Received: September 21, 2026
Accepted: November 4, 2026
Published: November 27, 2026

Acad Med J 2026;6(3):128-137
UDC:616.316-008.82:616.314-002
Original article

CORRELATION BETWEEN DMFT INDEX, SALIVARY FLOW RATE, SALIVARY PH, SALIVARY UREA, AND URIC ACID IN CARIES-ACTIVE AND CARIES-RESISTANT 12-YEAR-OLD CHILDREN

Gavriloska Petrovikj Verica[1], Jankulovska Mira[2], Ivanovski Kiro[3], Poposki Bojan[3], Pavlevska Meri[2], Zabokova Bilbilova Efka[2], Mladenovski Marko[4], Saveski Mirko[5], Maqellara Albert[6]

[1]PHO University Dental Clinic "St. Panteleimon", Department of Pediatric and Preventive Dentistry – Skopje, Republic of North Macedonia
[2]Faculty of Dentistry, Department of Pediatric and Preventive Dentistry, Ss. Cyril and Methodius University in Skopje, Republic of North Macedonia
[3]Faculty of Dentistry, Department of Oral and Periodontal diseases, Ss. Cyril and Methodius University in Skopje, Republic of North Macedonia
[4]PHO University Dental Clinic "St. Panteleimon", Department of Oral Pathology and Periodontology – Skopje, Republic of North Macedonia
[5]Faculty of Dentistry, Department of Restorative Dentistry and Endodontics, Ss. Cyril and Methodius University in Skopje, Republic of North Macedonia
[6]PHI General Hospital Extended Activity in Debar, Republic of North Macedonia
e-mail: dr.vericagavriloska@gmail.com

Abstract

Introduction: Saliva, as a biological fluid within the oral cavity, plays an important role in maintaining oral and general health. It is increasingly recognized as a non-invasive diagnostic medium for the detection of various oral and systemic diseases.

Objective: The aim of this study was to compare salivary flow rate, pH, urea, and uric acid levels between two study groups and to evaluate their association with the prevalence of dental caries.

Materials and methods: The study included 60 subjects of both sexes, aged 12 years, divided into a caries-active (CA) group and a caries-resistant (CR) group according to their DMFT index values. The DMFT index was determined for each subject, saliva samples were collected, and salivary flow rate, pH, urea, and uric acid levels were analyzed.

Results: A statistically significant difference in DMFT index values was found between the two groups. Salivary flow rate did not differ significantly between the groups, whereas salivary pH was significantly higher in the CR group. Salivary uric acid concentration was significantly lower in CA subjects. Higher salivary urea concentrations were observed in CR subjects. In addition, a significant negative correlation was found between salivary flow rate and the DMFT index.

Conclusion: The findings suggest that salivary parameters may play an important role in caries resistance. Higher salivary pH and urea concentrations may contribute to protection against dental caries, while the negative correlation between salivary flow rate and DMFT supports the protective role of salivary secretion in maintaining oral health.

Keywords: DMFT index, dental caries, salivary flow rate, salivary pH, salivary urea, uric acid

Introduction

Maintaining health has always been one of the fundamental responsibilities of every individual and society. Historically, health was viewed primarily from the perspective of diseases, while issues related to health maintenance were considered merely within the domain of healthcare. Health promotion represents a concept in which health is created through political and social processes in order to achieve the social, mental, and physical well-being of people[1].

Oral health is an integral part of general health and can significantly impact the quality of life. Good oral health encompasses much more than just healthy teeth; it is an integral part of overall health, and thus becomes essential for a good quality of life. Improvements in oral health are accompanied by increased public awareness, as well as enhanced knowledge and more positive attitudes toward oral health among both children and their parents.

From a socioeconomic perspective, the preservation and promotion of oral health would result in considerable savings of financial resources that would otherwise be spent on dental treatments, prosthetic rehabilitation, hospital and spa treatments, absence from work, and related healthcare costs. Furthermore, the psychological aspect should also be considered, since poor oral health, especially among young people, may lead to feelings of insecurity and lower self-esteem[2-4].

