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The Relationship between Salivary Sialic Acid Levels and Oral Health in Iraqi Pediatric Population

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Annotation: Salivary sialic acid levels have been identified as potential biomarkers for assessing oral health, particularly in pediatric populations. In the Iraqi pediatric population, studies suggest that higher levels of sialic acid in saliva are often associated with various oral health conditions, including dental caries and periodontal disease. This study investigates the diagnostic potential of salivary sialic acid and its association with oral health parameters in children aged 5–15 years. Salivary samples from 100 healthy participants were collected and analyzed using spectrophotometric and ELISA techniques. The study employed statistical methods, including ANOVA, Student's T-test, linear correlation, and multiple regression, with a significance level set at $p < 0.05$.

Keywords: Salivary Sialic Acid, Oral Health, Spectrophotometric, periodontal disease, Saliva.

Summary

Background

Gingivitis and periodontitis are prevalent chronic conditions on a global scale. 50% of persons are affected with plaque-induced gingivitis. If periodontitis is not treated, it may lead to the recession of the gums, When some bacteria and their byproducts establish themselves on the gum, they secrete proteolytic enzymes and reactive oxygen species (ROS) that elevate indicators of host tissue damage, leading to the development of periodontal disease. Periodontal tissue may be harmed by free radicals due to smoking, inadequate nutrition, and reduced antioxidant (AO) capability.

Smoking is a singular environmental risk factor that may be modified and has been shown to elevate the incidence of periodontal disease and alter periodontal characteristics.

The aim of the study

The aim of this study is to determine the diagnostic sialic acid percentage and its scavenger function in relation to oral health statistics.

Conclusion A statistical analysis reveals a noteworthy association between the properties of the oral cavity and the amounts of salivary sialic acid, as well as its impact on oral health.

Statistical Analysis: The data analysis was performed with SPSS version 19.0. The current research used many statistical techniques, including descriptive analysis, analysis of variance, student T-test, linear correlation, and multiple linear regression model. It is anticipated that the analysis will provide a significance level of $p < 0.05$.

Important terms: salivary, oral, importance, sialic acid.

CHAPTER 1

Periodontal disorders, such as gingivitis and periodontitis, are prevalent chronic conditions that significantly affect populations worldwide. Gingivitis is an inflammation of the gums caused by plaque accumulation and affects 50% of adults. Periodontitis however is the destruction of the structures that support the teeth, where failure to treat it may result in a severe consequence including gum recession, gingival tissue loss, and the eventual loss of alveolar bone underneath with which it comes into contact, and finally, the loss of the tooth. Such outcomes not only affect oral but may also compromise the mastication functionality, leading to dietary intake reduction and subsequently nutritional status [1-3].

The progression of periodontal disease is thought to be fueled by the attachment of specific bacteria to the gingival tissues along with their endogenous products. An abnormal immune host response with high levels of proteolytic enzymes and ROS further leads to tissue destruction. Markers indicative of such injury are increased concentrations of free radicals in the host tissue, denoting an oxidative imbalance between oxidative stress and the available antioxidant system. This condition, often triggered by environmental factors such as smoking and poor nutrition, contributes to the progression of periodontitis and gingivitis [4,5].

Smoking is an important modifiable risk factor associated with increased periodontal disease prevalence in populations. It disrupts blood flow, alters the functioning of neutrophils, impairs the production of cytokines and growth factors, inhibits fibroblast development, and reduces collagen production, which may lead to further tissue damage. In addition, smoking elevates free radical concentration and lipid peroxidation within periodontal tissues and thereby depletes antioxidants. Moreover, smoking-related health issues are associated with socioeconomic factors, poor oral hygiene, and dietary habits, which further increase the risk of periodontal diseases [6-8].

Laboratory tests, such as those examining plaque, saliva, or gingival crevicular fluid, offer more accurate measurements than clinical assessments. These tests are based on biomarkers that are derived from bacterial structures or the host inflammatory system and help identify individuals at increased risk of developing periodontal disease.

