Original Article

The Association between Hyperemesis Gravidarum and Periodontal Disease in Pregnancy

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Abstract

Purpose: Periodontal diseases (PDs) are considered a risk factor for some systemic conditions such as cardiovascular diseases, diabetes, and adverse pregnancy outcomes. Hyperemesis gravidarum (HG) is a common health problem, and inflammation is claimed to play a vital role in its etiopathogenesis. Here, we aimed for the first time to demonstrate the relationship between PD and HG. **Materials and Methods:** A total of 30 pregnant with HG and 30 healthy pregnant between the age group of 18 and 40 years were enrolled in the study. HG was diagnosed if the followings were present: at least one-positive ketonuria, >5% weight loss, and severe vomiting, which is >2 times a day. Periodontal status was evaluated by the plaque index (PI), gingival index (GI), probing pocket depth (PPD), and bleeding on probing index (BOPI), and these parameters were recorded. All measurements were performed at 6 points of each tooth (mesiobuccal, midbuccal, distobuccal, mesiolingual, midlingual, and distolingual) and compared between the groups. **Results:** Mean age was 29 ± 3 in HG and 28 ± 4 in the control group. There was no difference between two groups according to the age ($P = 0.421$), gravida (0.524), and parity, ($P = 0.54$). PI, GI, PPD, and BOPI were significantly higher in HG group as compared to controls. **Conclusions:** Gingival inflammation is more common in patients with HG, and it is possibly associated with insufficient tooth brushing because it may stimulate the gagging reflex and vomiting. Since there could be a vicious cycle between PD and HG, periodontal preventive programs are crucial for pregnant women with HG.

Keywords: Periodontal-systemic disease interactions, pregnancy, pregnancy complications

Introduction

Periodontal diseases (PDs) are common chronic infections affecting tooth-supporting tissues, with an incidence of 46% of the adult population in the United States.[1] It is probably caused by the disequilibrium between infectious pathogens and host-immune response.[2] PDs are considered a potential risk factor for some systemic inflammatory conditions such as cardiovascular diseases, rheumatoid arthritis, diabetes mellitus, and respiratory diseases.[3,4] Moreover, it has been found to be related with adverse pregnancy outcomes, and the main accused mechanism is inflammation for such adverse events.[5]

Previous studies have demonstrated that pregnant women with PD have a higher incidence of low-birth weight, preterm birth, and preeclampsia.[6,7] The effect of periodontal inflammation on adverse pregnancy outcomes has been theorized with two different pathways: direct and indirect. First, periodontal bacteria and/or their pathogenic products may directly spread to the fetal-placental unit hematologically or along the genitourinary tract from the oral cavity. Indirectly, local inflammatory mediators such as prostaglandin E2 (PGE2) and tumor necrosis factor-alpha (TNF)-α, which are produced in response to periodontal pathogens may enter the bloodstream, arrive the fetal-placental unit, and amplify the accumulation of this mediators. Similarly, they enter the liver and increase acute-phase protein reaction such as C-reactive protein (CRP) synthesis, and by this way, inflammation in the fetal-placental unit may become more severe.[2]

Furthermore, it has been considered that pregnancy could increase the severity of PDs due to hormonal changes.

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Increasing of sex steroid hormone levels during pregnancy cause vascular dilatation that leads swelling, bleeding, and redness of the gingiva. Tilakaratne *et al*. reported that gingival index (GI) scores were significantly higher in pregnant women than nonpregnant women even if there were no statistically significant differences between the plaque index (PI) scores of the groups.[8] Furthermore, many studies revealed that probing pocket depth (PPD) scores and bleeding on probing measurements are significantly elevated during pregnancy.[9,10]