Dental caries is a multifactorial disease affecting the hard dental tissues which, if left untreated, progressively compromises the structure and function of the teeth, ultimately resulting in their loss. Approximately 98% of the population in Europe is affected by dental caries, making it one of the most widespread chronic diseases in industrialized countries. The increasing prevalence of dental caries among children is particularly concerning. Over 40% of five-year-old children in developed countries already present with dental caries, while the prevalence is even higher in developing countries, resulting in long-term consequences for both oral and general health throughout life[5].

The World Health Organization (WHO) has reported that 60 to 90% of schoolchildren and nearly 100% of adults worldwide are affected by dental caries. Consequently, the prevention of dental caries plays a pivotal role in the promotion of public health[6].

Dental caries develops as a consequence of an imbalance between the processes of demineralization and remineralization taking place on the tooth surface. The development and progression of dental caries are influenced by numerous factors, including inadequate oral hygiene, tooth anatomy and morphology, dental status, dietary composition and food consistency, salivary flow rate and physicochemical characteristics, dental restorations, fluoride concentration in the enamel, medication use, and many other factors[7].

Recent research has highlighted the numerous biological functions of saliva mediated by its inorganic and organic components, which may be associated with the role of saliva in the etiology of dental caries. Some of these studies have introduced new perspectives on dental caries, emphasizing its nature as a bacterially-induced multifactorial disease[8].

The salivary glands are exocrine organs responsible for the production and secretion of saliva. They are classified according to their size, anatomical location, and histological structure. Both the quantity and quality of secreted saliva depend on the condition of the oral cavity, the functional status of the primary salivatory center, and the activity of specific regions of the cerebral cortex[9].

Reduced salivary flow rate, decreased salivary buffering capacity, and increased levels of *Streptococcus mutans* and *Lactobacillus* spp. in saliva are commonly associated with higher caries incidence and prevalence. When salivary secretion decreases below a critical threshold, the risk of dental caries increases dramatically. Dry mouth, or xerostomia, may occur as a result of salivary gland dysfunction, systemic conditions, the use of certain medications, radiotherapy, and the physiological aging process.

Xerostomia is diagnosed when the unstimulated salivary flow rate is less than 0.1-0.2 mL/min and the stimulated salivary flow rate is below 0.4–0.7 mL/min. In severe cases of xerostomia, saliva shows a low pH value and reduced buffering capacity. In addition, the concentrations of MUC5B and MUC7 mucins (high- and low-molecular-weight mucins) are also reduced[9].

Saliva contains specific buffering systems, such as bicarbonate, phosphate, and protein buffer systems, which not only provide buffering capacity but also create favorable conditions for the elimination of certain bacterial species that require a highly acidic environment to survive. The bicarbonate buffering system is primarily active under conditions of increased salivary flow, whereas the phosphate buffering system predominates when salivary flow is reduced. When salivary pH is higher than 6.0, saliva is supersaturated with phosphate ions. Conversely, when salivary pH falls below the critical value of 5.5, hydroxyapatite undergoes dissolution, releasing phosphate ions that attempt to restore the pH balance. Ultimately, this process depends on the concentrations of phosphate and calcium ions in the surrounding environment. The oral cavity is often exposed to foods and beverages with a lower pH value than that of saliva, under which circumstances the salivary buffering systems are activated to restore physiological pH as quickly as possible. A low salivary buffering capacity represents an important risk factor for dental caries, as it promotes demineralization and is indicative of reduced salivary secretion. Salivary proteins participate in the formation of the acquired enamel pellicle, to which oral bacteria adhere, thereby contributing to the demineralization process and creating favorable conditions for the development of dental caries. Furthermore, the formation of functional heterogeneous complexes among salivary molecules-including high-molecular-weight mucins, α-amylase, histatin-1, proline-rich proteins (PRPs), and statherin-is associated with dental plaque formation, which in turn represents one of the principal etiological factors involved in the initiation of dental caries[10].