Saliva is an important constituent of the oral cavity's defense mechanism, and certain biomarkers present in saliva, such as sialic acids, are critical for monitoring oral health. Sialic acids are acidic monosaccharides that function as systemic inflammatory markers, and their presence in saliva has been associated with the development of periodontal diseases. High levels of sialic acid are related primarily to periodontitis and they act on the scavenger capacity for free radicals and other types of agents protective in nature. The clinical study on human saliva using lipopolysaccharide-bound fractions for diagnosing periodontitis confirms the worthiness of employing the marker called sialic acid in diagnostic aspects of the disease [9,10].

Oral health issues in pediatric populations have become an area of great concern. Dental caries and periodontal diseases are very prevalent among children due to improper diet, inadequate oral hygiene, and less availability of dental services. Salivary biomarkers such as sialic acid do not appear to have been utilized in diagnosing and monitoring oral health conditions in children to any great extent. However, given the importance of early intervention in the prevention of long-term dental problems, there is a growing need to explore these biomarkers as potential tools in identifying children who are at risk of developing periodontal diseases. The evaluation of sialic acid levels in the Iraqi pediatric population may provide the necessary information into their oral health status, making it possible for more effective preventive and management measures.

CHAPTER 2

Literature review

2.1 pathogenesis

Numerous salivary biomarkers that have potential in relation to Parkinson's disease have been documented [11]. The development of periodontitis is associated with enzymatic changes, [5-8]. Superoxide dismutase (SOD) is an antioxidant enzyme found only in the periodontal ligaments of humans. It protects gingival fibroblasts from the damaging effects of superoxide [12]. Matrix metalloproteinases (MMPs), which degrade tissues and break down bones, are stimulated to develop by IL-1β. Three of the 24 distinct MMPs that have been successfully replicated so far have been discovered in humans. Enzymes such as collagenases, membrane-type metalloproteinases, stromelysins, matrilysins, and collagenase are categorised based on the substrates they are intended to break down.

[13].

MMP-8 and MMP9 are prominently recognised as indicators for periodontal disease among the MMPs. An office-based kit capable of conducting a 5-minute MMP-8 test has been developed [13,14]. Multiple risk variables, including periodontal infections, have the potential to impact the course of periodontal disease [15]. Smoking is the second most significant risk factor for Parkinson's disease (PD), behind dental plaque. Studies suggest that the occurrence of periodontitis is 3–6 times greater in those who smoke compared to those who do not smoke, and the heightened risk is directly related to the length of smoking and the rate of smoking. Smokers have more prominent clinical manifestations of Parkinson's disease (PD) compared to those who do not smoke. These manifestations include the presence of deeper pockets, a more comprehensive and severe loss of attachment, elevated levels of bone deterioration, and increased rates of tooth loss [16]. Furthermore, it has been shown that smoking has a detrimental impact on the efficacy of implant insertion as well as both non-surgical and surgical therapy [17].

2.2 Oral cavity

The mucosal surfaces found within the mouth cavity, along the gastrointestinal surfaces, and elsewhere in the body, play crucial roles in routinely protecting the areas beneath them, as well as blood vessels and other structural parts, from their external surroundings [17]. Various variables have an impact on the mucosal surfaces of the human oral cavity, which include distinctive anatomical characteristics such as the presence of teeth and tongue. The oral mucosa is often affected by environmental stimuli, including those present in the food, as well as localised impacts caused by the specific niches and areas inside the mouth, which have unique structural characteristics [18].

In conjunction with the aforementioned factors, a significant component of the human oral cavity is its inherent microbial communities that have an effect on the oral mucosa. The oral cavity's mucosal surface is inhabited by significant populations of both gram-positive and gram-negative bacteria, accompanied by fungus and other components that serve as supplementary inhabitants. The microflora present in the oral cavity may be seen in several locations, including supragingival plaque on the exposed surfaces of teeth, subgingival plaque below the gumline, and other specific niches such as the tongue and cheek surfaces. Saline microbial communities may be classified as planktonic components capable of facilitating the transportation of organisms over oral surfaces. In addition to the previous point, the regular consumption of food and its nutritional properties promote the growth of microorganisms, resulting in the production of various substances such as acids, toxins, components of microbial cell walls, and even those with immunogenic and pathogenic properties.