Hyperemesis gravidarum (HG), which is a condition of severe nausea and vomiting during pregnancy, can lead to electrolyte and fluid imbalance, weight loss, nutrition deficiency, and ketonuria.[11,12] Moreover, it has some catastrophic consequences such as central pontine myelinolysis, Wernicke's encephalopathy, vasospasm of cerebral arteries, rabdomyolysis, coagulopathy, and maternal and fetal death.[13-15] While HG generally occurs between the 8th and 10th gestational weeks of pregnancy, in 10% of all HG cases, it persists until the birth.[12] Previous HG history, multiple and molar pregnancy, gestational trophoblastic neoplasia, hyperthyroidism, gastrointestinal disorders, female offspring, and psychiatric disorders are the main risk factors for HG.[16] Increased human chorionic gonadotropin (β-hcg), thyroxine, prolactin, estrogen and progesterone levels, gastrointestinal dysmotility, decreased lower esophageal sphincter pressure, *Helicobacter pylori* infection, immunologic factors, disturbances in hypothalamic-pituitary-adrenal axis, and psychological factors are well-known proposed mechanisms.[17,18] Although the exact pathophysiological mechanisms have not been fully elucidated, inflammation is claimed to play a crucial role in its etiopathogenesis.[12,19]

Recent studies have demonstrated the increased levels of inflammatory markers such as interleukin (IL)-6, TNF-α, paraoxonase-1, and CRP in HG patients, which may be a sign to recognize HG as an inflammatory condition.[10,18] Another finding from the previous studies that led to this thought is related to the role of steroids in the treatment of HG. Steroids, which reduce the IL levels and provide dramatic responses even with a brief course, support the role of inflammation in HG.[19]

The main hypothesis of this study was that periodontal inflammation is more common in HG cases, and periodontal parameters are higher in a patient with HG than healthy pregnant women. In this study, we aimed for the first time to demonstrate the relationship between PD and HG.

Materials and Methods

This study was conducted on pregnant women at the obstetrics and gynecology department between the dates of March 2019 and August 2019. The present study was granted ethical approval by the Ethical Committee (Protocol Number: 108400-604.01.01-E.12586) and conducted in accordance with the guidelines of the Helsinki Declaration of 1975, as revised in 2000. All the participants were enlightened about the purpose and design of the study and signed written informed consent forms before the study. A total of 60 volunteer pregnant women ranging from the age group of 18 to 40 years participated in this study. Patients were allocated to two groups: the first group was constituted of participants with HG and named the HG group, and the second group was constituted of healthy pregnant women and named the control group.

Seventeen patients were excluded from this study according to the following criteria: antibiotic treatment within the past 6 months, any periodontal therapy and mouth rinse use within the previous 3 months, systemic diseases and chronic infections other than periodontitis, smokers, and presence of <20 teeth on oral examination. HG was diagnosed if the followings were present, at least one-positive ketonuria, >5% weight loss, and severe vomiting which is more than two times a day.

All clinical examination was performed within the 8th–10th week of pregnancy, periodontology department. Periodontal status was evaluated by PI,[20] GI,[21] PPD, and bleeding on probing index (BOPI).[22] All the measurements were recorded by the same, blinded and experienced researcher at 6 points of each tooth (mesiobuccal, midbuccal, distobuccal, mesiolingual, midlingual, and distolingual) by using Williams marked probe. The patients were classified as gingivitis (patients who had no periodontal pocket but had bleeding on more than 10% of the surfaces after light mechanical stimulation) and periodontitis (patients who had ≥4 mm pocket depth on two or more surfaces) based on the collected data.[23]

The prevalence of PD in pregnancy was reported between 30% and 100%. We expected the rate of PD in HG group (90%). Thus, the *post hoc* sample size and power calculation test revealed that >27 patients in each group would meet the statistical power with the following assumptions: 5% of α level, 0.8 of anticipated effect size, and 80% of statistical power level. Descriptive statistics are presented with frequency, percentage, mean, standard deviation, median, minimum, and maximum values. Pearson Chi-square test was used to analyze the categorical data. The normality assumption was evaluated by the Shapiro–Wilk test. In the analysis of the difference between the numerical data of the two groups, independent samples *t*-test was used in cases where the data corresponded to the normal distribution. Mann–Whitney U-test was used for nonnormally distributed variables. The analyses were performed using the IBM SPSS software version 23.0 program (Chicago, IL, USA). $P < 0.05$ was considered statistically significant.

