Chapter

The Influence of Salivary pH on the Prevalence of Dental Caries

Laura-Cristina Rusu, Alexandra Roi, Ciprian-Ioan Roi, Codruta Victoria Tigmeanu and Lavinia Cosmina Ardelean

Abstract

Dental caries is the most prevalent chronic oral disease, influencing the oral and systemic health of the individuals, being the result of the interaction of multiple factors, such as microbial agents, the oral environment, the salivary pH, and the host response. The main process that occurs in dental caries is the demineralization of the tooth enamel, process that is directly influenced by the salivary pH, exposing the dental structures to the action of pathological agents. The role of saliva in the etiology of dental caries is a major one, by influencing the homeostasis through the altering of its buffer capacity. The properties of saliva are influenced either by local pathogens or through a general mechanism with direct implications upon the salivary components. The alteration of the salivary pH, flow rate, and composition will further have repercussions upon the cariogenic activity, through a change of its physiochemical properties. Nevertheless, the salivary pH is strongly linked to the incidence of dental caries, any persistent imbalance due to various causes can be assessed as an indicator of the oral health status.

Keywords: dental caries, salivary pH, oral pathology, oral health, dentistry, buffer capacity

1. Introduction

Dental caries is considered one of the most common chronic diseases affecting the global population [1]. An important aspect associated to dental caries is the potential serious consequences upon the general health of the individuals [2]. Previous studies stated the fact that oral bacteria can spread and determine various systemic health implications, being responsible for secondary infections of different organs [2]. Multiple research studies discuss the involvement of persistent oral bacteria, due to an inadequate oral hygiene, specific dental procedures or periodontitis in the initiation of endocarditis [3]. The oral environment can be influenced, as well, by the general health status and treatments with a direct impact upon the oral microbiota balance, the salivary flow, and pH. A high interest has been shown in identifying the composition, properties, and implications of the oral microbiome and its consequences upon the salivary pH, oral pathologies, and systemic diseases. The prevalence of dental caries is still characterized by high values despite the prevention measures applied

worldwide. Its incidence continues to increase dramatically once the risk habits prevalence in the developing countries changes. However, it has been reported that a small percentage of young adults can still be characterized as being caries-free. Unfortunately, the efforts to identify risk populations by using a screening method had no significant result [4].

The etiology and the pathogenesis of dental caries are being considered complex multifactorial processes [5]. An important role is assigned to saliva, its rate and composition being most important in the initiation and progression of the cariogenic process. Being the body fluid, which is in permanent contact with the teeth and soft oral tissues, it is held responsible for their integrity and for the permanent remineralization of the dental structures, as well. The quantity of the salivary flow, the characteristics of saliva, and its buffer capacity are involved in maintaining a proper balance of the oral environment. Any alterations of these characteristics can influence the demineralization process and are consequently responsible for the development of caries. The salivary components may have a substantial implication in the reduction of the risk factors involved in dental caries incidence [5].

The factors associated with occurrence of dental caries are the host (the presence of teeth and saliva), the oral microbiome (the bacterial population), and the dietary habits (based on carbohydrates). Basically, all these factors contribute and conduct to the development of the disease. Caries is characterized by a progressive evolution, being reversible in early stages, and suggesting that the abovementioned factors must have a cumulative action for a certain period of time. Dental caries is the result of the interaction between the oral microbiome accumulated on teeth's surface (dental plaque) with the fermentable sugars form the diet, with consequences upon the buffering capacity of the saliva, lowering its pH, and weakening the normal remineralization process [6].

The demineralization and remineralization cycles of the enamel, under the action of the cariogenic bacteria from the dental plaque, are quite frequent mechanisms that occur in the oral cavity, episodically. Enamel has a unique structure, without any organic components that could contribute to its repair or defense against a potential cariogenic attempt. In the early stages of the demineralization process, the action of saliva combined with the mechanical removal of the dental plaque and application of topic fluorides may stop and reverse the process.

An accurate evaluation of the dental caries risk should take in consideration the implication of saliva in the process. The use of a salivary test in the assessment of the individual risk may have an impact upon the prevention strategies, screening, and early diagnosis of dental caries, making a difference in the incidence statistics of dental caries [6].

