ORAL PATHOLOGY

GINGIVAL INFLAMMATION AS A SIGN OF DIABETIC SYSTEMIC CHRONIC COMPLICATIONS

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ABSTRACT

Introduction: Diabetes mellitus (DM) is a chronic metabolic disorder and the high level of blood glucose has profound effects on various systems of the human body. DM increases the risk of periodontal disease and the severe periodontal disease often coexists in diabetic patients with poor glycemic control. The aim of the study was to analyse periodontal health in patients with diabetes mellitus type 2 related to diabetic complications and glycohemoglobin A1c values.

Methodology: One hundred patients with periodontitis and type 2 DM participated in the study. According to the glycohemoglobin A1c value they were divided in 4 groups: group 1 (4%-6% normal), group 2 (6.1%-7% good), group 3 (7.1%-8% moderately poor), group 4 (> 8% poor metabolic control). The presence of chronic systemic microvascular diabetic complications (retinopathy, nephropathy and neuropathy) was recorded and periodontal assessments (Plaque, Gingival, Calculus and Periodontal Disease Index) performed. The results were statistically analysed using MS Office Excel, program SPSS, 15.0 version.

Results: Gingival index values depended on the level of HbA1c values and higher values of the Gingival and Periodontal Disease Index were noticed as the value of glycohemoglobin A1c was rising ($p<0.001$). Gingival index values were higher in diabetics with diabetic chronic microvascular complications ($p<0.001$).

Conclusion: It is observed that pronounced gingival inflammation in diabetics is associated with systemic diabetic complications and poor glycemic control.

Keywords: diabetes mellitus, glycohemoglobin A1c, diabetic complications, gingival inflammation, periodontitis.

1. Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder caused by the ineffectiveness of the insulin produced or by deficiency in production of insulin by the pancreas. Among diabetic patients over 45 years old, more than 95% patients have type 2 DM1. The high level of glucose present in the blood has profound effects on various systems of the human body. The determination of glycohemoglobin A1c (HbA1c) levels provides an estimate of the average blood glucose level over the preceding one to three months. The higher average blood glucose levels reflect in higher HbA1c values2. HbA1c level is of major clinical values in assessment diabetes prognosis and correlates well with the development of diabetic complications. The recommended HbA1c target value for people with diabetes mellitus is <7.0% and achieving this goal is very difficult3. DM significantly increases the prevalence, severity, and rate of progression of periodontal disease, and periodontal disease is

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recognized as one of the complications of DM. What is less clear is the impact of periodontal disease on glycemic control of DM and the mechanisms through which this occurs. Some authors suggest that an intensive gingival inflammation relate to poor glycemic control and multiple diabetic complications. Periodontal disease may be more frequent and severe in diabetic individuals with more systemic complications. The evidence suggests that mechanisms which account for the development of systemic diabetic complications might also be crucial in the pathogenesis of increased periodontal destruction in DM. The diabetic state impairs the synthesis of collagen and glycosaminoglycans, enhances crevicular fluid collagenolytic activity which lead to the loss of periodontal fibres and loss of the alveolar supporting bone. This predisposes to chronic inflammation, progressive tissue breakdown and diminished tissue repair capacity. These mechanisms cause periodontal tissue breakdown and loosening of the teeth. The increased activity of periodontal disease in diabetic patients does not correlate with levels of plaque and calculus which do not have higher values in diabetic patients. Collectively, the evidence supports the theory that there is a relationship between the two diseases, especially in patients with poorly controlled DM. This proposed dual pathway of tissue destruction suggests that control of DM is necessary for achieving long-term control of periodontal disease.

2. The aim of the study
The aim of the study was to analyze periodontal health in patients with diabetes mellitus type 2 related to diabetic complications and HbA1c values.