Collectively, microbial variables constitute a significant component of the oral stress and inflammatory load. The links between the microbial load inside the human mouth and illness have been extensively documented in the literature, drawing upon data from surveys and clinical investigations. Current practices in the field of clinical dentistry revolve on the consistent adherence to good oral hygiene protocols in order to safeguard oral well-being. The use of toothpaste for toothbrushing is commonly acknowledged as a self-care practice that effectively cleanses the mouth and enhances oral appearance [19]. Despite the widespread availability and educational initiatives aimed at mitigating the prevalence of oral disorders, a substantial effect of these diseases is reported by the majority of people. Caries and periodontal disease are among the most often reported oral illnesses.

Without sufficient therapies, these disorders might result in tooth loss and alterations in appearance, which can have lasting effects on one's quality of life. Surveys indicate that, despite the widespread availability of high-quality dental treatment, only around 10% of persons in the UK report having good oral health. Reversible oral disorders, which include gingivitis; gingivitis refers to inflammation of the gums and their supporting components of the tooth, are frequently found in 90% of specific populations. A large body of laboratory and clinical research has been performed in an attempt to study the influence of microbial effects on the onset and course of such disorders [20].

CHAPTER 3

MATERIAL AND METHODS

Salivary Sample Collection

Salivary samples were collected from 100 healthy children aged between 5 and 15 years. The collection was done in the time period of 9:00 to 11:00 A.M. to avoid diurnal variations in salivary composition. The collection took 5 minutes, and it was done without any external stimulation to allow natural salivary flow. Participants were advised not to ingest, drink, or brush their teeth at least an hour before samples were taken for the purpose of not contaminating and getting uniformity.

Inclusion and Exclusion Criteria

- **Inclusion Criteria:**
- ✓ Healthy children aged 5-15 years.
- ✓ No history of systemic diseases or medications affecting salivary secretion.
- ✓ Consent obtained from parents or guardians.
- **Exclusion Criteria:**
- ✓ Presence of any oral or systemic conditions that interfere with salivary flow.
- ✓ Medications or treatments that could interfere with salivary biomarkers.
- ✓ Children reluctant or unable to adhere to the study protocol.

Analysis of Salivary Biomarkers

The main objective of this study was to investigate salivary biomarker parameters associated with age in the context of Parkinson's disease (PD). Salivary biomarkers were assessed according to the standard procedure described in the Preferred Reporting Items for Spectrophotometer and Enzyme-Linked Immunosorbent Assay (ELISA). These biomarkers were assessed to establish their utility as markers for gingival inflammation in children, thus helping pediatric dentists in the initiation of preventive measures.

Search queries in title and abstract fields employed a combination of plain text words that included synonyms and plural forms combined with a controlled vocabulary like Medical Subject Headings (MeSH) terms for an inclusive search strategy that should include literature relevant enough to validate the methodology and biomarker selection.

Statistical Analysis

The data collected was analyzed using SPSS software version 19.0. The choice of statistical tests was guided by the study's objectives, ensuring appropriate analysis of the salivary biomarkers.

➢ **Descriptive Analysis:**

✓ Used to summarize the demographic and baseline characteristics of the study population.

➢ **Analysis of Variance (ANOVA):**

✓ Applied to compare salivary biomarker levels across different age groups.

➢ **Student T-test:**

✓ Used to evaluate differences in biomarkers between specific subgroups.

➢ **Linear Correlation:**

✓ Conducted to identify relationships between age and salivary biomarker levels.

➢ **Multiple Linear Regression Model:**

✓ Implemented to assess the combined effect of age and other variables on salivary biomarkers.

A significance level of $p < 0.05$ was used in all statistical tests to ensure very robust conclusions. SPSS version 19.0 was validly used, as it contained a wide variety of statistical methods and was quite user-friendly, so that the researcher could easily execute the data for analysis. This study is anticipated to provide new insights into age-related changes and salivary biomarkers on gingival health and disease prevention in pediatric populations.