Aim

The aim of the present study was to compare salivary flow rate, salivary pH, salivary urea concentration, and salivary uric acid concentration between the two study groups, as well as to analyze the correlation between dental caries experience and the investigated salivary parameters.

Materials and methods

To achieve the study's objective, a total of 60 subjects of both sexes, aged 12 years, were enrolled and divided into two groups based on their DMFT index values (Klein–Palmer system): a caries-active (CA) group and a caries-resistant (CR) group. Saliva samples were collected from each subject. Salivary flow rate was determined, while salivary urea concentration was measured using the **UREA/BUN-UV** two-step enzymatic method, where urea is hydrolyzed into ammonia and carbon dioxide by the enzyme urease; salivary uric acid was determined using the **URICASE/PEROXIDASE** enzymatic method, also based on a coupled reaction, in which uric acid is hydrolyzed by the enzyme uricase into allantoin, carbon dioxide, and hydrogen peroxide. Salivary hydrogen ion concentration (salivary pH) was measured using a digital pH meter (PH-03(II) Pen-type pH Meter).

Results

In accordance with the inclusion and exclusion criteria, a total of 60 participants were included in the study, of whom 43(71.6%) were male and 17(28.4%) were female. The participants were divided into two equal groups, with 30 (50%) categorized as caries-active (CA) and 30(50%) as caries-resistant (CR).

Regarding sex distribution, the caries-active group comprised 19(63.3%) male and 11 (36.7%) female participants, whereas the caries-resistant group comprised 24(80.0%) male and 6 (20.0%) female participants. The sex distribution of the participants across the two groups is presented in Table 1.

Table 1. Descriptive analysis of the study sample according to sex

Sex	n	groups		p-value
		CA	CR	
Male	43(71.6%)	19(63.3%)	24(80%)	(χ^2=11.267;
Female	17(28.4%)	11(36.7%)	6(20%)	df=1; p=0.001)

According to the analysis of the DMFT index, the mean DMFT score in the caries-active (CA) group was 6.5±1.6, with a minimum value of 5 and a maximum value of 10 (Table 1). In the caries-resistant (CR) group, the mean DMFT score was 2.0±1.5, with a minimum value of 0 and a maximum value of 4 (Table 2).

Table 2. Analysis of the DMFT index between the CA and CR groups

	Num. (N)	Mean	Std. Dev.	Min	Max	Percentiles		
						25th	50th	75th
CA	30	6.5	1.6	5	10	5	6	8
CR	30	2	1.5	0	4	1	2	4

(Mann-Whitney U Test: Z=-6.698; p<0.001)

In the caries-active (CA) group, the mean salivary flow rate was **0.54±0.30 mL/min**, with values ranging from **0.20 mL/min** to **1.60 mL/min**. In the caries-resistant (CR) group, the mean salivary flow rate was **0.48±0.23 mL/min**, with a minimum value of **0.10 mL/min** and a maximum value of **1.25 mL/min**. Statistical analysis demonstrated no significant difference in salivary flow rate between the CA and CR groups (**Mann-Whitney U test:** Z= -0.451; p = 0.652) (Table 3).

Table 3. Analysis of salivary flow rate between CA and CR

	(N)	Mean	Std. Dev.	Min	Max	Percentiles		
						25th	50th	75th
CA	30	0.54	0.3	0.2	1.6	0.3	0.47	0.7
CR	30	0.48	0.23	0.1	1.25	0.34	0.5	0.6

(Mann-Whitney U Test: Z=-0.451; p=0.652)

In male subjects in the CA group, the salivary flow rate was 0.56±0.34 mL/min, with a minimum value of 0.2 mL/min and a maximum value of 1.6 mL/min. In female subjects in the CA group, the salivary flow rate was 0.50±0.25 mL/min, with a minimum value of 0.2 mL/min and a maximum value of 1.1 mL/min. No significant difference in the amount of salivary secretion was observed between male and female subjects in the CA group (Mann-Whitney U test: Z=-0.301; p=0.763) (Table 4)

In male subjects in the CR group, the salivary flow rate was 0.46±0.18 mL/min, with a minimum value of 0.15 mL/min and a maximum value of 0.91 mL/min. In female subjects in the CR group, the salivary flow rate was 0.57±0.38 mL/min, with a minimum value of 0.1 mL/min and a maximum value of 1.15 mL/min. No significant difference in the amount of salivary secretion was observed between male and female subjects in the CR group (Student's t-test: t=-1.023; p=0.315) (Table 4).