2. Saliva and its functions

The oral cavity and the teeth are permanently exposed to the action of saliva [7]. The oral fluid is the result of the secretion of multiple salivary glands: the parotid, submandibular, sublingual, and the minor salivary glands localized in multiple areas of the oral mucosa. Free epithelial cells, bacteria, crevicular fluid, inflammatory cells, and food particles are among the components of saliva. The implications of saliva and its functions contribute to the maintenance of the oral health [8]. One of its main roles is hydrating and lubrication of the surrounding tissues. The submandibular, parotid, sublingual, and minor salivary glands contribute with 60, 25, 8, and

DOI: http://dx.doi.org/10.5772/intechopen.106154

7%, respectively, to the whole saliva amount, when in unstimulated state. In case of salivary flow stimulation, their secretion increases with at least 10% [9]. The salivary flow varies from 0.3 ml/min up to 1.5–2.0 ml/min, depending of the state: stimulation period or rest. There are circadian variations involved, as well, during the day 0.5 liter of saliva is secreted, compared with night when the flow rate is highly decreased [9].

Saliva and its actions are dependent on its quantity and quality. Being in permanent contact with the oral tissues, it has influence on actions such as speaking, swallowing, and eating, protecting the mucosa and the surface of the teeth. The protective role of the saliva is supported by a proper viscosity, flow rate, balanced composition, pH, and buffer function [10]. Any alterations of these characteristics may result in developing oral pathologies such as dental caries (**Figure 1**).

Figure 1.
Roles and functions of the saliva.

To date, research has focused on identifying the relationship between the characteristics of saliva and the incidence of dental caries. Several studies reported that there was a connection between the viscosity of saliva and the development of dental caries [8]. The high cariogenic activity due to the alteration of the salivary characteristics could be explained by a reduced flow rate, a decreased clearance and buffer capacity, and a high glucose concentration. It has been shown that the salivary flow rate was significantly lower in individuals with active caries compared with caries-free ones [11]. The buffer capacity and the pH values have direct consequences upon the salivary flow rate and viscosity [10].

The composition and flow rate of saliva vary in relation with different factors, such as stimulation or rest periods [10]. In the rest periods, the salivary flow rate represents ¼ out of the total stimulated flow potential. During the stimulated flow, the composition and pH of the saliva change, a more serious saliva consistency facilitates the digestive process and increases the clearance function [12]. The immune surveillance role of the saliva is due to immunoglobulins, secreted by the plasma cells of the lymphoid tissue belonging to the major salivary glands. The epithelial cells localized in the salivary acini produce proteins with a protective role against bacteria and viruses.

Because of its complex composition, saliva has multiple actions in the oral environment. In vitro studies, focused on the interaction between the cariogenic microorganisms in the dental plaque and the salivary proteins, suggest that interleukins, lysozyme, mucins, and lactotransferrin contribute to the cell aggregation, inhibition action, and adherence of the bacteria, suggesting that the salivary proteins may have a diagnostic potential, allowing the development of personalized treatments [13, 14].

Dental caries is represented by a localized demineralization with progressive loss of the tooth components. The healthy oral environment is in symbiosis with the oral microbiome, in case of a neutral pH value. The bacteria from the oral biofilm are responsible for metabolizing the carbohydrates and producing permanent organic acid products, which are able to lower the pH, with effects upon the tooth