CHAPTER 4

Results and discussion

This study aims to establish the correlation between salivary biomarkers and oral health parameters in children aged 5–15 years. A particular emphasis was laid on the concentration of sialic acid levels along with other biomarkers in assessing the possible use of salivary parameters for oral and systemic health conditions. The findings demonstrate correlations between salivary parameters and key clinical indices, thereby offering insights into the diagnostic utility of non-invasive salivary assessments.

Table 1: Correlation Between Sialic Acid Levels and Parameters

Parameters	Sialic Acid Level (saliva)
Salivary Flow Rate	r = -0.104, p = 0.30 (NS)
DMFs	r = 0.053, p = 0.59 (NS)
CI	r = 0, p < 0.001 (S)
FS	r = -0.197, p = 0.042 (S)
Ds	r = 0.057, p = 0.56 (NS)

Table 1 presents the correlation between sialic acid levels in saliva and various oral health parameters. The analysis reveals a significant positive correlation between sialic acid levels and the Caries Index (CI) ($r = 0$, $p < 0.001$), suggesting its potential role in caries assessment. Additionally, there is a significant negative correlation with the number of filled surfaces (FS) ($r = -0.197$, $p = 0.042$), indicating that higher sialic acid levels might be associated with fewer restorative dental interventions. However, no significant correlations were observed with salivary flow rate ($r = -0.104$, $p = 0.30$), DMFs ($r = 0.053$, $p = 0.59$), or decayed surfaces (Ds) ($r = 0.057$, $p = 0.56$), suggesting that these parameters may not be directly influenced by sialic acid levels.

Descriptive Analysis of Salivary Biomarkers

Table 2 presents the mean and standard deviation of salivary biomarkers. Significant differences were noted for most parameters, emphasizing their potential diagnostic value.

Table 2: Descriptive Statistics of Salivary Biomarkers

Salivary Biomarker	Mean ± SD	Significance (p-value)
Sialic Acid (nmol/µL)	0.14 ± 0.02	p < 0.001
Activity of LDH (nmol/min/mg)	896.56 ± 264.14	N/A
IL-1β (pg/mL)	251.35 ± 81.19	p < 0.0001
Cortisol (pg/mL)	417.16 ± 99.67	p < 0.0001
SOD (U/mL)	50.41 ± 4.25	p < 0.001
Urea (mg/dL)	5.6 ± 1.2	N/A
Creatinine (mg/dL)	0.9 ± 0.06	N/A

Table 2 summarizes the descriptive statistics of various salivary biomarkers measured in the study, highlighting their mean values, standard deviations, and levels of statistical significance. Sialic acid, a critical biomarker for oral health, exhibited a mean concentration of 0.14 ± 0.02 nmol/µL, with a highly significant p-value ($p < 0.001$), suggesting its strong diagnostic relevance. The activity of lactate dehydrogenase (LDH) was observed at 896.56 ± 264.14 nmol/min/mg, though its significance was not assessed (N/A). Pro-inflammatory biomarker interleukin-1 beta (IL-1β) showed a mean level of 251.35 ± 81.19 pg/mL ($p < 0.0001$), indicating its importance in systemic and oral inflammatory responses. Similarly, cortisol levels (417.16 ± 99.67 pg/mL, $p < 0.0001$) and superoxide dismutase (SOD) activity (50.41 ± 4.25 U/mL, $p < 0.001$) demonstrated significant associations, reflecting stress and oxidative status. In contrast, biomarkers such as urea (5.6 ± 1.2 mg/dL) and creatinine (0.9 ± 0.06 mg/dL) were not statistically analyzed, likely due to their stable physiological ranges.

Discussion

This study evaluated the relationship between salivary biomarkers, particularly sialic acid, and various oral health parameters in children aged 5–15 years. Findings point to substantial correlations between the concentration of salivary sialic acid and some major indicators of oral health, like Caries Index (CI) and FS, while it is also focused on the role of other biomarkers in systemic and oral health. The findings may contribute importantly to understanding the potential of salivary biomarkers for diagnostic purposes in pediatric oral health.

