

Association Between Dental Caries and Oxidative Stress Parameters in Children

Çocuklarda Diş Çürüğü ile Oksidatif Stres Parametreleri Arasındaki İlişki

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Abstract

Background: The body's oxidant/antioxidant balance and oxidative stress can impact or change dental caries. The main aim of this study was to investigate the association between dental caries and total oxidant status (TOS), total antioxidant status (TAS), and oxidative stress index (OSI).

Materials and Methods: This study was designed in two groups including the control group (DMFS/dfs =0) and the case group with dental caries (DMFS/dfs \geq 5). The number of samples in this study includes 94 children, including 42 healthy children and 52 children with dental caries. Unstimulated saliva samples were gathered from all children mid-morning. Participants' saliva samples were obtained by requesting them to spit for 5 min. Then, the specimens were frozen and preserved at a temperature of four °C before being maintained at -80°C until further examination.

Results: Children's mean age and mean weight were 6.55 \pm 3.52 years and 20.51 \pm 9.67 kg, respectively. There was no significant difference between the case and control groups regarding total oxidant status ($p < 0.01$). There was a significant difference between case and control groups in terms of oxidative stress index ($p < 0.01$).

Conclusions: The TOS and OSI were significantly higher in the case group. The TOS and OSI can be employed as markers of oxidative stress caused by dental caries.

Keywords: Dental caries, Total oxidant status, Total antioxidant status, Oxidative stress index

Öz

Amaç: Vücudun oksidan/antioksidan dengesi ve oksidatif stres, diş çürüğünü etkileyebilir veya değiştirebilir. Bu çalışmanın temel amacı, diş çürüğü ile toplam oksidan durumu (TOS), toplam antioksidan durumu (TAS) ve oksidatif stres indeksi (OSI) arasındaki ilişkiyi araştırmaktır.

Materyal ve metod: Bu çalışma, kontrol grubu (DMFS/dfs = 0) ve diş çürüğü olan vaka grubu (DMFS/dfs \geq 5) olmak üzere iki grup halinde tasarlanmıştır. Bu çalışmadaki örnek sayısı, 42 sağlıklı çocuk ve 52 diş çürüğü olan çocuk olmak üzere toplam 94 çocuğu kapsamaktadır. Tüm çocuklardan sabah ortasında uyarılmamış tükürük örnekleri alınmıştır. Katılımcılardan 5 dakika boyunca tükürmeleri istenerek tükürük örnekleri alınmıştır. Daha sonra örnekler dondurulmuş ve 4°C sıcaklıkta muhafaza edilmiş, daha sonra -80 °C'de daha sonraki incelemeye kadar saklanmıştır.

Bulgular: Çocukların ortalama yaşı ve ortalama ağırlığı sırasıyla 6,55 \pm 3,52 yıl ve 20,51 \pm 9,67 kg idi. Vaka ve kontrol grupları arasında toplam oksidan durumu açısından anlamlı bir ilişki bulunmadı ($p < 0,01$). Oksidatif stres indeksi açısından vaka ve kontrol grupları arasında anlamlı bir ilişki vardı ($p < 0,01$).

Sonuç: TOS ve OSI, vaka grubunda anlamlı derecede daha yüksekti. TOS ve OSI, diş çürüğünün neden olduğu oksidatif stresin belirteçleri olarak kullanılabilir.

Anahtar Kelimeler: Diş çürüğü, Toplam oksidan durumu, Toplam antioksidan durumu, Oksidatif stres indeksi

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Introduction

Dental caries is a chronic disease, common among children. The World Health Organization (WHO) has recognized it as a global problem with a prevalence of 60%-90% among school-age children (1). In this disease, hard dental tissue, such as enamel, loses calcium and phosphorus minerals, and treatment generally involves restoration of the lost dental hard tissue using restorative materials (2).