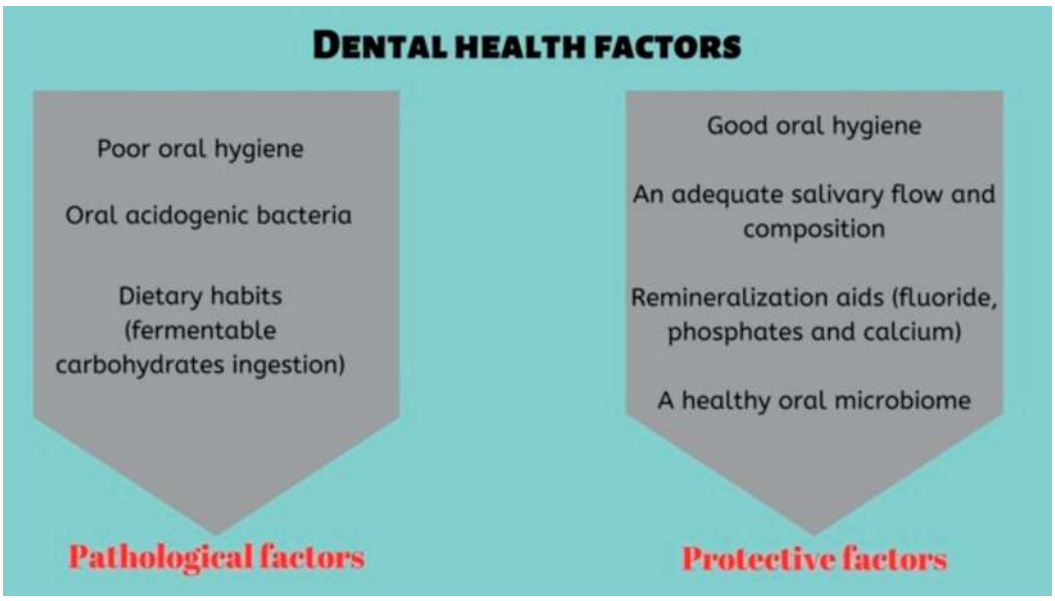

Figure 2.
The contribution of the pathological and protective factors.

composition and biofilm [15]. A long-time persistence of a lower pH value influences the bacterial population of the biofilm, producing a shift in the oral microbiome and promoting the acidogenic bacteria [16]. These changes will eventually have repercussions upon the oral environment by the acidification process. A low pH value will result in the extraction of phosphate and calcium from the tooth structures, in order to attempt to equilibrate the acid environment, determining their demineralization. These types of actions take place several times per day and are being influenced by numerous other mechanisms and factors such as oral hygiene, diet, oral microbiome diversity, genetics, dental anatomy, biofilm, salivary flow, buffer capacity, and composition (**Figure 2**).

Saliva has an important role in maintaining a healthy oral environment and proper digestion, and its alterations can be the cause of multiple diseases, including dental caries.

3. Salivary pH and buffer capacity

The buffer capacity of saliva plays an important role in mediating the relationship between the tooth surface and the biofilm, normally exhibiting a protective role against the development of dental caries [17]. This specific characteristic of saliva is represented by the concentration of the bicarbonate ion. The buffer capacity may be quantified and assessed, in case of active-caries individuals, by a titration method, from salivary samples. The implications of the buffer action rely on reducing the acid formation in the dental biofilm. In case of a pathogenic action, the neutralization of an acidic pH environment, and shifting it into a neutral one, has proven to be quite difficult [18].

The composition of saliva has an important contribution in maintaining and increasing the value of the pH biofilm. Among its main constituents, which efficiently determine the pH to increase are sialin (that contains arginine and lysine) and urea. Further hydrolyzation of each of these molecules results in releasing ammonia, with a direct contribution in increasing the pH.

In order to maintain the oral health and the integrity of the tooth surface, the pH value should be kept around the value of 6.7. The ion concentration and activity are responsible for demineralization and remineralization processes through the solubility of hydroxyapatite [19]. A decreased and critical pH value is considered at a value of/under 5.5.

The pH value is directly related to the concentration of the phosphate and calcium ions. Salivary flow and its variations have consequences upon the pH value, by exhibiting different concentrations of calcium and phosphate. It has been reported that the pH value can be increased by one unit only through stimulating the salivary flow rate. Differences between the unstimulated and stimulated saliva have been identified, as the unstimulated saliva has a lower pH value compared with the stimulated one, due to its higher concentration in phosphate [20]. The critical pH value presents individual variations, as the salivary concentrations of calcium and phosphate vary from one person to another. It should also be mentioned that the critical pH fluctuations are dependent on multiple factors [21].

