The assessment of the relationship between the severity of gingivitis and the glycosylated hemoglobin levels in adolescent and adult patients with type 1 diabetes

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Abstract

Background. Diabetes and periodontitis belong to the group of civilizational diseases, which are not associated with any specific bacterial or viral infection but with the rapid development of civilization and technological advances that affect comfort and quality of life. Civilizational diseases occur in highly developed and developing societies. Glycosylated hemoglobin A1c (HbA1c) is one of the standard indicators for the assessment of metabolic compensation in diabetes that reflects the risk of disease complications. One of the significant complications of diabetes that manifests in the oral cavity is gingival and periodontal inflammation, which is directly related to increased insulin resistance and worsened diabetes compensation. Factors influencing inflammation are the patient's age, directly linked with fine motor skills when it comes to cleaning teeth, and patients' awareness related to cause-and-effect relationship between dental hygiene, gingival and periodontal inflammation, and HbA1c testing during routine check-ups.

Objectives. To compare the relationship between gingival inflammation and metabolic compensation (HbA1c levels), depending on the patient's age.

Materials and methods. The study involved 100 patients (50 adolescents and 50 adults, 42 M; 58 F) with type 1 diabetes. The study group was divided according to sex and age into 19 male adolescent patients (10–18 years old; mean age 15.5) and 23 male adult patients (19–45 years old; mean age 27.1). The mean duration of diabetes was 7 years in the group of adolescents and 11 years in the group of adults. The HbA1c levels and gingival index (GI) were measured in all patients. The obtained results were statistically analyzed.

Results. By comparing the study groups, higher HbA1c values were reported in the group of adolescents. HbA1c has been shown to correlate with the GI in adolescents and adults. Despite poorer compensation for diabetes (higher HbA1c), GI values were similar in adolescents and adults.

Keywords

Type 1 diabetes • gingival inflammation • glycosylated hemoglobin • disease of civilization

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Background

Diabetes mellitus is a systemic metabolic disease caused by an absolute or relative insulin deficiency. The healing process in diabetes is impaired due to monocyte and macrophage dysfunction, chronically elevated levels of proinflammatory cytokines, and decreased expression of growth factors inhibiting cell proliferation and extracellular matrix synthesis [1, 2]. Increased fibroblast apoptosis with concomitant accumulation of advanced glycation end-products (AGEs) is another suggested mechanism of impaired healing in diabetes [3]. Glycated hemoglobin HbA1c is considered the gold standard for assessing the compensation of diabetes [4]. HbA1c reflects the average glycemia over the last 3–4

months, with about 50% of the HbA1c formed in the month prior to sampling [5].

HbA1c has been shown to have a strong predictive power for chronic diabetic complications [1] including micro- and macroangiopathy [6]. Gingivitis and periodontitis have been considered clinical complications in diabetic patients, manifested by increased gingival crevicular bleeding, pocket probing depth, and the loss of connective tissue attachment [7, 8, 9]. At the same time, the course of diabetes is affected by many inflammatory mediators produced locally in the periodontal tissues and secreted into the bloodstream, such as interleukin- β (IL- β) and tumor necrosis factor- α (TNF- α). Tumor necrosis factor- α and IL-1 β increase serine phosphorylation of insulin receptor substrate (IRS-1 and IRS-

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2) proteins on the surface of the insulin target cells [10]. This process leads to impaired signal transduction and weaker insulin action on cells [11], making cells less sensitive to insulin and reducing blood glucose uptake and tissue glucose storage. This leads to disturbed glucose metabolism and hyperglycemia, both having adverse effects on periodontal tissues [12]. Management of comorbid periodontal disease in patients with diabetes may significantly improve the compensation of diabetes [13]. There are still no conclusive data on the relationship between diabetes, gingivitis, and periodontitis. However, a close bidirectional relationship between these two disease entities has been found. There is a complex relationship between uncompensated diabetes and chronic inflammation in the periodontal tissues [14, 15].

Objectives

This study aimed to evaluate the association between the severity of gingivitis and HbA1c levels in adolescents and adults with type 1 diabetes.