Dental caries is a multifactorial disease in which the major contributing factors include the host (tooth structure and saliva), cariogenic microorganisms, dietary habits, and time. These factors collectively influence the initiation and progression of carious lesions. Recent studies have suggested that dental caries may disrupt the balance between reactive oxygen species (ROS) and antioxidant defense mechanisms, leading to increased oxidative stress and free radical production. Oxidative stress resulting from an imbalance between oxidants and antioxidants has been implicated in several oral inflammatory conditions (3). Excessive reactive oxygen species production may damage dental pulp cells through lipid peroxidation, mitochondrial dysfunction, and inflammatory signaling pathways, leading to impaired odontoblast function and altered mineral metabolism. Disruption of trace element homeostasis may further affect hydroxyapatite stability and dentin mineralization, thereby weakening the structural integrity of hard dental tissues (4,5). In addition, dental caries and its associated symptoms may negatively affect the physical, psychological, and social well-being of children.

Antioxidants play an important protective role by reducing the harmful effects of ROS and free radicals in the human body (6). The salivary antioxidant defense system consists of several enzymatic and non-enzymatic components, including salivary peroxidase, uric acid, glutathione peroxidase, catalase, superoxide dismutase, vitamins C, E, and A, melatonin, and glutathione (8,9). Total antioxidant status (TAS) reflects the overall antioxidant capacity of biological fluids such as saliva and serum and is considered an important indicator of antioxidant defense (7).

ROS-related tissue damage occurs through oxidative modification of cellular and extracellular macromolecules, including lipids, proteins, and DNA. When antioxidant defense mechanisms become insufficient, excessive ROS accumulation may damage healthy cells, impair immune function, and increase susceptibility to infection (3–8). Therefore, several biomarkers, including total oxidant status (TOS), total antioxidant status (TAS), and oxidative stress index (OSI), have been used to evaluate oxidative stress in biological samples (10). Among oxidative stress assessment methods, measurements of lipid peroxidation products in body

fluids such as saliva and serum are among the most commonly used approaches (11,12).

The analysis of blood is of great importance in diagnosing the disease and evaluating the treatment process. Likewise, saliva analysis is also important in forensic medicine follow-up and diagnosis of systemic and local conditions (13). Salivary biomarkers have been recognized for their role in the early diagnosis of some systemic disorders, such as chronic kidney disease, chronic heart failure, psoriasis, neurodegenerative diseases. Salivary biomarkers can also be used for the diagnosis of periodontitis and oral cancers (14). Changes in FRs, reactive oxygen products, and antioxidant levels in saliva are claimed to be effective in the initiation and progression of tooth decay. The values of these factors in the saliva may be useful in determining an individual's caries risk (15). The present study aimed to evaluate the association between dental caries and salivary oxidative stress parameters, including TAS, TOS, and OSI, and to assess their potential utility as biomarkers of oxidative stress in children with dental caries.

Materials and Methods

Ethical Approval

Ethical approval for the study was obtained from the Ethics Committee of Harran University Faculty of Medicine (approval no: 18/12/05, date: December 10, 2018). Written informed consent was obtained from the parents or legal guardians of all participants prior to their inclusion in the study. All procedures performed in this study were conducted in accordance with the ethical standards of the institutional ethics committee and the principles of the Declaration of Helsinki.

Study Population

The study was conducted between December 1, 2018, and May 1, 2019, at Harran University, with a total of 94 participants (number of boys=44 and number of girls=50). The patient's age in the study varied from 1 to 15.83 years. The study included children in the mixed dentition period; therefore, both primary (dmfs/dfs) and permanent (DMFS/DFS) caries indices were recorded according to age. Participants were categorized based on their clinical dentition status, and caries assessment was performed accordingly.

Study Design

Participants were divided into two groups according to their caries status:

- Control group: children without dental caries (dmfs/DMFS = 0) (N:42)
- Caries group: children with dental caries (dmfs/DMFS ≥5)

(N:52)

Because the study population included children at different dentition stages, both primary and permanent dentition indices were evaluated according to age and clinical dentition status.

The sample size was estimated according to previous studies investigating oxidative stress markers in oral diseases. Considering an alpha error of 0.05, statistical power of 80%, and moderate effect size, the minimum required sample size was calculated as 84 participants. To compensate for possible sample loss, 94 children were included.