Table 4. Analysis of salivary flow rate between CA and CR by gender

	(N)	Mean	Std. Dev.	Min	Max	Percentiles		
						25th	50th	75th
CA								
Male	19	0.56	0.34	0.2	1.6	0.3	0.53	0.72
Female	11	0.5	0.25	0.2	1.1	0.35	0.45	0.62
(Mann-Whitney U Test: Z=-0.301; p=0.763)								
CR								
Male	24	0.46	0.18	0.15	0.91	0.31	0.47	0.6
Female	6	0.57	0.38	0.1	1.15	0.34	0.52	0.7
(Student's t-test: t=-1.023; p=0.315)								

In the CA group of subjects, salivary pH was 6.92 ± 0.37, with a minimum value of 6.14 and a maximum value of 7.52. In the CR group, salivary pH was 7.19 ± 0.39, with a minimum value of 6.15 and a maximum value of 7.73. A statistically significant difference was found between the salivary pH values of the CA and CR groups (Student's t-test: t = −2.708; p = 0.009) (Table 5). The CR group of subjects had a significantly higher salivary pH value than the CA group.

Table 5. Analysis of salivary pH between CA and CR

	(N)	Mean	Std. Dev.	Min	Max	Percentiles		
						25th	50th	75th
CA	30	6.92	0.37	6.14	7.52	6.53	6.99	7.19
CR	30	7.19	0.39	6.15	7.73	6.9	7.24	7.54
(Student's t-test: t=-2.708; p=0.009)								

In the CA group of subjects, the salivary urea concentration was 2.9 ± 1.76 mmol/L, with a minimum value of 0.88 mmol/L and a maximum value of 10.08 mmol/L. In the CR group, the salivary urea concentration was 4.99 ± 2.03 mmol/L, with a minimum value of 2.93 mmol/L and a maximum value of 11.66 mmol/L.

A statistically significant difference was found between the salivary urea concentrations in the CA and CR groups (Mann–Whitney U test: Z = −4.858; p < 0.001) (Table 6). The salivary urea concentration was significantly higher in subjects from the CR group compared with subjects from the CA group.

Table 6. Analysis of salivary urea concentration between CA and CR

	(N)	Mean	Std. Dev.	Min	Max	Percentiles		
						25th	50th	75th
CA	30	2.9	1.76	0.88	10.08	1.97	2.35	3.36
CR	30	4.99	2.03	2.93	11.66	3.36	4.76	5.33
(Mann-Whitney U Test: Z=-4.858; p<0.001)								

In the CA group of subjects, the salivary uric acid concentration was 142.3 ± 53.1 µmol/L, with a minimum value of 55 µmol/L and a maximum value of 297 µmol/L. In the CR group of subjects, the salivary uric acid concentration was 112.8 ± 47.2 µmol/L, with a minimum value of 44 µmol/L and a maximum value of 330 µmol/L.

Table 7. Analysis of salivary uric acid concentration between CA and CR

	(N)	Mean	Std. Dev.	Min	Max	Percentiles		
						25th	50th	75th
CA	30	142.3	53.1	55	297	111	135	163
CR	30	112.8	47.2	44	330	98	109	122
(Mann-Whitney U Test: Z=-2.914; p=0.004)								

A statistically significant difference was found between the salivary uric acid concentrations in the CA and CR groups (Mann–Whitney U test: Z = −2.914; p = 0.004) (Table 7). The salivary uric acid concentration was significantly higher in the CA group compared with the CR group of subjects.