3. Methodology
3.1. Study design and subjects
This clinical study was carried out as a joint collaboration between the Department of Endocrinology and Department of Periodontology and Oral medicine, Niš University, Faculty of Medicine. The study protocol was reviewed and approved by the Niš University Faculty of Medicine Institutional Ethical Committee (identification number 01-2800-7) and in accordance with the Helsinki Declaration of 1975, as revised in 2000.

3.2. Subjects
Patients with periodontitis and DM were selected from the pool of followed patients at the Department of Endocrinology, Niš University Medical Center. After the patient history was taken, patients who had acute systemic or oral disease, autoimmune diseases, hemorrhagic disorders, who had undergone antibiotic and corticosteroid therapy in the last three months, as well as patients who had periodontal treatment in the last three months were not included in the study.

One hundred patients with periodontal disease and type 2 DM, 48 (48%) women and 52 (52%) men, the mean age 62.57±8.57 years participated in the study. The HbA1c level was taken from the patient records. In the analysis according to the HbA1c values patients were divided in four groups: group 1 (4%-6% HbA1c; normal metabolic control), group 2 (6.1%-7% HbA1c; good metabolic control), group 3 (7.1%-8% HbA1c; moderate poor metabolic control), group 4 (> 8% HbA1c; poor metabolic control). The presence of chronic systemic microvascular diabetic complications (retinopathy, nephropathy and neuropathy) was recorded from patients records, and according to presence of these complications patients were divided in groups: patients with chronic systemic DM complications (group A) and patients without chronic systemic DM complications (group B).

3.3. Oral examination protocol
The periodontal assessments were performed by a single examiner on four sites per tooth (mesio-buccal, disto-buccal, mesio-lingual, disto-lingual) for all (third molars excluded) fully erupted permanent teeth, using a manual periodontal probe. Using the tip of the periodontal probe inserted into the pocket with constant probing force the following were evaluated: Plaque index (PI), Gingival Index (GI), Calculus index (Cal), and Periodontal Disease Index (PDI). Afterwards, all of the patients received oral hygiene instructions and full-mouth scaling and root planning.

3.4. Diabetes-related variables
The following information were collected from medical records: sex, duration of DM (years since diagnosis) and patient age. For the metabolic assessment, the HbA1c level was calculated from the patient records.

3.5. Analytical methods
The statistical analysis was performed using SPSS software program and parameters were shown as mean values (X) and standard deviations (SD). Student t-test, Leven method, Tukey HSD test and Dunnett T3 test were used for analysis of statistically important difference between mean values of two groups. The results are shown tabularly using MS Office Excel, program SPSS, 15.0 version.

4. Results
The study population included patients with DM type 2 aged 22-83 years, 51 women and 49 men. Mean HbA1c value was 8.70±0.45% and the mean DM duration 14.68±3.43 years.

Comparing mean values and standard deviations (X±SD) of PI, Izk, Ikon, Gi and PDI indexes according to HbA1c values, ANOVA analysis showed that Gi values depended on the level of HbA1c values (p<0.001). Higher values of investigated indexes were noticed as the value of HbA1c was rising (p<0.001) (Table 1).

Comparing mean values and standard deviations (X±SD) of PI, Izk, Ikon, Gi and PDI indexes according to presence of chronic systemic DM complications, it was noticed that only Gi values were higher in the group with chronic systemic DM complications (retinopathy, nephropathy and neuropathy) (t=5.42, p<0.001) (Table 2).
5. Discussion

DM and periodontal disease are common chronic diseases in adults\textsuperscript{22,23}. The general opinion is that there is no effect of gender on elevated blood glucose in diabetic patients, as noticed in this study, whereas both sexes were uniformly represented\textsuperscript{24}. Diabetic patients with poor metabolic control are at a high risk for a poor periodontal prognosis\textsuperscript{7,8}. Most studies suggest that the situation for periodontal disease is similar to that for the other systemic complications of DM\textsuperscript{3,7,8}. The metabolic control in diabetic patients is an important variable in the onset and progression of periodontal disease and chronic systemic DM complications\textsuperscript{5}. Lalla et al.\textsuperscript{24} noticed that HbA1c was positively and significantly correlated with gingival bleeding. The presence of periodontal pockets and attachment loss were not significantly correlated with HbA1c higher values in diabetic patients. These findings suggest that changes in the periodontal microvasculature are related to the level of metabolic control. The results of this investigation were similar to literature data\textsuperscript{25}. The “poor metabolic control” shown through the high values of HbA1c clearly increases the risk of activation of gingival inflammation and higher values of GI index are present as the value of HbA1c was rising (p<0.001).