Exclusion criteria were as follows:

- Acute periodontal or apical infections
- Periodontal disease
- Autoimmune diseases
- Diabetes mellitus
- Neurodegenerative disorders
- Other systemic inflammatory diseases

Clinical Examination

All oral examinations were performed by an experienced pediatric dentist using a dental mirror and explorer under standard clinical conditions. Dental caries were diagnosed according to WHO diagnostic criteria. Radiographic examination was not routinely performed.

Saliva Collection and Biochemical Analysis

Unstimulated whole saliva samples were collected between 09:00 and 11:00 a.m. to minimize circadian variation. Participants were instructed not to eat, drink, or brush their teeth for at least 1 hour before saliva collection.

Saliva samples were collected by passive drooling/spitting into sterile tubes over a 5-minute period while the participants were

seated comfortably. Samples were immediately transferred on ice to the laboratory and centrifuged at 3000 rpm for 10 minutes to remove cellular debris. Supernatants were initially stored at 4°C for short-term preservation and then kept at -80°C until biochemical analysis.

Total antioxidant status (TAS) and total oxidant status (TOS) levels were measured using automated colorimetric methods developed by Erel. Oxidative stress index (OSI) values were calculated as the ratio of TOS to TAS.

Statistical Analysis

Statistical analyses were performed using NCSS 2007 software (Kaysville, Utah, USA). Data distribution was evaluated using the Shapiro-Wilk test and graphical methods. Normally distributed variables were compared using Student's t-test, whereas non-normally distributed variables were analyzed using the Mann-Whitney U test. Categorical variables were compared using the Pearson chi-square test. Pearson or Spearman correlation analyses were used according to data distribution. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the predictive performance of TOS and OSI parameters. A p value <0.05 was considered statistically significant.

Results

A total of 94 children participated in this study, of which 53.2% (n=50) were girls and 46.8% (n=44) were boys. The ages of the patients participating in the study ranged between 1 and 15.83 years, and the mean age was 6.55±3.52 years. The weight of the participants ranged between 9.5-60 kg, and the mean weight was 20.51±9.67 kg. Their height ranged from 76-161 cm, with an average of 110.46±19.9 cm. The body mass index (BMI) measurements ranged from 10.03-23.15 kg/m², with an average of 16.10±2.56 kg/m². The demographic features of the children are shown in Table 1.

Table 1. Evaluation of demographic features by groups

		Group			Test value
		Total	Patient (n=52)	Control (n=42)	p
Age	Min-max (Median)	1-15.83 (5.42)	2.08-15.83 (5.58)	1-15.17 (4.96)	Z:-0.753
	Mean± SD	6.55±3.52	6.48±2.90	6.64±4.19	a0.451
Gender	Woman	50 (53.2)	26 (52.0)	24 (48.0)	χ ² :0.476
	Man	44 (46.8)	26 (59.1)	18 (40.9)	b0.490
Weight (kg)	Min-Max (Median)	9.5-60 (17.5)	11-60 (18)	9.5-43 (16.6)	Z:-0,696
	Mean ± SD	20.51±9.67	20.37±9.22	20.69±10.32	a0.486

Length (cm)	Min-Max (Median)	76-161 (109.5)	76-161 (111)	78-156 (104.5)	Z:-1.191
	Mean \pm SD	110.46 \pm 19.9	111.4 \pm 17.5	109.29 \pm 22.69	a0.234
BMI (kg/m ²)	Min-Max (Median)	10.03-23.15 (15.65)	10.03-23.15 (15.17)	12.25-22.72 (16.17)	t:-0.962
	Mean \pm SD	16.10 \pm 2.56	15.88 \pm 2.87	16.37 \pm 2.13	c0.339

^aMann Whitney U Test, ^bPearson Chi-Square Test, ^cStudent-t Test, SD: Standard deviation, Min: Minimum, Max: Maximum, BMI>: Body Mass Index

No statistically noteworthy distinction was observed in terms of age and gender distribution, weight, height, and BMI of the

subjects of the two the groups ($p>0.05$). The distribution of tooth decay among the subjects is presented in Table 2.