In the total sample, according to the Spearman's rank correlation analysis, the following findings were established:

-At $p<0.05$, there was a statistically significant negative correlation between the salivary flow rate and the DMFT index ($R(60)=-0.555$; $p<0.001$). As the salivary flow rate increased, the DMFT index significantly decreased (Table 8).

At $p<0.05$, there was a statistically significant positive correlation between the salivary uric acid concentration and the DMFT index ($R(30)=0.348$; $p=0.006$). As the salivary uric acid concentration increased, the DMFT index significantly increased (Table 8).

Table 8. Correlation between salivary parameters and dental caries prevalence

Correlations	Spearman's rho	p
DMFT index and salivary pH	-0.197	0.131
DMFT index and salivary buffering capacity	-0.111	0.398
DMFT index and salivary flow rate	-0.555	<0.001
DMFT index and salivary urea concentration	-0.243	0.062
DMFT index and total salivary protein concentration	0.073	0.578
DMFT index and salivary uric acid concentration	0.348	0.006

A statistically significant difference in DMFT index values was found between the two study groups; however, no statistically significant difference was found in the percentage of restored teeth between the subjects. A statistically significant difference was found in the percentage of decayed and extracted teeth comprising the DMFT index between the two study groups. No statistically significant difference was found in the percentage of restored teeth between the two study groups. Salivary uric acid levels were significantly lower in subjects with active dental caries.

Discussion

Saliva is a biological fluid in the oral environment and a secretory product of the major and minor salivary glands. It is generally accepted that saliva is crucial for maintaining oral health. Its buffering capacity contributes to the regulation of pH in the oral environment; however, it is particularly important to emphasize that most of its components act synergistically in preventing the development of dental caries through physiological mechanical cleansing, antimicrobial activity, and, of course, the salivary remineralization capacity [1,2]. Since saliva plays an important role in preventing the development of dental caries, a significant reduction or impairment of its functions may contribute to the development of dental caries[3]. Caries risk assessment is of great importance because it provides opportunities to improve oral hygiene and dietary practices and, through motivation, education, and the implementation of appropriate individual or population-based preventive measures, to achieve better oral and general health, as well as an improved quality of life and better public health[4,5].

Dental caries is most commonly expressed using the DMFT index, which represents the total number of decayed, missing due to caries, and filled teeth[6]. The DMFT index was first introduced by Klein *et al*., (1938)[7] and represents a cumulative measure of dental caries that reflects its occurrence and prevalence. It remains the most widely used epidemiological index for assessing dental caries. This index is widely accepted and applied, enabling the assessment of caries risk at the population level for the purposes of planning and developing public health and dental health strategies[8-10].

In this study, the DMFT index value was 6.8±1.6, with a minimum value of 5 and a maximum value of 10 among male subjects, whereas among female subjects in the caries-active group, the DMFT index was 6.2±1.6, with a minimum value of 5 and a maximum value of 10. No significant difference was observed between male and female subjects. In contrast to our findings, Gonzales A. *et al*., reported an inverse distribution of caries prevalence by sex. In our study, female subjects had lower DMFT index values than male subjects, whereas in their study, male subjects had lower DMFT index values. Interestingly, Gonzales A. *et al*., did not observe a single extracted tooth among their subjects[11].

In the caries-active group, the pH value obtained was 6.92±0.37, with a minimum value of 6.14 and a maximum value of 7.52. Gonzales A.E. *et al*., in their study conducted among 12-year-old children, obtained results similar to ours. In the group of patients with DMFT ≥ 5, corresponding to our caries-active group, the pH of unstimulated saliva was 6.9 (±0.54)[11]. In the caries-resistant group, salivary pH was 7.19±0.39, with a minimum value of 6.15 and a maximum value of 7.73. In the study by Gonzales A.E. *et al*., patients with DMFT <5 had a result similar to that observed in our caries-resistant group-7.1 (±0.49)[11]. These findings are also consistent with the study by Pyati SA, in which the caries-active group had a salivary pH of 6.64±0.54, whereas the caries-resistant group had a value of 7.47±0.45[14].