Saliva has three buffering systems, which are represented by phosphate, bicarbonate, and protein systems. The major system being considered is the acid/bicarbonate one, present in the stimulated salivary secretion. Its action starts with food intake, by decreasing the pH value and increasing the concentration of bicarbonate. The

phosphate buffer system and its effectiveness are dependent on the salivary concentration of the phosphate ion and have been reported to have a moderate action in case of unstimulated saliva [22]. The salivary proteins represent another buffer system, through their action of absorbing and releasing protons. Their action may result in increasing the saliva viscosity when the pH value is low, protecting the tooth structure from acid production, by exhibiting a physical barrier [20].

The pH value during rest periods has been reported to have the ability to predict the caries status of the patient and outline the buffering capacity of the saliva. Patients with resting salivary pH value of approximately 7.0 have been reported to have a lower caries activity compared with those with pH values of 5.5, who exhibited a high caries incidence. In individuals with pH values between 5.5 and 7.0, the caries incidence was less severe. A lower value of a resting pH suggests a lower pH value when exposed to carbohydrates, with a prolonged maintenance of this lower value, until returning to the resting pH [8]. These facts suggest that the changes during a lower pH value result in exposing the tooth structure to an acidic environment, for a longer period of time, without the possibility of neutralizing it.

The presence of dental caries influences the carbohydrate clearance, resulting in a prolonged contact with the dental plaque and a continuous decrease of the salivary pH value [11]. The presence of dental caries and alteration of the oral environment promote the production of acid, supplementary bacterial adhesion, and low salivary clearance activity. A previous published study concluded that the salivary flow rate, the buffer capacity, and pH value were decreased in active-caries children compared with the caries-free group [23].

The implication of the salivary pH in the multiplication and survival of oral microorganisms is an important aspect in the etiology of dental caries. In case of a low pH, the acidophilic microorganisms will multiply, considerably increasing the caries risk [24]. A high incidence of dental caries, dysphagia, and other oral pathologies has been linked to a decreased salivary flow, clearance, and buffer capacity. Special attention should be paid to the patients with decreased saliva secretion, with repercussions upon the oral mucosa, upon the viscosity and buffer capacity, favoring the development of opportunistic infections and increasing the risk of dental caries [25].

4. PH variations and dental caries risk in systemic conditions

The oral cavity and the salivary composition and characteristics may be defined as the mirror of the general health status. Saliva represents the first body fluid, which comes in contact with multiple pathogens, being responsible for their neutralization, and for the homeostasis of the oral environment. Recent studies have revealed the importance of assessing the levels of salivary antioxidants and reactive oxygen species, which have a high implication in the incidence of dental caries.

A clinical study conducted on children diagnosed with iron deficiency anemia revealed its impact upon the salivary pH value and buffer capacity. By collecting unstimulated saliva and serum samples from the patients, before and after treatment, the salivary buffer capacity and pH values have been quantified. The serum ferritin levels were measured, in order to outline their role as dental caries and iron deficiency anemia biomarkers. The results showed that 3 months after treatment, the buffering capacity and the salivary pH have increased, suggesting a direct implication of the iron deficiency anemia in altering the salivary functions with secondary implications in the cariogenic activity [26].

The salivary dysfunction related to primary Sjögren's syndrome may be the cause of multiple oral manifestations. The results of several studies discuss the fact that patients diagnosed with primary Sjögren's syndrome have a high incidence of dental caries, exhibiting mostly cervical carious lesions, despite an acceptable oral hygiene status [27]. Several salivary factors that have been encountered in primary Sjögren's syndrome patients have been linked to the high incidence of caries. The main problem related to this pathology is the influence upon the saliva formation, patients experiencing a decreased salivary flow rate, and an alteration in the salivary composition, due to the presence of focal lymphocytic infiltrate in the salivary glands. Pedersen et al. [28] conducted a study that aimed to identify and evaluate the salivary flow and composition and the incidence of dental caries in patients diagnosed with primary Sjögren's syndrome. The results showed that the included patients exhibited a decreased salivary flow rate, and the pH and bicarbonate concentration of the parotid gland's saliva were significantly decreased compared with the control group. Although patients had accurate oral hygiene habits and reported using dental floss and fluoride toothpaste, the caries incidence and gingival index were high. These patients also had a higher number of acidophilic, cariogenic bacteria in the dental plaque compared with the control group, and a relationship between the decreased salivary flow and the high incidence of Lactobacillus has been observed. Among all the oral manifestations, oral dryness and a reduced salivary flow rate were the main accuses of the patients [29].

