OXIDATIVE STRESS AND ORAL HEALTH IN PEDIATRIC TYPE 1 DIABETES: A COMPARATIVE STUDY OF ANTIOXIDANT ENZYME ACTIVITY AND LIPID PEROXIDATION MARKERS

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Abstract

Objectives: This study investigates the relationship between Type 1 diabetes mellitus (T1DM) and periodontal health in pediatric patients, focusing on oxidative stress markers and antioxidant enzyme activity. T1DM in children is associated with elevated levels of oxidative stress, which exacerbates inflammatory responses and increases susceptibility to periodontal disease. Materials and methods: In this observational study, clinical periodontal parameters, such as Plaque Index (PI), Bleeding on Probing (BOP), Probing Depth (PD), and Clinical Attachment Loss (CAL), were compared between two groups: healthy children and children with T1DM. Additionally, plasma malondialdehyde (MDA), superoxide dismutase (SOD), and glutathione peroxidase (GPx) levels were assessed to evaluate oxidative stress and antioxidant capacity. Results and Discussion: Results indicated significantly higher BOP, PD, and CAL in the T1DM group, highlighting an elevated risk of periodontal disease. Paraclinical findings also showed increased MDA and reduced SOD and GPx activity in the T1DM group, suggesting compromised antioxidant defenses. Conclusions: This study emphasizes the need for integrated periodontal and systemic oxidative stress management in pediatric T1DM to mitigate complications and improve health outcomes.

Key-words: oral diagnosis, type 1 diabetes mellitus, pediatric oral status, periodontal parameters, oxidative stress, anxiety

Introduction

Type 1 diabetes mellitus (T1DM) is a chronic autoimmune condition characterized by the destruction of insulin-producing beta cells in the pancreas, resulting in an inability to regulate blood glucose levels effectively [1]. T1DM is among the most prevalent endocrine disorders in pediatric populations and commonly manifests in childhood or adolescence [2]. This early onset of T1DM necessitates a comprehensive and lifelong approach to disease management, significantly influencing both the affected children and their families [3].

The precise etiology of T1DM remains unclear; however, it is understood to arise from a complex interplay of genetic predisposition and environmental triggers, such as viral infections, which initiate the autoimmune destruction of pancreatic beta cells [4]. Unlike Type 2 diabetes, T1DM is unrelated to lifestyle factors and, thus, cannot be prevented or mitigated through dietary or exercise interventions [5, 6]. The onset is often abrupt, with hallmark symptoms including polyuria (frequent urination), polydipsia (increased thirst), unexplained weight loss, and fatigue. These

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symptoms reflect the body's inability to utilize glucose for energy due to the lack of insulin, an essential hormone for glucose uptake [4].

The absence of insulin production in T1DM necessitates lifelong exogenous insulin administration to manage blood glucose levels and prevent both acute and long-term complications. In the acute setting, poor glycemic control can precipitate episodes of hypoglycemia (low blood sugar) and hyperglycemia (high blood sugar), both of which present immediate health risks [7]. One of the most severe acute complications is diabetic ketoacidosis (DKA), a potentially life-threatening condition arising from prolonged hyperglycemia and requiring urgent medical intervention. Long-term, inadequate glycemic control in T1DM increases the risk of microvascular and macrovascular complications, including retinopathy, nephropathy, neuropathy, and cardiovascular disease [8], with early-onset diabetes predisposing children to an earlier manifestation of these complications.

Oxidative stress plays a significant role in the pathophysiology of T1DM in children [9], contributing to both the onset of the disease and the progression of its complications. Oxidative stress refers to an imbalance between the production of reactive oxygen species (ROS) and the body's ability to neutralize them with antioxidants. In children with T1DM, chronic hyperglycemia increases oxidative stress [10], which not only affects glycemic control but also leads to cellular and tissue damage over time.

One significant and often underappreciated aspect of T1DM's impact is its effect on oral health, particularly in relation to periodontal status. Research has established a bidirectional relationship between diabetes and periodontal disease [11-13], with each condition exacerbating the other. In individuals with T1DM, this relationship becomes particularly pronounced, as they are at higher risk of developing periodontal disease and experiencing more severe disease progression than non-diabetic individuals [14].