An increase in salivary pH following the intraoral application of urea was first described by Stephan RM (1943). This author demonstrated, in both *in vitro* and *in vivo* studies, that urea can shift pH from acidic to alkaline, i.e., it can increase plaque pH to as high as 9[16].

The amount of salivary secretion is an important factor in maintaining the health of the oral environment and in protecting against and controlling dental caries, as it facilitates self-cleansing and the elimination of bacterial metabolites, thereby protecting oral surfaces. Reduced salivary flow may lead to accelerated accumulation and maturation of dental biofilm, resulting in acidification of the environment and the presence of acidogenic bacteria[12,13]. In our subjects, the amount of salivary secretion in the caries-active group was 0.54±0.3 mL/min, whereas in the caries-resistant group it was 0.48±0.23 mL/min. Based on these results, we conclude that there was no significant difference in the salivary flow rate between the two study groups. In contrast, studies conducted by González AE *et al*., and Pyati SA *et al*., reported significantly lower salivary flow rates in the caries-active group compared with the caries-resistant group[11,14]. In contrast, Saveski M. (2023), in a study conducted among 12-year-old children from the Skopje region, obtained results consistent with our findings. The mean and median salivary flow rates measured in the caries-active group were 0.495 mL and 0.499 mL, respectively, compared with those in the caries-resistant group[15].

Urea is the diamide of carbonic acid. The salivary glands do not synthesize urea; rather, it reaches them through ultrafiltration of blood serum at the level of the acinar cells of the salivary glands. Urea, as the end product of protein catabolism, behaves as a moderately alkaline compound in solution. It is a low-molecular-weight compound that readily penetrates through the layers of deposits, particularly the layers of dental biofilm[17]. Salivary urea present in the oral cavity is hydrolyzed into carbon dioxide and ammonia by bacterial urease. Ammonia produced through the metabolism of arginine and urea has been identified as a mechanism by which oral bacteria protect themselves against acidification, maintain a relatively neutral pH that may suppress the development of cariogenic microflora, and prevent the attainment of a bioenergetic advantage, including an increase in pH[18-21].

Peterson S. *et al*., provided indirect evidence that oral urea metabolism may increase caries resistance. They included patients with chronic renal failure and observed a low prevalence of carious lesions despite a carbohydrate-rich diet. In these subjects, salivary urea concentrations were 10-50 times higher than those observed in healthy individuals. Therefore,

the alkalogenic potential of saliva could represent a promising strategy for preventing or controlling dental caries[21,22].

Similar findings were reported in the study by Zabokova B.E. *et al*., [23] In their study, higher urea levels were found in subjects with lower DMFT index values compared with subjects with higher DMFT index values. In this context, similar results were reported in a study by Raj G. *et al*., [24] conducted among university students, in which significantly higher urea levels were found in caries-free individuals compared with caries-active subjects.

Based on the analysis performed in our study, we determined the salivary urea concentration in the caries-active and caries-resistant groups and found a significant difference between the two groups. Salivary urea concentration was significantly higher in subjects from the caries-resistant group compared with subjects from the caries-active group.

Another antioxidant component among the salivary parameters examined in our study was uric acid concentration. The analysis of uric acid concentration in the caries-active and caries-resistant groups showed that uric acid had mean and median values of 154.5±60.3 μmol/L and 121.2±29 μmol/L, respectively, in the caries-active group, and 116.8±51.3 μmol/L and 97±29.6 μmol/L, respectively, in the caries-resistant group. Statistical analysis confirmed significantly higher uric acid levels in subjects with active dental caries.