Salvi\textsuperscript{26} investigated diabetics with mean HbA1c of 8.1%, and concluded that in diabetic patients with “poor metabolic control” the bleeding tendencies were higher than in those with lower values of HbA1c. Similar findings were noticed in the present investigation. Mean GI values in groups with “moderately poor” and “poor metabolic control” were higher comparing to the values in group with “good metabolic control” (p<0.05).

Lalla E et al.\textsuperscript{24} measured attachment loss and gingival bleeding separately, and similarly as previous investigators noticed that HbA1c was positively and significantly correlated with gingival bleeding, but not with attachment loss alone\textsuperscript{24,27}. Similar findings were noticed in the present investigation where mean GI values in groups with “moderate poor” and “poor metabolic control” were higher comparing to group with “good metabolic control” (p<0.05).

Some authors emphasize that an intensive gingival inflammation suggests the existence of poor glycemic control and multiple systemic diabetic complications\textsuperscript{7-11}. Similar noticed in the present study where diabetics with chronic systemic diabetic complications also had higher values of GI.

The evidence suggests that mechanisms which account for the development of systemic diabetic chronic microvascular complications might also be operating in the pathogenesis of increased gingival inflammation in DM\textsuperscript{12-13}. Potentially a number of factors could contribute to the periodontal disease in DM (oral microflora, phagocytic and connective-tissue defects) and exploring the complex pathogenic mechanisms underlying these associations was beyond the scope of this study. Further studies with larger sample sizes are needed to investigate the pathogenic mechanisms between gingival inflammation and systemic diabetic chronic complications.

The general opinion is that diabetic patients exhibit poorer periodontal health and poorer therapeutic response than systemically healthy patients\textsuperscript{28}. Good glycemic control might be essential in the prevention of periodontal complications in patients with DM\textsuperscript{29,30}. During routine dental checkup, dentists detecting pronounced gingival inflammation in patients with DM can suspect the presence of undiagnosed diabetic chronic complications and refer a patient

\textbf{Table 1. Mean values and standard deviations (X±SD) of PI, Izk, Ikon, Gi and PDI indexes and statistically important differences between groups according to HbA1c values}

<table>
<thead>
<tr>
<th>Groups according to HbA1c</th>
<th>N</th>
<th>PI</th>
<th>Izk</th>
<th>Ikon</th>
<th>Gi</th>
<th>PDI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (4%-6%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 (6.1%-7%)</td>
<td>22</td>
<td>2.33±0.58</td>
<td>2.00±0.00</td>
<td>2.67±0.58</td>
<td>1.00±0.00</td>
<td>4.68±0.79</td>
</tr>
<tr>
<td>3 (7.1%-8%)</td>
<td>16</td>
<td>2.57±0.53</td>
<td>1.86±0.69</td>
<td>2.57±0.53</td>
<td>1.75±0.46</td>
<td>5.00±0.00</td>
</tr>
<tr>
<td>4 (&gt; 8%)</td>
<td>62</td>
<td>2.28±0.68</td>
<td>1.98±0.66</td>
<td>2.58±0.55</td>
<td>2.00±0.00</td>
<td>5.25±0.46</td>
</tr>
</tbody>
</table>

\textsuperscript{*}-1vs2, -1vs3, -1vs4, -2vs3, -2vs4, -3vs4; **p<0.05, ***p<0.01, ****p<0.001