The relationship between T1DM and periodontal health is significant in pediatric populations [15], as children with T1DM face unique challenges due to the early onset of the disease and its potential impact on growth and development. The interplay between T1DM and periodontal disease in children is complex, with hyperglycemia contributing to an elevated risk of periodontal issues, while periodontal inflammation can, in turn, complicate glycemic control [15]. Understanding and managing this relationship is essential to protect children's health and quality of life with T1DM.

The objective of the study was to evaluate the periodontal health and oxidative stress levels in children diagnosed with Type I diabetes mellitus in comparison to healthy children.

Materials and Methods

This observational study evaluated indicators of periodontal health between healthy children and those diagnosed with type I diabetes mellitus (T1DM). The research was conducted following the Declaration of Helsinki, and informed consent was secured from all participants' parents or guardians prior to the study's initiation.

A total of 48 children were selected for the study and categorized into

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two groups: those classified as healthy (n=24) and those diagnosed with Type 1 Diabetes Mellitus (T1DM) (n=24). The inclusion criteria stipulated that participants must not have any systemic health conditions besides T1DM for the relevant study group, possess non-restorable teeth, fully erupted permanent teeth, and be engaged in stable orthodontic treatment. Children who had recently utilized antibiotics, anti-inflammatory medications, or other systemic medications that might impact periodontal health were excluded from participation to uphold the integrity of the results.

A comprehensive clinical examination was conducted to assess oral health thoroughly. Periodontal indices were evaluated utilizing a UNC-15 periodontal probe to measure several critical parameters: Plaque Index (PI), Probing Depth (PD), Clinical Attachment Loss (CAL), and Bleeding on Probing (BOP).

A single examiner was responsible for clinically assessing all these parameters, ensuring the measurements' consistency and accuracy. To minimize variability and guarantee adequate reproducibility, the examiner underwent a calibration procedure before the commencement of the study. Intra-examiner calibration was performed on a subset of 10% of patients, which involved duplicate measurements of PD and CAL taken 48 hours apart. An examiner was regarded as calibrated when a statistically significant correlation and a statistically insignificant difference were observed between duplicate measurements ($r = 0.85$ for PD and 0.90 for CAL).

The thiobarbituric acid reactive substances (TBARS) assay was used to assess plasma malondialdehyde (MDA) levels, a marker of lipid peroxidation and oxidative stress. Plasma was collected and prepared by isolating it from other blood components. MDA in the plasma reacts with thiobarbituric acid under acidic and high-temperature conditions, typically in a boiling water bath for a specified time. The reaction forms a pink-colored MDA-TBA complex, which indicates MDA presence. The absorbance of the MDA-TBA complex is measured at 532 nm. The intensity of the color is directly proportional to the MDA concentration. MDA levels were calculated using a standard curve expressed in micromoles per liter (µmol/L).

The assessment of plasma superoxide dismutase (SOD) activity involved a spectrophotometric assay that measures the enzyme's ability to catalyze the dismutation of superoxide radicals (O_2^-) into oxygen (O_2) and hydrogen peroxide (H_2O_2). The change in absorbance is measured at 560 nm, which reflects the inhibition of the indicator's reduction due to SOD activity. SOD activity was calculated based on the percentage of inhibition expressed in units per milliliter (U/mL). One unit of SOD activity is defined as the amount of enzyme causing a 50% inhibition in the reduction of the indicator.

The assessment of plasma glutathione peroxidase (GPx) activity was also conducted through the spectrophotometric method that measured the enzyme's ability to reduce hydrogen peroxide (H_2O_2) in the presence of reduced glutathione (GSH). The change in absorbance is measured at a specific wavelength (340 nm) over time. This change reflects the consumption of NADPH (if coupled with glutathione reductase) or the depletion of GSH, both indicators of GPx activity. GPx activity is calculated based on the rate of change in

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absorbance, expressed in units per liter (U/L), where one unit corresponds to the amount of enzyme that catalyzes the conversion of 1 µmol of substrate per minute under the assay conditions.