The results of this study are consistent with studies conducted by Raj G *et al*., Hendi SS *et al*., who, among other parameters, determined uric acid concentrations as a component of the antioxidant capacity of saliva in both study groups. Higher uric acid levels were demonstrated in the caries-active group compared with the control group, i.e., the dental caries-resistant group[24,25]. In contrast to the findings of our study, Saveski M reported opposite results. In his study, lower uric acid concentrations were found in the caries-active group (104.12±62.7 μmol/L and 89.8 μmol/L) compared with subjects in the caries-resistant group (172.27±88.8 μmol/L and 181.8 μmol/L)[15]. A statistically significant positive correlation was found between salivary uric acid concentration and the DMFT index ($R(30)=0.348$; $p=0.006$), indicating that an increase in salivary uric acid concentration was associated with a significant increase in the DMFT index.

There are very limited data in the literature demonstrating an association between uric acid and dental caries, indicating a need for further research to elucidate its influence on oral and dental health.

Conclusion

The salivary flow rate did not show significant differences between subjects in the two study groups, whereas salivary pH showed a statistically significant difference between the groups. Subjects categorized as resistant to dental caries had higher salivary pH values, which most likely indicates more effective neutralization of acids in their oral environment. In the caries-active group of subjects, a statistically significant negative correlation was observed between salivary pH and the amount of salivary secretion, indicating that increased salivary secretion may be accompanied by lower salivary pH values.

A significant negative correlation was found between the salivary flow rate and the DMFT index. This indicates that increased salivary secretion may contribute to a reduction in caries incidence, which is an important aspect of preventive dentistry. The increased salivary urea concentration observed in caries-resistant subjects suggests a potential protective role against dental caries. The statistically significant negative correlation between the amount of salivary secretion and the DMFT index indicates a protective effect of salivary secretion. The higher pH observed in caries-resistant subjects may indicate more effective neutralization of acids in the oral environment.

The absence of a significant association between the DMFT index and oral hygiene and dietary habits suggests that multiple factors contribute to the etiology of dental caries, supporting the need for further epidemiological research.

Conflict of interest statement. None declared.

References

1. Preethi BP, Reshma D, Anand P. Evaluation of flow rate, pH, buffering capacity, calcium, total proteins and total antioxidant capacity levels of saliva in caries-free and caries-active children: an in vivo study. *Indian J Clin Biochem* 2010; 25(4): 425-428. doi: 10.1007/s12291-010-0062-6.
2. Kaur A, Kanwardeep K, Kamboj P. Evaluation of non-microbial salivary caries activity parameters and salivary biochemical indicators in predicting dental caries. *J Indian Soc Pedod Prev Dent* 2012; 30(3): 212-217. doi: 10.4103/0970-4388.105013.
3. Gopinath VK, Arzreanne AR. Saliva as a diagnostic tool for assessment of dental caries. *Arch Orofac Sci* 2006; 1: 57-59.
4. Pannu P, Gambhir R, Sujlana A. Correlation between the salivary Streptococcus mutans levels and dental caries experience in adult population of Chandigarh, India. *Eur J Dent* 2013; 7(2): 191-195. doi: 10.4103/1305-7456.110169.
5. Mohamedhussein NM, Hussein M, Bhaskar S, Al Radaideh A. Caries risk assessment in children using salivary parameters. Int J Adv Dent Sci Technol. 2014;1(1):25-34. http://medical.cloud-journals.com/index.php/IJADST/article/view/Med-174.
6. World Health Organization. Global data on dental caries prevalence (DMFT) in children aged 12 years. Geneva: World Health Organization; 2000. Report No.: WHO/NMH/MNC/ORH/Caries.12y.00.3.
7. Klein H, Palmer CE, Knutson JW. Studies on dental caries. I. Dental status and dental needs of elementary school children. *Public Health Rep* 1938; 53: 751-65. doi: 10.2307/4582532.
8. Al-Darwish M, El Ansari W, Bener A. Prevalence of dental caries among 12-14 year old children in Qatar. *Saudi Dent J* 2014; 26(3): 115-125. doi: 10.1016/j.sdentj.2014.03.006.
9. Jakobsen JR, Hunt RJ. Validation of oral status indicators. *Community Dent Health* 1990; 7(3): 279-284. PMID: 2076505.
10. Broadbent JM, Thomson WM. For debate: problems with the DMF index pertinent to dental caries data analysis. *Community Dent Oral Epidemiol* 2005; 33(6): 400-409. doi: 10.1111/j.1600-0528.2005.00259.x.
11. González-Aragón Pineda AE, García Pérez A, García-Godoy F. Salivary parameters and oral health status amongst adolescents in Mexico. *BMC Oral Health* 2020; 20(1): 190. doi: 10.1186/s12903-020-01182-8.
12. Do T, Damé-Teixeira N, Naginyte M, Marsh PD. Root surface biofilms and caries. *Monogr Oral Sci* 2017; 26: 26-34. doi: 10.1159/000479304.
13. Marsh PD, Do T, Beighton D, Devine DA. Influence of saliva on the oral microbiota. *Periodontol 2000*. 2016; 70(1): 80-92. doi: 10.1111/prd.12098.
14. Pyati SA, Naveen Kumar R, Kumar V, Praveen Kumar NH, Parveen Reddy KM. Salivary flow rate, pH, buffering capacity, total protein, oxidative stress and antioxidant capacity in children with and without dental caries. *J Clin Pediatr Dent* 2018; 42(6): 445-449. doi: 10.17796/1053-4625-42.6.7.
15. Saveski M. Salivary biomarkers in correlation with predisposition to dental caries [master's thesis]. Skopje: Ss. Cyril and Methodius University in Skopje, Faculty of Dentistry; 2023.