\textbf{Table 2. Mean values and standard deviations (X±SD) of PI, Izk, Ikon, Gi and PDI values and statistically important differences between groups according to chronic systemic DM complications}

<table>
<thead>
<tr>
<th>Groups according to DM complications</th>
<th>N</th>
<th>PI</th>
<th>Izk</th>
<th>Ikon</th>
<th>Gi</th>
<th>PDI</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (with DM complications)</td>
<td>70</td>
<td>2.23±0.69</td>
<td>1.63±0.69</td>
<td>1.66±0.76</td>
<td>1.92±0.27</td>
<td>4.91±0.61</td>
</tr>
<tr>
<td>B (without DM complications)</td>
<td>30</td>
<td>1.87±0.74</td>
<td>1.47±0.52</td>
<td>1.73±0.96</td>
<td>1.64±0.50</td>
<td>4.53±0.83</td>
</tr>
</tbody>
</table>

\textsuperscript{*}-AvsB gr, **p<0.05, ***p<0.01, ****p<0.001

Good glycemic control might be essential in the prevention of periodontal complications in patients with DM\textsuperscript{29,30}. During routine dental checkup, dentists detecting pronounced gingival inflammation in patients with DM can suspect the presence of undiagnosed diabetic chronic complications and refer a patient
to an endocrinologist for prompt treatment of the underlying disease and DM complications. For proper dental care the dentist should be aware of the diabetic status of each patient. Information on the levels of HbA1c over a longer period of time and the presence/absence of any diabetic complications is needed in assessing periodontal prognosis and the need for periodontal therapy on individual basis. Close collaboration between the patient, the primary health care and oral health professionals, and application of new therapeutic modalities could be a way of improving the diabetic patient’s general and oral health.6,7,8

6. Conclusion
It is observed that pronounced gingival inflammation in diabetics is associated with systemic diabetic chronic microvascular complications and poor glycemic control. As periodontal disease is a complex multifactorial disease related to DM, the prevention and control of periodontal disease must be considered an integral part of DM control. The findings in this study highlight a need to promote oral health in patients with DM as an integral component of total patient care.

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REFERENCES

Doctor Radmila Obradovic is an Assistant Professor at the Department of Oral Medicine and Periodontology, Dental Clinic, Faculty of Medicine, Niš University; Serbia. She is also a member of the Dental Clinic’s Ethical Committee and Medical Faculty’s Disciplinary Board. She is a member of the Serbian Medical Society and Serbian Oral Laser Society (SOLAS). She participated in national projects, many dental courses and conferences as a lecturer, and published many papers in dental and medical journals.

Questions

Regarding diabetic periodontitis:
- a. Mechanisms which account for the development of systemic diabetic complications might also be crucial in the pathogenesis of increased periodontal destruction;
- b. Diabetes mellitus has no influence on periodontitis;
- c. Periodontitis has no influence on diabetes mellitus;
- d. Diabetes mellitus and periodontitis have no influence on each other.

Regarding this study:
- a. 100 patients with periodontal disease and type 2 DM participated in this study;
- b. 100 patients with periodontal disease and type 1 DM participated in this study;
- c. 100 patients with periodontal disease and gestational DM participated in this study;
- d. Patients with DM did not participate in this study.

Regarding to the glycohemoglobin A1c value patients were divided in:
- a. 4 groups;
- b. 3 groups;
- c. 2 groups;
- d. 5 groups.

Regarding gingival inflammation and diabetic microvascular complications:
- a. Pronounced gingival inflammation in diabetics is associated with systemic diabetic chronic microvascular complications and poor glycemic control;
- b. Pronounced gingival inflammation in diabetics is not associated with systemic diabetic chronic microvascular complications and poor glycemic control;
- c. Systemic diabetic chronic microvascular complications have no influence on gingival health;
- d. Glycemic control has no influence on gingival health.