Results

The mean age in the Healthy Group was 12.31 years, with a standard deviation (SD) of 1.28, whereas the T1DM Group had a mean age of 11.73 years, accompanied by an SD of 1.55 (Table 1). In the Healthy Group, there were 13 male participants (54.17%) and 11 female participants (45.83%). Meanwhile, in the T1DM Group, 14 participants were male (58.33%) and ten were female (41.67%) (Table 1).

The Healthy Group consisted of 18 subjects (75.00%) hailing from urban areas and 6 (25.00%) from rural regions. Conversely, the T1DM Group included 19 participants (79.17%) from urban locations and five (20.83%) from rural areas (Table 1).

The demographic data showed a comparable distribution of age, gender, and environmental background across both groups, allowing for a balanced comparison between the healthy participants and those with Type 1 diabetes.

Table 1. Demographic data for the study groups

Parameter		Healthy Group (n=24)	T1DM Group (n=24)
Age (Mean ± Standard Deviation)		12.31±1.28 (11.8, 12.82)	11.73±1.55 (11.11, 12.35)
Gender [n, (%)]	Male	13 (54.17%)	14 (58.33%)
	Female	11 (45.83%)	10 (41.67%)
Environment [n, (%)]	Urban	18 (75.00%)	19 (79.17%)
	Rural	6 (25.00%)	5 (20.83%)

The Healthy Group demonstrated a mean Plaque Index of 0.62, accompanied by a standard deviation (SD) of 0.13, revealing no statistically significant difference when compared to the T1DM Group, which exhibited a mean Plaque Index of 0.70 ($P = 0.256$) (Table 2).

Furthermore, the mean Bleeding on Probing (BOP) score for the Healthy Group was 2.32 ± 0.33, significantly lower than that of the T1DM Group, which had a mean BOP score of 4.62 ± 0.38 ($P < 0.001$) (Table 2).

The mean Probing Depth within the Healthy Group was recorded at 1.17 mm, with an SD of 0.19, whereas the mean Probing Depth for the T1DM Group was 2.82 ± 0.61 mm. The P-value of 0.003 indicates a statistically significant difference between the two groups, with the T1DM Group exhibiting a greater probing depth (Table 2).

Similarly, the Clinical Attachment Loss (CAL) values mirrored the trend observed in Probing Depth. The Healthy Group's mean CAL was 0.31 mm, with an SD of 0.05, while the T1DM Group displayed a mean CAL of 2.10 ± 0.44 mm. The derived P-value of 0.003 indicates a statistically significant difference, indicating that the T1DM Group experienced greater clinical attachment loss (Table 2).

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Table 2. Clinical findings in the study groups

Parameter	Healthy Group (n=24)	T1DM Group (n=24)	P-Value
PI	0.62±0.13 (0.57, 0.67)	0.70±0.18 (0.63, 0.77)	0.256
BOP	2.32 ±0.33 (2.19, 2.45)	4.62 ±0.38 (4.47, 4.77)	<0.001
PD (mm)	1.17±0.19 (1.09, 1.25)	2.82±0.61 (2.58, 3.06)	0.003
CAL (mm)	0.31±0.05 (0.29, 0.33)	2.10±0.44 (1.92, 2.28)	0.003

Values are expressed as Mean ± Standard Deviation, (Confidence Interval set at 95%); BMI: Body Mass Index; PI: Plaque Index; BOP: Bleeding on Probing Index; PD: Probing Depth; CAL: Clinical Attachment Loss

The Healthy Group exhibited a mean MDA level of 0.75 µmol/L with a standard deviation (SD) of 0.07. In contrast, the T1DM Group demonstrated a significantly elevated mean MDA level of 3.56 µmol/L, accompanied by an SD of 0.22. The P-value for this comparison was less than 0.001, indicating a statistically significant difference between the two groups, with the T1DM Group presenting higher MDA levels. This elevation implies an increase in oxidative stress among children diagnosed with T1DM (Table 3).

