Galgali, 2018) which found a statistically significant association between HT and increased periodontal probing depths. Although those authors considered the effect of plaque control, their sample size was relatively small (n = 102) and included participants not yet old enough to have been screened for HT. Our results also revealed a disproportionately greater number of women with hypothyroidism, which is consistent with known characteristics of that disease (Chaker *et al*., 2017).

The complete mechanism through which HT could affect periodontal disease currently is unknown. However, quantitative and qualitative intestinal microbial dysbiosis occurs in HT, often with increased E. coli concentrations (Ishaq *et al*., 2017; Shin *et al*., 2020; Su *et al*., 2020). In mice, experimentally-induced gastrointestinal (GI) dysbiosis has been shown to affect thyroxine levels in healthy animals, suggesting that conditions that affect GI flora might indirectly affect thyroid function (Su *et al*., 2020). Similarly, periodontal disease is characterized by dysbiosis affecting the periodontium. Multiple reports have described the relationship between oral bacteria and the GI microbiome (Kato *et al*., 2018; Kobayashi *et al*., 2020). Indeed, some studies have specifically demonstrated that Porphyromonas gingivalis, an oral bacterium commonly associated with periodontitis, facilitates GI dysbiosis when found in the intestine (Olsen & Yamazaki, 2019).

Since periodontal pathogens can affect GI microbiota, and GI dysbiosis alters thyroid function, it is conceivable that an altered microbiome secondary to periodontal disease also might influence the pathogenesis of other conditions, including HT. Additionally, there also is evidence that HT might alter the composition of the oral microbiota in addition to the GI microbiota since, during pregnancy, certain bacteria have been found at significantly higher or lower abundances in patients with HT, compared with individuals with normal thyroid function (Wang *et al*., 2020). Although evidence exists that GI microbiota can affect thyroid hormone synthesis and cause hydrolysis of hormone conjugates, the effect of a dysbiotic microbiota on thyroid disorders remains to be elucidated (Ejtahed *et al*., 2020). Therefore, despite the support of an association between HT and periodontitis suggested by those findings, additional studies are required to determine if the current results can be generalized to different populations, and to understand the precise mechanisms through which the pathogenesis of HT and periodontal disease might be interrelated.

Limitations of our study include those inherent in a cross-sectional retrospective design, such as lack of specific information regarding the dose, duration, and frequency of hypothyroid medication prior to the time of examination. It also is possible that patients with undiagnosed HT were inadvertently included in the non-HT control group. However, in that case, the observed association of HT with an increased proportion of elevated probing depths would be partially obscured, leading to a more conservative assessment of the actual HT effect than we have shown. Compared to previous reports, the current study generally represents a larger sample size, uses a patient population with an appropriate age distribution, and applies more defined criteria for diagnosis of periodontal disease and hypothyroidism. Indeed, in the current study, the presence of HT was assessed through confirming an existing physician diagnosis of HT, as well as documented thyroid supplementation with levothyroxine or liothyronine. Consequently, it addresses the study objective and expands upon the previously published abstract from this workgroup (Yerke *et al*., 2019) by providing evidence supporting the existence of a potential relationship between HT and periodontal disease complexity in patients with moderate to severe periodontitis. The positive association between periodontal disease and hypothyroidism reported in our study also is consistent with previous reports, as reviewed by Aldulaijan *et al*. (2020). In the current study population, patients with HT have an approximately 30% greater proportion of ≥ 5 mm and ≥ 6 mm probing depths compared to individuals without HT. Based on those results, interprofessional collaboration might be considered to care for patients who suffer from both conditions. Indeed, screening of patients with moderate to severe periodontitis and who exhibit some of the clinical signs associated with HT might be valuable for identification of subclinical or previously undiagnosed or subclinical HT.

Conclusions

Among patients with stage III to IV, grade B to C, generalized periodontitis, a greater percentage of elevated probing depths occur among those also diagnosed with HT. In an effort to further elucidate the relationship between HT and periodontitis, prospective studies using larger patient sample sizes currently are underway in our laboratory. Collectively, the findings suggest that referral for comprehensive periodontal examination might be considered by endocrinologists for individuals diagnosed with hypothyroidism. Similarly, dentists should be aware of signs consistent with HT among their patients with moderate to severe periodontitis to help assess when medical consultation might be useful to assist in the detection of undiagnosed or preclinical HT.

References

Albandar, J. M., Susin, C., & Hughes, F. J. (2018). Manifestations of systemic diseases and conditions that affect the periodontal attachment apparatus: Case definitions and diagnostic considerations. *J Periodontol*, **89** Suppl 1, S183-s203. https://doi.org/10.1002/jper.16-0480

Aldulaijan, H. A., Cohen, R. E., Stellrecht, E. M., Levine, M. J., & Yerke, L. M. (2020). Relationship between hypothyroidism and periodontitis: A scoping review. *Clinical and experimental dental research,* **6**(1), 147-157.

Casanova, L., Hughes, F., & Preshaw, P. (2014). Diabetes and periodontal disease: a two-way relationship. *Br Dent J*, **217**(8), 433-437.

Chaker, L., Bianco, A. C., Jonklaas, J., & Peeters, R. P. (2017). *Hypothyroidism*. Lancet, **390**(10101), 1550-1562. https://doi.org/10.1016/s0140-6736(17)30703-1

Ejtahed, H.-S., Angoorani, P., Soroush, A.-R., Siadat, S.-D., Shirzad, N., Hasani-Ranjbar, S., & Larijani, B. (2020). Our little friends with big roles: alterations of the gut microbiota in thyroid disorders. *Endocrine, Metabolic & Immune Disorders-Drug Targets (Formerly Current Drug Targets-Immune, Endocrine & Metabolic Disorders)*, **20**(3), 344-350.