Number of teeth decay (n=52)	Min-Max (Median)	1-9 (4)
	Mean \pm SD	4.23 \pm 2.05
Number of missing teeth (n=52)	No	9 (17.3)
	1 Tooth	7 (13.5)
	2 Teeth	32 (61.5)
	3 Teeth	2 (3.8)
	4 Teeth	2 (3.8)
	Min-Max (Median)	0-4 (2)
	Mean \pm SD	1.63 \pm 0.95
Number of filled teeth (n=52)	No	7 (13.5)
	1 Tooth	7 (13.5)
	2 Teeth	37 (71.2)
	3 Teeth	1 (1.9)
	Min-Max (Median)	0-3 (2)
	Mean \pm SD	1.62 \pm 0.75
DMFT Index (n=52)	Min-Max (Median)	0.05-0.35 (0.18)
	Mean \pm SD	0.19 \pm 0.07
Tooth decay number group (n=94)	1	23 (44.23)
	2	16 (30.77)
	3	13 (25)

SD: Standard deviation

The decayed teeth number of patient group cases participating in the study ranged from 1 to 9 with an average of 4.23 \pm 2.05. The number of missing teeth was 1 in 13.5% of patients (n=7), 2 in 61.5% (n=32), 3 in 3.8% (n=2), and 4 in 3.8% (n=2), while

no missing teeth were found in 17.3% (n=9) of patients. The number of missing teeth in the participants ranged from 0 to 4, with an average of 1.63 \pm 0.95. Of the patients, 13.5% (n=7) had one restored tooth, 71.2% had two, and 1.9% (n = 1) had

three, while 13.5% of the subjects had no restored teeth ($n=7$). The number of filled teeth in the cases ranged from 0 to 3, with an average of 1.62 ± 0.75 . DMFS/dfs index measurements of the patient group ranged in the interval of 5-9.96, and the mean was 7.48 ± 0.07 . While one decayed tooth was observed in 44.23% ($n = 23$) of the cases, two decayed teeth in 30.77% ($n = 16$), and three decayed teeth in 25% ($n = 13$).

Upon conducting the assessments, a cut-off point of ≥ 10.59 was determined for the TOS. For TOS ≥ 10.59 , the sensitivity was 84.62%, specificity was 50%, the positive predictive value was 67.7%, and the negative predictive value was 72.4%. In the receiver operating characteristic (ROC) curve obtained for TOS, the area under the curve was 67.4% and the standard error was 5.6% (Table 3, Figure 1).

Table 3. Diagnostic screening tests and ROC curve results for TOS and OSI by groups

	Diagnostic scan					ROC curve		p
	Cut-off	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Area	95% confidence interval	
TOS	≥ 10.59	84.62	50	67.7	72.4	0.674	0.564-0.785	0.004**
OSI	≥ 8.70	84.62	50	67.7	72.4	0.661	0.547-0.774	0.008**

TOS: Total oxidant status, OSI: Oxidative stress index, ** $p<0.01$

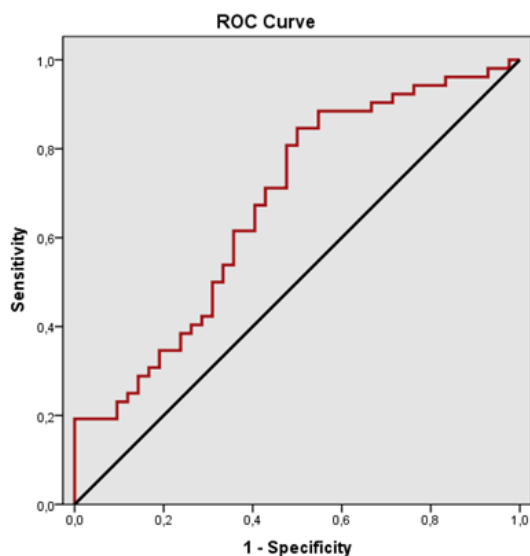


Figure 1. ROC Curve for TOS by Groups

Upon conducting the assessments, a cut-off point of ≥ 8.7 was determined for the OSI. For OSI ≥ 8.7 , the specificity, sensitivity, positive predictive value, and negative predictive value were 50%, 84.62%, 67.7%, and 72.4%, respectively. In the ROC curve obtained for OSI, the area under the curve was 66.1% and the standard error was 5.8% (Table 3, Figure 2).