The increasing sialic acid levels with Caries Index correlated well with previous studies, which have shown that increased salivary sialic acid levels correlate with increased microbial activity and caries progression. Studies have shown that the sialic acid component of glycoproteins plays a role in the adhesion of cariogenic bacteria such as Streptococcus mutans to the enamel surface of the teeth, making it more susceptible to caries. Furthermore, the significant association of sialic acid levels with filled surfaces (FS) supports its utility in monitoring past dental interventions, as previously suggested in pediatric dental research.

The role of sialic acid in systemic inflammation and immune responses has also been extensively documented. Elevated sialic acid levels may indicate a systemic response to chronic low-grade inflammation in the oral cavity, as reflected by correlations with biomarkers such as IL-1β and cortisol. The high levels of IL-1β observed in this study align with findings in inflammatory conditions, reinforcing its role in the pathogenesis of gingivitis and early periodontal disease.

Sialic acid may influence oral health through several mechanisms. As a terminal sugar residue in mucins and glycoproteins, sialic acid plays a critical role in maintaining oral mucosal integrity and microbial defense. It contributes to the lubrication of the oral cavity, enhancing the protective barrier against mechanical damage and pathogenic invasion. However, its increased concentration in saliva may also provide additional nutrient sources for acidogenic bacteria, promoting dental caries. Additionally, sialic acid can modulate immune responses, acting as an anti-inflammatory agent under normal conditions, but potentially exacerbating inflammation in diseased states.

Limitations of the Study

Despite its valuable contributions, this study has several limitations. First, the cross-sectional design limits the ability to establish causal relationships between salivary biomarkers and oral health outcomes. Longitudinal studies would be more effective in understanding temporal dynamics and causality. Second, the study population was restricted to a specific age group (5–15 years), which may limit the generalizability of findings to other pediatric populations or adults. Furthermore, the sample size, while sufficient for preliminary analysis, may not capture the full variability in salivary biomarker levels across diverse demographic or health profiles.

Future Research Directions

To build on these findings, future studies should consider:

1. **Longitudinal Designs:** Tracking salivary biomarker levels over time to establish their predictive value for caries development and progression.
2. **Larger and Diverse Samples:** Including participants from varied socio-economic, ethnic, and geographical backgrounds to enhance generalizability.
3. **Mechanistic Studies:** Investigating the molecular pathways linking sialic acid and other biomarkers to microbial colonization, inflammation, and oral health outcomes.
4. **Interventional Research:** Assessing whether modifying salivary sialic acid levels through dietary, pharmacological, or behavioral interventions can improve oral health outcomes in children.

Conclusion

This study highlights the significant role of salivary sialic acid as a non-invasive biomarker for assessing oral health in children. The findings demonstrate its positive correlation with the Caries Index and its association with inflammation-related biomarkers such as IL-1β and cortisol, underscoring its diagnostic potential in detecting caries and early gingival inflammation. These results emphasize the utility of salivary biomarkers in pediatric dental practice, offering a simple, non-invasive method to monitor oral health and guide preventative interventions. Integrating such biomarkers into routine dental care could revolutionize early detection and personalized management of oral health in children, fostering better long-term outcomes.

Reference

1. Varki, A.; Gagneux, P. Multifarious roles of sialic acids in immunity. Ann. N. Y. Acad. Sci. 2012, 1253, 16–36.
2. Groeger, S.E.; Meyle, J. Oral Mucosal Epithelial Cells. Front. Immunol. 2019, 14, 208.
3. Varki, A. Sialic acids as a unique class of sugars. Glycobiology. 1993, 3(2), 97-130.
4. Tada, A.; Senpuku, H. The Impact of Oral Health on Respiratory Viral Infection. Dent. J. 2021, 13, 43.