A decreased salivary flow has been reported in diabetic patients, the incidence of type I diabetes among young patients may have repercussions on the oral health, especially teeth integrity. The association between dental caries and diabetes has been one of the most researched subjects. As type I diabetes is associated with the critical years of dental eruption, the attention in identifying its potential implication on the dental status has been considered a necessity. Studies have reported a high incidence of dental caries, dry mouth (xerostomia), and gingival inflammation in young patients diagnosed with type I diabetes compared with healthy ones. One of the main causes that could explain this outcome, besides a poor oral hygiene, could be the decreased salivary flow rate and alteration of the composition of saliva. Elevated glucose concentration has been identified in the saliva, sustaining an acidogenic oral environment and the colonization of bacteria. All these changes in the flow rate, salivary composition, and an inadequate oral hygiene influence the incidence of dental caries [29]. Studies including patients with type I diabetes showed that the salivary flow and pH value were significantly reduced compared with the control group, the prevalence and severity of dental caries in type I diabetes being a high one [29].

High incidence of dental caries, mucositis, and inflammation has been identified in acute lymphoblastic leukemia. The main changes are related to the compromised immune system, influencing the oral environment as well. Hegde et al. [30] conducted a study focusing on the implication of acute lymphoblastic leukemia on the oral health and dental status. They aimed to identify the direct action of the disease, as well as the influence of chemotherapy on the salivary flow and dental caries incidence. The study included patients divided into four groups (without chemotherapy, at the beginning of chemotherapy treatment, after 4 weeks of chemotherapy, and a control group). The results showed that all three groups with acute lymphoblastic leukemia experienced a low salivary flow rate and pH values compared with the control group. The antioxidant salivary levels were increased in the first two groups and decreased in the third group of leukemia patients. Poor oral hygiene and gingival inflammation were reported in all leukemia patients, and the incidence of dental

caries was a high one. The influence of chemotherapy on the salivary flow through the hypoplasia of the salivary glands is a common consequence of this treatment. Another cause for the poor dental health status, besides the abovementioned salivary changes, could be the discomfort caused by the inflammation of the oral mucosa that reduces the possibility of maintaining a proper oral hygiene [30].

The role of saliva in the diagnosis of multiple diseases through its composition and actions is currently accepted. The salivary secretion is controlled by a reflex arc influenced by multiple actions. For the salivary flow and composition, the parasympathetic and sympathetic systems are responsible. Multiple studies were conducted in identifying the stress-related consequence upon the saliva [31]. Results show an increase in the acidity levels of saliva in case of anxiety and a decrease of the salivary flow and pH value with consequences upon the tooth structure [31]. Said et al. [32] conducted a study, which aimed to identify the relationship between the anxiety levels and the changes encountered in the saliva. The results outline the existence of a low pH value in the study group, compared with the control group, revealing a higher prevalence among males with a low anxiety level. These alterations could be a further explanation for the prevalence of dental caries among these patients.

Systemic health plays an important role in maintaining an adequate oral environment. Changes specific to various diseases can directly influence the salivary production, composition, and functions, with influence on the prevalence of dental caries. Over the past years, research has opened a new path that includes the use of saliva for screening, diagnosis, and monitoring of multiple pathologies.

5. Conclusions

Among the numerous factors linked to the incidence of dental caries, the oral microorganisms and saliva are of most importance. The role of saliva cannot be underestimated, its composition revealing important information regarding the involvement of systemic and oral conditions. Research has focused on outlining the importance of the salivary functions and characteristics in the development of dental caries. Connections between the pH values and the prevalence of caries have been pointed out, the influence of local and general factors, as well as the impact of pH variations upon the tooth structure. An acidogenic oral environment results in an imbalanced demineralization and remineralization process, with a multiplying community of acidophilic bacteria. The key in the management of dental caries is addressing the causative factors, both general and local, and obtaining a neutral oral pH.

Conflict of interest

The authors declare no conflict of interest.