The TAS values ranged from 0.07 to 2.08, with an average of 1.22 ± 0.30 . TOS measurements ranged from 2.36 to 59.72, with an average of 16.47 ± 10.64 , while OSI measurements ranged

from 2.22 ± 53.53 , with an average of 14.26 ± 9.55 . The values of the evaluated TAS, TOS, and OSI are shown in Table 4. No statistically discernible difference was found between the TAS of both groups ($p>0.05$). The TOS and OSI of the patient group was significantly higher than that of the control group ($p<0.01$). There was no discernible relationship between the DMFS/dfs index and the TAS, TOS, and OSI ($p>0.05$) (Table 5).

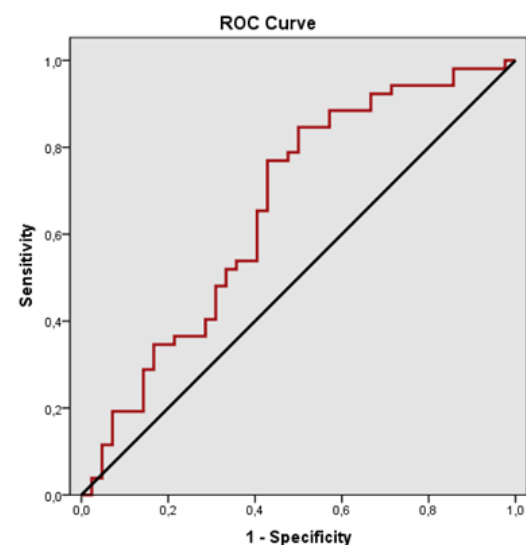


Figure 2. ROC Curve for OSI by Groups

		Group			Test Value
		Total	Patient (n=52)	Control (n=42)	p
TAS	Min-Max (Median)	0.07-2.08 (1.25)	0.64-2.08 (1.23)	0.07-1.65 (1.28)	t:0.287
	Mean±SD	1.22±0.30	1.23±0.27	1.21±0.34	^c 0.775
TOS	Min-Max (Median)	2.36-59.72 (14.98)	3.15-59.72 (15.93)	2.36-28.87 (10.62)	Z:-2.898
	Mean±SD	16.47±10.64	19.36±12.24	12.90±6.83	^a 0.004**
OSI	Min-Max (Median)	2.22-53.53 (11.57)	3.44-47.66 (12.31)	2.22-53.53 (8.93)	Z:-2.669
	Mean±SD	14.26±9.55	15.86±9.34	12.29±9.56	^a 0.008**
^a Mann Whitney U Test		^c Student-t Test			**p<0.01

	DMFT Index	
	r	p
TAS	0.114 ^d	0.420
TOS	0.197 ^e	0.161
OSI	0.176 ^e	0.211
^d r=Pearson Correlation Coefficient ^e r=Spearman's Correlation Coefficient		

Discussion

Dental caries is a common, chronic, yet preventable, oral disease prevalent in childhood. When there is a disparity or imbalance between the quantities of ROS and antioxidants, oxidative stress manifests (16). Numerous studies have reported the involvement of oxidative stress in the pathogenesis of various diseases. ROS can damage tissues by damaging lipids, DNA, enzymes, and proteins, and its reaction with lipids leads to lipid peroxidation (17). This process can affect the pathology of many diseases, including that of oral diseases.