Table 3. Paraclinical findings in the study groups

Parameter	Healthy Group (n=24)	T1DM Group (n=24)	P-Value
MDA (µmol/L)	0.75±0.07 (0.72, 0.78)	3.56±0.22 (3.47, 3.65)	<0.001
SOD (U/mL)	173.21±32.12 (160.36, 186.06)	82±11.30 (77.48, 86.52)	<0.001
GPx (U/L)	380.33±39.53 (364.51, 396.15)	160±23.19 (150.72, 169.28)	<0.001

Values are expressed as Mean ± Standard Deviation, (Confidence Interval set at 95%); MDA: malondialdehyde; SOD: superoxide dismutase; GPx: glutathione peroxidase

Furthermore, the Healthy Group displayed a mean SOD activity of 173.21 U/mL with an SD of 32.12, whereas the T1DM Group recorded a reduced mean SOD activity of 82 U/mL, with an SD of 11.30. The P-value here was also less than 0.001, signifying a statistically significant decrease in SOD activity within the T1DM Group. This reduction indicates a compromised antioxidant defense capacity in children living with T1DM (Table 3).

In terms of GPx activity, the Healthy Group had a mean value of 380.33 U/L and an SD of 39.53. The T1DM Group, however, presented a substantially lower mean GPx activity of 160 U/L, accompanied by an SD of 23.19. The P-value was found to be less than 0.001, illustrating a statistically significant difference, with the T1DM Group exhibiting lower GPx levels. This decline in GPx activity suggests an impaired capability to mitigate oxidative stress among children with T1DM (Table 3).

Discussion

The association between periodontal disease and Type 1 diabetes

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mellitus in pediatric populations has increasingly been acknowledged as bidirectional, wherein each condition can aggravate the other [16]. Periodontal disease, fundamentally an inflammatory response to bacterial infection of the periodontal tissues, is influenced by numerous factors, including systemic conditions such as diabetes mellitus [17]. In pediatric patients with Type 1 diabetes, this interrelationship assumes even greater significance given the combined challenges posed by hormonal and immunological alterations during growth.

One of the principal connections between Type 1 diabetes and periodontal disease is inflammation. Elevated blood glucose levels associated with diabetes result in the increased production of inflammatory mediators [18], thereby rendering children more vulnerable to infections, including those impacting the periodontal tissues. Research indicates that diabetic children frequently display elevated levels of gingival inflammation and plaque accumulation [19], which are precursors to periodontal disease. The hyperglycemia characteristic of diabetes cultivates an optimal environment for detrimental oral bacteria to proliferate, thereby expediting the progression of periodontal disease.

Conversely, periodontal inflammation can make blood sugar management more difficult for children with diabetes [15]. Infections, including those of the periodontal tissues, can exacerbate insulin resistance, leading to increased blood glucose levels. This cyclical effect highlights the importance of oral health in managing diabetes effectively. For children, poor glycemic control due to unmanaged periodontal infections may result in more complications over time, such as delayed growth, increased susceptibility to other diseases [20], and complications in dental development.

The demographic data in our study indicate a well-matched distribution of age, gender, and environmental background between the Healthy and T1DM groups. Both groups have similar proportions of urban and rural residents and comparable male-to-female ratios, supporting that the observed clinical and paraclinical differences are likely attributed to T1DM rather than demographic variables. This controlled demographic background enhances the reliability of the comparisons made between groups.

Our results revealed significant differences in several clinical periodontal parameters between the two groups. Children with T1DM exhibit higher values in Bleeding on Probing (BOP), Probing Depth (PD), and Clinical Attachment Loss (CAL), each with a P-value indicating strong statistical significance. These findings align with current literature [21], which suggests that individuals with T1DM are at an elevated risk of periodontal disease due to hyperglycemia-induced inflammatory responses. Elevated blood glucose levels in T1DM lead to the accumulation of advanced glycation end-products (AGEs), triggering an increased inflammatory response and making periodontal tissues more susceptible to bacterial colonization and infection [14].

Interestingly, while the Plaque Index (PI) does not show a statistically significant difference, the BOP, PD, and CAL measures do. This suggests that the periodontal challenges in children with T1DM are not merely due to increased

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plaque accumulation but are likely a result of systemic metabolic factors that affect the periodontium independently of plaque levels. These results highlight the need for enhanced periodontal care in children with T1DM, focusing on reducing inflammation and managing the unique periodontal complications associated with diabetes.