Author details

Laura-Cristina Rusu[1], Alexandra Roi[1], Ciprian-Ioan Roi[2], Codruta Victoria Tigmeanu[3] and Lavinia Cosmina Ardelean[3]*

1 Department of Oral Pathology, Multidisciplinary Center for Research, Evaluation, Diagnosis and Therapies in Oral Medicine, "Victor Babes" University of Medicine and Pharmacy, Timisoara, Romania

2 Department of Anaesthesiology and Oral Surgery, Multidisciplinary Center for Research, Evaluation, Diagnosis and Therapies in Oral Medicine, "Victor Babes" University of Medicine and Pharmacy, Timisoara, Romania

3 Department of Technology of Materials and Devices in Dental Medicine, Multidisciplinary Center for Research, Evaluation, Diagnosis and Therapies in Oral Medicine, "Victor Babeș," University of Medicine and Pharmacy, Timisoara, Romania

*Address all correspondence to: lavinia_ardelean@umft.ro

IntechOpen

References

[1] Frencken JE, Sharma P, Stenhouse L, Green D, Laverty D, Dietrich T. Global epidemiology of dental caries and severe periodontitis - a comprehensive review. Journal of Clinical Periodontology. 2017;**44**(Suppl. 18):S94e105

[2] Kim JK, Baker LA, Davarian S, Crimmins E. Oral health problems and mortality. Journal of Dental Science. 2013;**8**:115-120. DOI: 10.1016/j.jds.2012.12.011

[3] Kriebel K, Hieke C, Muller-Hilke B, Nakata M, Kreikemeyer B. Oral biofilms from symbiotic to pathogenic interactions and associated disease-connection of periodontitis and rheumatic arthritis by peptidylarginine deiminase. Frontiers in Microbiology. 2018;**9**:53

[4] Anderson MH. Current concepts of dental caries and its prevention. Operative Dentistry Supplement. 2001;**6**:11-18

[5] Vellore G, Arzreanne AR. Saliva as a diagnostic tool for assessment of dental caries. Archives of Orofacial Sciences. 2006;**1**:57-59

[6] Jepsen S, Blanco J, Buchalla W, Carvalho JC, Dietrich T, Dörfer C, et al. Prevention and control of dental caries and periodontal diseases at individual andpopulation level: Consensus report of group 3 of joint EFP/ORCA workshop on the boundaries between caries and periodontal diseases. Journal of Clinical Periodontology. 2017;**44**(Suppl. 44):S85-S93. DOI: 10.1111/jcpe.12687

[7] Sreebny LM. Saliva in health and disease: An appraisal and update. International Dental Journal. 2000;**50**:140-161

[8] Hicks J, Garcia-Godoy F, Flaitz C. Biological factors in dental caries: Role of saliva and dental plaque in the dynamic process of demineralization and remineralization (part 1). Journal of Clinical Pediatric Dentistry. 2004;**28**:47-52

[9] Khan GJ, Javed M, Ishaq M. Effect of smoking on salivary flow rate. International Journal of Molecular Sciences. 2010;**8**:221-225

[10] Lagerlöf F, Oliveby A. Caries-protective factors in saliva. Advances in Dental Research. 1994;**8**:229-238. DOI: 10.1177/08959374940080021601

[11] Aminabadi NA, Najafpour E, Rohani ZR, Deljavan AS, Ghojazadeh M, Jamali Z. Linear reciprocal interaction between dental caries and salivary characteristics. Journal of Oral Science. 2013;**55**:337-342

[12] Schenkels LCPM, Veerman ECI, Amerongen AVN. Biochemical composition of human saliva in relation to other mucosal fluids. Critical Reviews in Oral Biology & Medicine. 1995;**6**:161-175

[13] Cogulu D, Onay H, Ozdemir Y, Aslan I, G, Ozkinay F, Kutukculer N, Eronat C. Associations of interleukin (IL)-1β, IL-1 receptor antagonist, and IL-10 with dental caries. Journal of Oral Science. 2015;**57**:31-36. DOI: 10.2334/josnusd.57.31

[14] Andrade FB, Oliveira JC, Yoshie MT, Guimarães BM, Gonçalves RB, Schwarcz WD. Antimicrobial activity and synergism of lactoferrin and lysozyme against cariogenic microorganisms. Brazilian Dental Journal. 2014;**25**:165-169. DOI: 10.1590/0103-6440201302257