16. Stephan RM. The effect of urea in counteracting the influence of carbohydrates on the pH of dental plaques. *J Dent Res* 1943; 22(1): 63-71. doi: 10.1177/00220345430220010801.
17. Ivanovski K, Peshevska S, Dirjanska K, Ristoska S, Poposki B. Oral biochemistry and physiology. Skopje: Faculty of Dentistry, Ss. Cyril and Methodius University; 2025.
18. Firestone AR, Schmid R, Mühlemann HR. Effect of topical application of urea peroxide on caries incidence and plaque accumulation in rats. *Caries Res* 1982; 16(2): 112-117. doi: 10.1159/000260586.
19. Geddes DAM. Diet patterns and caries. *Adv Dent Res* 1994; 8(2): 221-224. doi: 10.1177/08959374940080021401.
20. Mueller WA, Courts FJ, Tapley PM. Relationship of salivary urea to caries incidence in CRF patients. *J Dent Res* 1984; 63(3): Special Issue: Abstract 120.
21. Schipper RG, Silletti E, Vingerhoeds MH. Saliva as research material: biochemical, physicochemical and practical aspects. *Arch Oral Biol* 2007; 52(12): 1114-1135. doi: 10.1016/j.archoralbio.2007.06.009.
22. Peterson S, Woodhead J, Crall J. Caries resistance in children with chronic renal failure: plaque pH, salivary pH, and salivary composition. *Pediatr Res* 1985; 19(8): 796-799. doi: 10.1203/00006450-198508000-00003.
23. Zabokova Bilbilova E, Sotirovska Ivkovska A, Ambarkova V. Correlation between salivary urea level and dental caries. *Prilozi* 2012; 33(1): 289-302. PMID: 22983064.
24. Raj G, Kumar D, Suma BS, Mangal G. Salivary urea and uric acid levels as biomarkers in dental caries: in vivo study. *Int J Community Med Public Health* 2022; 9(6): 2574-2578. doi: 10.18203/2394-6040.ijcmph20221537.
25. Hendi SS, Goodarzi MT, Moghimbeigi A, Ahmadi-Motamayel F. Evaluation of the status of salivary antioxidants in dental caries. *Infect Disord Drug Targets* 2020; 20(6): 816-821. doi: 10.2174/1871526519666191031100432.
26. Alves dos Santos GN, Meneses AMF, Vasconcelos US, de Assis RC, Fonseca e Souza AIA, Amorim GC, *et al*. Analysis of oxidative stress biomarkers in caries-free and caries-active children and adolescents. *Int J Dev Res* 2020; 10: 20585. https://doi.org/10.37118/ijdr.20585.12.2020.