Garber, J. R., Cobin, R. H., Gharib, H., Hennessey, J. V., Klein, I., Mechanick, J. I., Pessah-Pollack, R., Singer, P. A., Endocrinologists, W. f. t. A. A. o. C., & American Thyroid Association Taskforce on Hypothyroidism in Adults, K. A. (2012). Clinical practice guidelines for hypothyroidism in adults: cosponsored by the *American Association of Clinical Endocrinologists and the American Thyroid Association*. Thyroid, **22**(12), 1200-1235.

Hollowell, J. G., Staehling, N. W., Flanders, W. D., Hannon, W. H., Gunter, E. W., Spencer, C. A., & Braverman, L. E. (2002). Serum TSH, T(4), and thyroid antibodies in the United States population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III). *J Clin Endocrinol Metab*, **87**(2), 489-499. https://doi.org/10.1210/jcem.87.2.8182

Ishaq, H. M., Mohammad, I. S., Guo, H., Shahzad, M., Hou, Y. J., Ma, C., Naseem, Z., Wu, X., Shi, P., & Xu, J. (2017). Molecular estimation of alteration in intestinal microbial composition in Hashimoto's thyroiditis patients. *Biomedicine & Pharmacotherapy*, **95**, 865-874.

Jain, R. (2015). Thyroid profile of the reference United States population: Data from NHANES 2007-2012. *Int Arch Endocrinol Clin Res*, **1**(1).

Kato, T., Yamazaki, K., Nakajima, M., Date, Y., Kikuchi, J., Hase, K., Ohno, H., & Yamazaki, K. (2018). Oral administration of Porphyromonas gingivalis alters the gut microbiome and serum metabolome. *mSphere*, **3**(5).

Kobayashi, R., Ogawa, Y., Hashizume-Takizawa, T., & Kurita-Ochiai, T. (2020). Oral bacteria affect the gut microbiome and intestinal immunity. *Pathogens and Disease.*

Olsen, I., & Yamazaki, K. (2019). Can oral bacteria affect the microbiome of the gut? J*ournal of oral microbiology*, **11**(1), 1586422.

Page, R. C., & Eke, P. I. (2007). Case definitions for use in population-based surveillance of periodontitis. *J Periodontol,* **78**, 1387-1399.

Papapanou, P. N., Sanz, M., Buduneli, N., Dietrich, T., Feres, M., Fine, D. H., Flemmig, T. F., Garcia, R., Giannobile, W. V., & Graziani, F. (2018). Periodontitis: Consensus report of workgroup 2 of the 2017 *World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. J Periodontol*, **89**, S173-S182.

Rahangdale, S. I., & Galgali, S. R. (2018). Periodontal status of hypothyroid patients on thyroxine replacement therapy: A comparative cross-sectional study. *J Indian Soc Periodontol*, *22*(6), 535.

Sanz, M., Marco del Castillo, A., Jepsen, S., Gonzalez-Juanatey, J. R., D'Aiuto, F., Bouchard, P., Chapple, I., Dietrich, T., Gotsman, I., & Graziani, F. (2020). Periodontitis and cardiovascular diseases: Consensus report. *Journal of Clinical Periodontology*, *47*(3), 268-288.

Shin, N. R., Bose, S., Wang, J. H., Nam, Y. D., Song, E. J., Lim, D. W., Kim, H. B., Lim, Y. S., Choi, H. S., & Kim, H. (2020). Chemically or surgically induced thyroid dysfunction altered gut microbiota in rat models. *The FASEB Journal.*

Silness, J., & Löe, H. (1964). Periodontal disease in pregnancy II. Correlation between oral hygiene and periodontal condition. *Acta odontologica scandinavica,* **22**(1), 121-135.

Su, X., Zhao, Y., Li, Y., Ma, S., & Wang, Z. (2020). Gut dysbiosis is associated with primary hypothyroidism with interaction on gut-thyroid axis. *Clinical Science.*

Tonetti, M. S., Greenwell, H., & Kornman, K. S. (2018). Staging and grading of periodontitis: Framework and proposal of a new classification and case definition. *Journal of Periodontology*, **89**, S159-S172.

von Elm, E., Altman, D. G., Egger, M., Pocock, S. J., Gotzsche, P. C., & Vandenbroucke, J. P. (2014). The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement: guidelines for reporting observational studies. *Int J Surg*, **12**(12), 1495-1499. https://doi.org/10.1016/j.ijsu.2014.07.013

Wang, B., Xu, Y., Zhang, M., Zhang, J., Hou, X., Li, J., Cai, Y., Sun, Z., Ban, Y., & Wang, W. (2020). Oral and intestinal microbial features in pregnant women with hypothyroidism and their correlations with pregnancy outcomes. *American Journal of Physiology-Endocrinology and Metabolism*, **319**(6), E1044-E1052.

Yerke, L., Levine, M., & Cohen, R. (2019). MON-616 Potential Relationship between Hypothyroidism and Periodontal Disease Severity. *Journal of the Endocrine Society,* **3**(Supplement_1), MON-616.

Yerke, L. M., Levine, M. J., & Cohen, R. E. (2020). Hypothyroidism among Periodontally Healthy Adults in Western New York. *New York State Dental Journal*, **86**(3), 10-15.

Zahid, T. M., Wang, B.-Y., & Cohen, R. E. (2011). The effects of thyroid hormone abnormalities on periodontal disease status. *Journal of the International Academy of Periodontology*, **13**(3), 80-85. http://europepmc.org/abstract/MED/22220370