[15] Takahashi N, Nyvad B. The role of bacteria in the caries process: Ecological perspectives. Journal of Dental Research. 2011;**90**:294-303

[16] Ferjeskov O, Nyvad B, Kidd E. Dental Caries: The Disease and its Clinical Management. 3rd ed. Oxford: Wiley-Blackwell; 2015 480p

[17] Xiao J, Klein MI, Falsetta ML, Lu B, Delahunty CM, Yates JR III, et al. The exopolysaccharide matrix modulates the interaction between 3D architecture and virulence of a mixed-species oral biofilm. PLoS Pathogens. 2012;**8**:e1002623. DOI: 10.1371/journal.ppat.1002623

[18] Koo H, Falsetta ML, Klein MI. The exopolysaccharide matrix: A virulence determinant of cariogenic biofilm. Journal of Dental Research. 2013;**92**:1065-1073

[19] Aframian DJ, Davidowitz T, Benoliel R. The distribution of oral mucosal pH values in healthy saliva secretors. Oral Disease. 2006;**12**:420-423

[20] Ramezani J, Khaligh MR, Ansari G, Yazdani Y, Mohammadi S. Association of salivary physicochemical characteristics and peptide levels with dental caries in children. Journal of Indian Society of Pedodontics and Preventive Dentistry. 2021;**39**:189-195

[21] Dawes C. What is the critical pH and why does a tooth dissolve in acid? Journal of Canadian Dental Association. 2003;**69**:722-724

[22] Bardow A, Moe D, Nyvad B, Nauntofte B. The buffer capacity and buffer systems of human whole saliva measured without loss of CO2. Archives of Oral Biology. 2000;**45**:1-2

[23] Gandhy M, Damle SG. Relation of salivary inorganic phosphorus and alkaline phosphatase to the dental caries status in children. Journal of Indian Society of Pedodontics and Preventive Dentistry. 2003;**21**:135-138

[24] Jeong SJ, Apostolska S, Jankulovska M, Angelova D, Nares S, Yoon MS, et al. Dental caries risk can be predicted by simply measuring the pH and buffering capacity of saliva. Journal of Dental Hygiene Science. 2006;**6**:159-162

[25] Mojabi KB, Esfahani M, Hashemi HJ. Evaluation of unstimulated salivary flow rate and oral symptoms in menopausal women. Journal of Dentistry Tehran. 2007;**4**:103-106

[26] Mahantesha T, Reddy KP, Ellore VPK, Ramagoni NK, Iitagi V, Anitha KS. Evaluation and association of iron deficiency anemia with salivary pH and buffering capacity in children aged 6-12 years. National Journal of Physiology, Pharmacy and Pharmacology. 1970;**4**:229-229

[27] Pedersen AM, Nauntofte B. Primary Sjögren's syndrome: Oral aspects on pathogenesis, diagnostic criteria, clinical features and approaches for therapy. Expert Opinion on Pharmacotherapy. 2001;**2**:1415-1436

[28] Pedersen AML, Bardow A, Nauntofte B. Salivary changes and dental caries as potential oral markers of autoimmune salivary gland dysfunction in primary Sjögren's syndrome. BMC Clinical Pathology. 2005;**5**:1-13

[29] Rai K, Hegde A, Kamath A, Shetty S. Dental caries and salivary alterations in type I diabetes. Journal of Clinical Pediatric Dentistry. 2011;**36**:181-184

[30] Hegde AM, Joshi S, Rai K, Shetty S. Evaluation of oral hygiene status, salivary characteristics and

dental caries experience in acute lymphoblastic leukemic (ALL) children. Journal of Clinical Pediatric Dentistry. 2011;**35**:319-323

[31] Yaribeygi H, Panahi Y, Sahraei H, Johnston TP, Sahebkar A. The impact of stress on body function: A review. EXCLI Journal. 2017;**16**:1057-1072

[32] Said OB, Razumova S, Velichko E, Tikhonova S, Barakat H. Evaluation of the changes of salivary pH among dental students depending on their anxiety level. European Journal of Dentistry. 2020;**14**:605-612