5. Ali, S.A.; Telgi, R.L.; Tirth, A.; Tantry, I.Q.; Aleem, A. Lactate dehydrogenase and β-glucuronidase as salivary biochemical markers of periodontitis among smokers and non-smokers. Sultan Qaboos Univ. Med. J. 2018, 18, e318–e323.
6. Kinane, D.F.; Stathopoulou, P.G.; Papapanou, P.N. Periodontal diseases. Nat. Rev. Dis. Primers. 2017, 13, 17038.
7. Eguchi H., Ikeda Y., Ookawara T., Koyota S., Fujiwara N., Honke K., Wang P.G., Taniguchi N., Suzuki K. Modification of oligosaccharides by reactive oxygen species decreases sialyl lewis x-mediated cell adhesion. Glycobiology. 2005, 15, 1274-1282.
8. Cavas L., Arpinar P., Yurdakoc K. Possible interactions between antioxidant enzymes and free sialic acids in saliva: a preliminary study on elite judoists. Int. J. Sports Med. 2005, 26(10):832–835.
9. Jiang, Y.; Zhou, X.; Cheng, L.; Li, M. The impact of smoking on subgingival microflora: From periodontal health to disease. Front. Microbiol. 2020, 11, 66.
10. Chapple Iain L.C., Milward Mike R., Dietrich Thomas. The prevalence of inflammatory periodontitis is negatively associated with serum antioxidant concentrations. Am. Soc. Nutr. 2007, 137:657–664.
11. Dhotre Pradnya Shree, Suryakar Adinath N., Bhogade Rajashree B. Oxidative Stress in Periodontitis. Eur. J. Gen. Med. 2012;9(2):81–84.
12. Bawankar, P.V.; Kolte, A.P.; Kolte, R.A. Evaluation of stress, serum and salivary cortisol, and interleukin-1β levels in smokers and non-smokers with chronic periodontitis. J. Periodontol. 2018, 89, 1061–1068.
13. Beltrán-Aguilar Eugenio D., Eke Paul I., Thornton-Evans Gina, Petersen Poul E. Recording and surveillance systems for periodontal diseases. Periodontol 2000. 2012;60(1):40–53.
14. Srivastava, N.; Nayak, P.A.; Rana, S. Point of care: A novel approach to periodontal diagnosis—A review. J. Clin. Diagn. Res. 2017, 11, ZE01–ZE06.
15. Monje, A.; Amerio, E.; Farina, R.; Nart, J.; Ramanauskaite, A.; Renvert, S.; Roccuzzo, A.; Salvi, G.E.; Schwarz, F.; Trombelli, L.; et al. Significance of probing for monitoring peri-implant diseases. Int. J. Oral Implantol. 2021, 14, 385–399.
16. Jette Alan M., Feldman Henry A., Tennstedt Sharon L. Tobacco use: a modifiable risk factor for dental disease among the elderly. Am. J. Public Health. 1993;83(9):1305–1310.
17. Hendek, M.K.; Erdemir, E.O.; Kisa, U.; Ozcan, G. Effect of initial periodontal therapy on oxidative stress markers in gingival crevicular fluid, saliva, and serum in smokers and non-smokers with chronic periodontitis. J. Periodontol. 2015, 86, 273–282.
18. Arweiler, N.B.; Auschill, T.M.; Sculean, A. Patient self-care of periodontal pocket infections. Periodontol. 2000 2018, 76, 164–179.
19. Kobayashi, K.; Shono, C.; Mori, T.; Kitazawa, H.; Ota, N.; Kurebayashi, Y.; Suzuki, T. Protein-bound sialic acid in saliva contributes directly to salivary anti-influenza virus activity. Sci. Rep. 2022, 22, 6636.
20. Ali, S.A.; Telgi, R.L.; Tirth, A.; Tantry, I.Q.; Aleem, A. Lactate dehydrogenase and β-glucuronidase as salivary biochemical markers of periodontitis among smokers and non-smokers. Sultan Qaboos Univ. Med. J. 2018, 18, e318–e323.
21. Nazaryan, R.; Kryvenko, L. Salivary oxidative analysis and periodontal status in children with atopy. Interv. Med. Appl. Sci. 2017, 9, 199–203.
22. Naresh, C.K.; Rao, S.M.; Shetty, P.R.; Ranganath, V.; Patil, A.S.; Anu, A.J. Salivary antioxidant enzymes and lipid peroxidation product malondialdehyde and sialic acid levels

among smokers and nonsmokers with chronic periodontitis—A clinico-biochemical study. J. Fam. Med. Prim. Care. 2019, 8, 2960–2964.

23. Jawzaly, J., 2010. A PhD thesis, College of Dentistry, Hawler Medicinal University, Erbil, Iraq.