Results

During the research period, sixty pregnant women who met the inclusion criteria were evaluated. Table 1 shows the patient's characteristics. There were no statistically significant differences between the two groups in terms of age, gravida, and parity. In the HG group, the number of patients with periodontitis was statistically significantly higher than that of the control group ($P < 0.001$) [Table 2].

The mean values of the clinical parameters indicating that oral hygiene and periodontal status of the HG and control groups are given in Table 3. The results showed that HG group had statistically significantly higher PI, GI, PPD, and BOPI levels ($P < 0.05$) compared with the control group [Table 2]. The distributions of PI, GI, PPD, and BOPI of HG and control groups are shown in the box-plot graph format [Figures 1 and 2].

Discussion

PDs are known to be a risk factor for systemic conditions and diseases such as cardiovascular diseases, rheumatoid arthritis, diabetes mellitus, respiratory diseases, and adverse pregnancy outcomes, including premature birth, low-birth weight, miscarriage, or dead birth.[6,9]

The relationship between periodontal inflammation and systemic conditions could be related to two different mechanisms. First, translocation of bacteria from the inflamed periodontal tissues into the systemic circulation can cause bacteremia.[4]

Table 1: Characteristics of study participants

	Control	HG	*P*
Age (year)	28±4	29±3	0.421
Gravida	1.7±1.23	1.9±1.15	0.524
Parity (range)	0±1	1±0.8	0.54

HG: Hyperemesis gravidarum

Table 2: Multiple comparisons among the different periodontal measurements

Group Diagnosis[$]	Control, *n* (%)	HG, *n* (%)	*P*
Gingivitis	24 (80)	11 (36.67)	<0.001*
Periodontitis	6 (20)	19 (63.33)	

[$]Pearson Chi-square test, *$P<0.05$. HG: Hyperemesis gravidarum

Table 3: Comparison between clinical periodontal indices and hyperemesis gravidarum

Group	Mean±SD	*P*
PI[#]		
Controls	1.00±0.30	0.04*
HG	1.20±0.40	
GI[+]		
Controls	1.35±0.16	0.009*
HG	1.55±0.25	
PPD[+]		
Controls	1.94±0.18	<0.001*
HG	2.15±0.20	
BOPI[#]		
Controls	48.70±16.25	0.03*
HG	62.33±27.21	

[#]Independent samples *t*-test, [+]Mann-Whitney U-test, *$P<0.05$. HG: Hyperemesis gravidarum, SD: Standard deviation, PI: Plaque index, GI: Gingival index, PPD: Probing pocket depth, BOPI: Bleeding on probing index

Furthermore, it is shown that levels of proinflammatory cytokines such as IL-1, IL-6, PGE2, and TNFα are high in inflammatory gingival tissues, gingival crevicular fluids, and plasma in periodontitis patients.[24] This locally derived mediators can enter the bloodstream and stimulate acute-phase protein production such as CRP in the liver.[2,4]

Nausea and vomiting affect more than 80% of pregnant women, especially during the first trimester.[25] HG is a rare (0.3%–1.5%) and stringent condition of nausea and vomiting that may cause nutritional deficiencies, dehydration, electrolyte imbalance, and ketonuria and has a significant detrimental impact on the quality of life.[26,27] Even if the etiology of HG is not well understood, inflammation could be a risk factor for its development. Kaplan *et al*. were found significantly elevated serum levels of TNF-α, IL-1, and IL-6 in patients with HG compared with nonpregnant women and healthy pregnant women.[18] Kuscu *et al*. also observed higher levels of IL-6 in HG patients.[19] In addition, in another study showed that significantly higher immunoglobulin (Ig) G, IgM, C3, C4 levels, and lymphocyte count in HG patients.[28] Thus, the immune reactions may play a role in the etiology of HG. However, it is not clear yet whether the high levels of inflammatory markers in patients with HG cause or are produced by hyperemesis.