The paraclinical results indicate a significant imbalance in oxidative stress markers between the Healthy and T1DM groups. Children with T1DM show elevated malondialdehyde (MDA) levels alongside reduced superoxide dismutase (SOD) and glutathione peroxidase (GPx) activities, each with p-values below 0.001. Similarly, Grabia et al. [22] documented that the Type 1 Diabetes Mellitus (T1DM) group exhibited elevated Total Oxidative Status (TOS) compared to healthy controls. Furthermore, Aral et al. [23] conducted an examination of salivary TOS in T1DM patients at the time of diagnosis in comparison to systemically healthy children both with gingivitis (G) and those without gingivitis (H). Their findings revealed that salivary TOS was significantly greater in the T1DM group than in the H group. This pattern suggests an increase in oxidative stress, as evidenced by higher MDA, a marker of lipid peroxidation, coupled with a diminished antioxidant defense system, as seen in the reduced levels of SOD and GPx.

This oxidative stress imbalance is a hallmark of T1DM and has implications for both systemic and periodontal health. Chronic hyperglycemia in T1DM patients enhances the production of reactive oxygen species (ROS) [24], which, combined with lower antioxidant enzyme activities, creates a pro-oxidative state. This environment can exacerbate inflammation and tissue damage, particularly in periodontal tissues. The low SOD and GPx levels suggest that children with T1DM have a compromised ability to counteract oxidative stress, further elevating the risk of periodontal disease and systemic complications. These findings underscore the potential benefit of antioxidant support in T1DM management to mitigate oxidative damage.

The combined clinical and paraclinical findings suggest a synergistic effect of T1DM on both periodontal and systemic oxidative stress levels. The elevated BOP, PD, and CAL scores observed in T1DM children are consistent with the oxidative stress markers, as high oxidative stress can exacerbate periodontal inflammation and tissue breakdown. The imbalance in MDA, SOD, and GPx levels in T1DM children may contribute to this inflammatory state, making periodontal tissues more susceptible to disease progression and exacerbating systemic inflammation that hinders glycemic control.

The results emphasize the importance of addressing oxidative stress as part of periodontal and diabetes management in children with T1DM. Clinical protocols could benefit from integrating antioxidant therapies or dietary modifications to support antioxidant capacity [25, 26]. In addition, these children may require more frequent periodontal assessments and targeted interventions to manage the systemic effects of hyperglycemia on periodontal tissues.

Nevertheless, our study presents a series of limitations. The study included only 24 children in each group, which may limit the generalizability of the findings. A larger, more diverse sample size could provide a broader understanding of the relationship between T1DM and

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periodontal health across different pediatric populations. Moreover, the study primarily assesses associations rather than intervention effects. Exploring the impact of targeted periodontal treatments or antioxidant supplementation on oxidative stress and periodontal health in T1DM patients would add practical implications to the findings.

These findings call for a multidisciplinary approach to managing T1DM in pediatric patients, integrating endocrinological, dental, and nutritional support. Regular periodontal assessments should be considered a standard part of care for children with T1DM to monitor and address early signs of periodontal disease. From a research perspective, further studies could explore the efficacy of antioxidant supplementation and glycemic control strategies targeted explicitly at reducing periodontal inflammation and oxidative stress in T1DM.

Management of periodontal health is essential for improving glycemic control in children with Type 1 diabetes. Preventive dental care, regular dental check-ups, and good oral hygiene practices should be integrated into diabetes management plans. Encouraging these children and their caregivers to adopt stringent oral health habits can minimize inflammation, reduce the bacterial load in the mouth, and help stabilize blood glucose levels, ultimately leading to a better quality of life and reducing the risk of long-term complications.

Conclusions

This research underscores the correlation between type 1 diabetes mellitus (T1DM), periodontal health, and oxidative stress. It indicates that children diagnosed with T1DM experience an elevated risk of periodontal complications as a result of heightened oxidative stress and inflammatory responses. By addressing both periodontal challenges and systemic oxidative factors within diabetes management, it is possible to improve health outcomes and the overall quality of life for children suffering from T1DM.

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