To assess the presence of oxidative stress, this study measured TAS, TOS, and OSI as biomarkers in the saliva samples of children with and without dental caries. According to the study results, children suffering from dental caries demonstrated significantly higher TOS and OSI levels in comparison to the control group. However, there was no significant difference between the TAS of children with dental caries and the control group. Contrary to our findings, other studies have shown that children with dental caries have higher TAS than healthy children (1,3,12,18,19). Ahmadi –Motamayel et al. investigated the TAS of saliva and its relationship to dental caries. They stated that the level of TAS

in the saliva of the active caries group was significantly higher than in those without caries (20). In this study, we excluded all children with systemic diseases and periodontitis to examine only the effect of dental caries on the participants' antioxidant levels. At the end of the study, although there was no difference in the TAS values between the groups, significant differences were found in the TOS and OSI.

Zieniewska et al. had indicated that apart from oral cavity diseases, dental treatments can also cause oxidative stress. The report highlights that sources of ROS in the oral cavity, as identified by the authors, encompass filling materials such as glass ionomer materials, amalgam and composites, bonding systems, materials used in endodontic treatment, surgical and periodontal methods, and orthodontic treatment fabrics (21).

Araujo et al. determined that the total protein, total antioxidant capacity, superoxide dismutase (enzymatic antioxidant activity), and uric acid (non-enzymatic antioxidant activity) levels increased with caries severity. They stated that the severity of caries is directly related to the total antioxidant capacity of the saliva (22).

Kamodyová et al. reported that tooth brushing and intake of vitamin C increased the antioxidant levels in the saliva (23). In

our study, the OSI and TOS were found to be low in children with good oral hygiene.

OSI is a novel parameter that indicates the level of systemic diseases (24). This parameter is usually based on the measurement of the body's oxidant and antioxidant imbalance. In this study, the OSI values were different between two groups. The OSI and TOS levels were significantly higher for the study group. Therefore, the measurement of OSI can be employed as a reliable indicator of oxidative stress, and TOS can be used as a direct measure of oxidative stress. Various studies have shown that TOS can play a useful role in predicting oxidative stress (24-26). These findings are consistent with our results; therefore, TOS can also be used to effectively predict oxidative stress.

The findings indicated that there was no significant relationship observed between the measurements of dmft index and the TAS, TOS, and OSI measurements. Therefore, it can be concluded that there is no significant relationship between dmft and the oxidative stress status of individuals. In our study, OSI, in addition to more accurately representing oxidative stress than other parameters, more clearly indicated the relationship between excitatory stress and periodontal status. Studies have shown that by eliminating infection and preventing caries and periodontitis, the values of OSI, TOS, and TAS can be significantly reduced (27,28).

Oxidative stress recreates an essential function in the pathogenesis of many diseases, and underlying diseases such as diabetes, systemic diseases, smoking, and pregnancy can contribute to oxidative stress. In our study, patients with underlying diseases were excluded from the study to investigate only the effect of tooth decay on the parameters of oxidative stress. The oral hygiene index was not measured in our study. Other studies have shown that the oral hygiene index can affect the TAS and TOS (29-31). Many other common and complex factors, such as diet, smoking, level of physical activity, and levels of antioxidants, can also affect the levels of oxidative stress. However, it has not been determined exactly if dental caries increase oxidative stress values or whether oxidative stress values trigger dental caries. Longitudinal studies are needed on this subject.

Conclusion

Our results showed that the parameters of TOS and OSI were significantly higher in the group of patients with dental caries.

OSI and TOS can be used as markers of oxidative stress caused by dental caries. The TAS showed no discernible differences between the two groups. Further investigations are warranted to explore the impacts of dental caries on oxidative stress levels in more detail.

Ethical Approval: Ethical approval for the study was obtained from the Ethics Committee of Harran University Faculty of Medicine (approval no: 18/12/05, date: December 10, 2018).

Author Contributions:

Concept: M.D., M.S.D.

Design: M.D., M.S.D.

Data Collection or Processing: M.D., A.G., A.K.

Analysis or Interpretation: M.S.D., M.D., A.G., A.S., A.D., A.K.

Literature Search: A.G., M.D., A.K., A.D., E.Ç., M.S.D.

Writing: A.G., M.D., A.K., A.D., E.Ç., M.S.D.

Critical Review: A.G., M.D., A.K., A.D., E.Ç., M.S.D.

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