Material and methods

With the approval of the Bioethics Committee at Poznan University of Medical Sciences, we enrolled 100 patients with type 1 diabetes: 50 adolescents (19 males; mean age 15.5 years) and 50 adults (23 men; mean age 27.1 years). The mean duration of the disease was 7 and 11 years, respectively (Table 1). All study participants gave informed consent to participate in the study; however, in the case of adolescents, consent was given by legal guardians or by the patients themselves if they were over 16. The study exclusion criteria were current orthodontic treatment and pregnancy. The gingival status of all patients was clinically examined according to the gingival index (GI) [16]. To objectify study results, all assessments were performed by a single physician. Gingival index was assessed at teeth 16, 11, 24, 36, 31, 44, and in the case of unerupted or missing teeth

24 and/or 44, at teeth 26 and/or 46. The assessment was performed according to a four-grade gingival status index: 0 – healthy gingiva, pale pink in color; 1 – mild inflammation, a slight color change and mild structural change of the gingival tissue, no bleeding on probing; 2 – moderate inflammation: redness, swelling, glossy and hypertrophic gingiva, bleeding on pressure or probing; 3 – severe inflammation: significant redness and swelling, ulceration, tendency to spontaneous bleeding [9, 17].

Fasting HbA1c was measured in all patients using standard laboratory methods [13, 18].

The results were statistically analyzed with STATISTICA v. 10.0. A p-value < 0.05 was considered statistically significant. The correlation analysis was performed using Spearman's rank correlation coefficient (Rs). All variables were tested for a normal distribution using the Kolmogorov-Smirnov test with Lilliefors correction. Nonparametric tests were used for data analysis. Statistical analyses were performed using Mann-Whitney U test and chi-square test. Results were presented as counts, means, and interquartile ranges (IQR).

Results

The study involved 50 adolescents (19 males) and 50 adults (23 males). In the whole study group, the mean age was 21.3 years, the level of HbA1c was 9.9%, and the gingival index (GI) was 0.79 (Table 2). The mean age of the adolescent patients was 15.5 years, and of the adult patients 27.1 years ($p=0.000001$). Compared to the group of adults, adolescent patients had worse metabolic compensation expressed by higher HbA1c (11.7% vs. 8.2%; $p = 0.000001$) and higher GI values (0.83 vs. 0.76; $p=0.46$) (Table 3). These differences were sex-independent.

Discussion

It may be difficult to compare study results on diabetes metabolic compensation in relation to gingival and

Table 1. Characteristics of the studied groups

Adolescents (n=50)	Minimum	Maximum	Average	SD	IQR	Adults (n=50)	Minimum	Maximum	Average	SD	IQR
Age	10	18	15.5	3.7	12–16	Age	19	45	27.1	7.7	21–32
Duration of diabetes [years]	4	10	7	1.8	5–8	Duration of diabetes [years]	4	15	11	2.8	8–13
Sex [f/m; n]	31/19					Sex [f/m; n]	27/23				

Table 2. Total value of parameters in the study group

Total n=100	Mini- mum	Maxi- mum	Aver- age	SD	IQR
Age	10	45	21.3	8.2	16–25
Duration of diabetes [years]	3	15	7	2.3	6–11
HbA1c [%]	5.6	15.2	9.9	2.4	7.8–12.0
GI	0.07	1.67	0.79	0.46	0.43–1.03
sex [f/m; n]	58/42				

periodontal disease. This ambiguity of interpretation is often related to the small sample size and different indices to assess oral health status [19]. In our study, gingival health status was assessed with GI in a group of 100 patients with type 1 diabetes. We chose GI because of its ease of use in the outpatient setting and because it helped exclude patients with symptoms of supportive tissue destruction. However, we reported gingivitis in 100% of the study participants, and GI values ranged from 0.2 to 2.8. Therefore, our study group differs from other groups in terms of the sample size and the status of periodontal tissues. In a group of Brazilian children aged 13 ± 3.5 years, gingivitis was reported in 21% and periodontitis in 6% of the study participants [20, 21]. In a group of Lithuanian children aged 10–15 years with type 1 diabetes, gingivitis was recorded in 27% compared to 13% in nondiabetics [22]. It is also important to note that in these studies the mean GI values in children aged 5–9 years was 1.54 ± 0.5 , and 1.14 ± 0.5 in the healthy control, whereas in children aged 10–14 years these indices were, respectively, 1.98 ± 0.6 and 1.17 ± 0.5 [5], so significantly higher than in the Polish population (mean 0.83 for adolescents vs. mean 0.76 for adults).