The previous studies showed that pregnant women exhibited significantly higher levels of gingivitis than nonpregnant women. Although the plaque levels remained unchanged, the results indicate that gingival scores and PPDs were significantly greater in pregnant women compared with nonpregnant controls.[8,9] The increase in severity of gingivitis during pregnancy has been attributed to increased hormonal levels of estrogen and progesterone. Although this may cause hyperemia, edema, increased gingival exudate, and bleeding in periodontal tissues could not affect periodontal attachment.[29,30] The possible reason for the lack of attachment loss is probably that a 9-month period is insufficient to cause periodontal destruction.

Taani *et al*. observed a positive correlation between GI and PPDs in patients who vomited during pregnancy compared

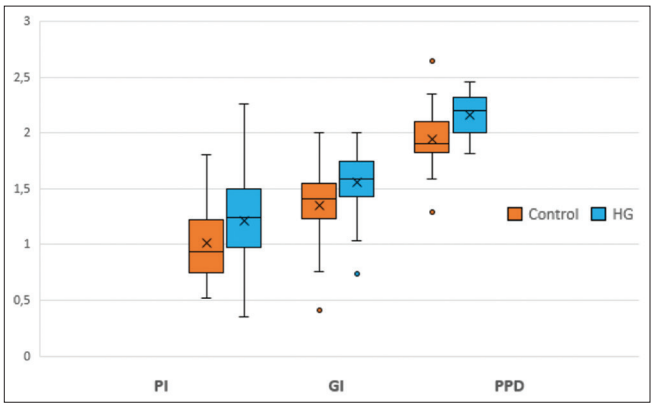

Figure 1: Distribution of plaque index, gingival index and probing pocket depth between the groups

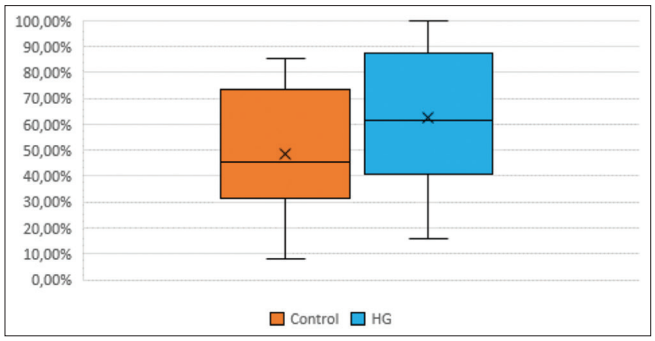

Figure 2: Distribution of bleeding on probing index between the groups

with those who did not.[9] Gürsoy *et al*. reported the greatest peak in the plaque scores appeared during the first trimester.[10] They speculated that brushing may stimulate a gagging reflex and vomiting, and women may avoid brushing their teeth. Toygar *et al*. in their study of 3576 women found that GI and PD were increased with vomiting and nausea, but did not find a relationship between periodontal status and nausea and vomiting.[6] However, none of these studies evaluated the severity of nausea and vomiting. This is the first study comparing the gingival inflammation and oral hygiene between pregnant women with and without HG. In our study, we found a significant association between PI, GI, PPD, BOPI, and HG. At the same time, the number of patients with periodontitis in the HG group was significantly higher than the control group. Although patients with HG may have difficulties in brushing their teeth, this is not expected to increase periodontal attachment loss in such a short time. In this case, periodontitis may contribute to the formation of HG by increased inflammatory mediators in the systemic circulation.

Conclusions

There could be a two-way relationship between HG and periodontitis. We assume that periodontitis can contribute the etiopathogenesis of HG, and thus, patients with an increased incidence of vomiting cannot brush their teeth properly, and PI, GI, and BOPI may increase. These findings indicate a likely association, but large and well-designed further studies are needed to determine the possible relationship with HG and periodontal inflammation.

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Conflicts of interest

There are no conflicts of interest.

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