Current studies indicate that treatment of gingival and periodontal inflammation can improve HbA1c values by 0.4% [2, 23]. In periodontitis, chronic infection of the oral tissues increases insulin resistance, which contributes to seemingly worse metabolic compensation for diabetes [24, 25]. The interaction of bacterial by-products with phagocytes and fibroblasts leads to chronic release of proinflammatory cytokines, including interleukin 1 beta (IL-1 β), interleukin 6 (IL-6), tumor necrosis factor (TNF- α), prostaglandin E2 (PGE2), and acute phase C-reactive protein (CRP) [14, 26]. We observed a statistically significant correlation between HbA1c levels and GI values (Table 4). Moreover, we reported a statistically significant correlation between age and metabolic control in patients with type 1 diabetes. Compared to adults, adolescent patients had worse metabolic control (mean HbA1c 11.7 vs. mean HbA1c 8.2; $p = 0.000001$, respectively). Younger patients were less aware of their disease as compared to adults who had been educated about diabetes over a longer period of time. The same trend was noted for oral hygiene [23, 27].

Conclusions

The higher mean GI values observed in the group of adolescents (0.83 compared to 0.76 in adults) can be attributed to their hygienic habits. This may be due to the fact that adult patients have better manual skills, better techniques of oral hygiene, and more available oral hygiene tools [20]. In younger patients, the period of tooth replacement negatively affects GI and, consequently, gingival and periodontal inflammatory markers [28]. Studies show that the mixed dentition period is associated with higher gingival inflammation and thus with higher GI values [6, 29]. Gingivitis in patients with type 1 diabetes may be age-dependent, but is closely related to

Table 3. Comparison of children and adults in relation to the studied parameters

Adolescents (n=50)	Mini- mum	Maxi- mum	Average	SD	IQR	Adults (n=50)	Mini- mum	Maxi- mum	Average	SD	IQR	Adults vs. adolescents	p
Age	10	18	15.5	3.7	12–16	age	19	45	27.1	7.7	21–32	15.5 vs. 27.1	0.000001
Duration of diabetes [years]	4	10	7	1.8	5–8	duration of diabetes [years]	4	15	11	2.8	8–13	7 vs. 11	0.00001
HbA1c [%]	9.6	15.2	11.7	1.7	9.8– 12.9	HbA1c [%]	5.6	14.4	8.2	1.7	7.2–8.7	11.7 vs. 8.2	0.000001
GI	0.07	1.67	0.83	0.6	0.38– 1.15	GI	0.00	1.38	0.76	0.3	0.5–1.0	0.83 vs. 0.76	0.46

Table 4. Correlation between gingival index and HbA1c levels in the study groups

Correlated variables	Study group (total)	Adolescents	Adults
HbA1c & GI	Rs = 0.24; p = 0.0157	Rs = 0.29; p = 0.039	Rs = 0.50; p = 0.0002

*p < 0.05: the level of statistical significance.

metabolic compensation (expressed by HbA1c levels) [30, 31]. Regardless of age, patients with diabetes and coexisting gingival and periodontal disease should be informed and properly educated about the interaction between oral hygiene, periodontal status, and general health [32]. Treatment of gingivitis and periodontitis involves hygienization, correction, and maintenance [33]. The first two stages constitute an active treatment, and the third phase is to maintain treatment results [34]. Effective treatment of diabetes requires good cooperation between a diabetologist and a dentist, because of the bidirectional relationship between diabetes and periodontal disease [35]. Patients with undiagnosed diabetes who present to the dentist with diabetic symptoms should be referred to a specialist (diabetologist) for additional testing in order to establish a diagnosis and undertake appropriate treatment [36]. Early diagnosis of diabetes and good glycemic control positively affect the course of the underlying disease and the periodontal presentation [37]. Treatment of periodontal disease in diabetic patients may reduce the incidence of diabetic complications. Therefore, diabetologists should refer all patients without dental insurance to a dentist for diagnosis, prevention, and, if necessary, treatment of periodontal disease [38, 39].

Authors' Contribution

J.L.: Supervising the project, acquisition of data, data analysis and interpretation, writing (original draft preparation) review and editing, literature review, final proofreading and approval of the version for publication; **D.B.:** Acquisition of data, data analysis and interpretation; **A.D.S.:** Research concept and design, supervising the project, data analysis and interpretation; **M.W.Ś.:** Research concept and design, prewriting the project, writing (original draft preparation), review and editing, literature review, final proofreading and approval of the version for publication.

Conflict of Interest

The authors have no potential conflicts of interest to declare.

Ethics Approval

Due to the nature of the research, the consent of the ethics committee was not required.

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