

The Effect of Dental Implants on Secretory IgA Level in Saliva

Taghreed Ahmed M Al-Kibsi¹, Fatima Mohammed Abdullal Al-Rohmi², Hassan Abdulwahab Al-Shamahy^{3,*}, Khaled A AL-Haddad⁴ Omar Ahmed Ismael Al-Dossary^{3,4}, and Basheer Hamed Hamood Al-Shameri⁵

¹Department of Oral and Maxillo-Facial Surgery, Faculty of Dentistry, Sana'a University, Republic of Yemen

²Department of Conservative Dentistry, Faculty of Dentistry, Sana'a University, Republic of Yemen

³Department of Basic Sciences, Faculty of Dentistry, Sana'a University, Republic of Yemen

⁴Orthodontics, Pedodontics and Prevention Department Faculty of Dentistry, Sana'a University, Yemen.

⁵Department of Restorative and Esthetic Dentistry, Faculty of Dentistry, Sana'a University, Republic of Yemen

***Corresponding author:** Hassan Abdulwahab Al-Shamahy, MD, PhD, Department of Basic Sciences, Faculty of Dentistry, Sana'a University, Republic of Yemen, Phone: +967-770299847; E-mail: shmahe@yemen.net.ye; al-shamahy@gust.edu.ye

Received: 03 Nov, 2023 | Accepted: 15 Dec, 2023 | Published: 21 Dec, 2023

Citation: Al-Kibsi TAM, Al-Rohmi FMA, Al-Shamahy HA, AL-Haddad KA, Al-Dossary OAI, et al. (2023) The Effect of Dental Implants on Secretory IgA Level in Saliva. Int J Dent Oral Health 9(2): dx.doi.org/10.16966/2378-7090.411

Copyright: © 2023 Al-Kibsi TAM, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Background and aims: The host immune response is altered by a series of physiological and pathological factors such as age, gender, inflammation, surgery, and medications. This study was conducted to evaluate differences in salivary IgA (S-IgA) levels in individuals who underwent dental implant surgery and compare them to individuals who were not exposed to dental treatments. S-IgA levels were determined at least 3 months after implant installation.

Methods: A total of 60 healthy individuals were included in the study; 30 participants received implant treatment (Implant Group) and were compared with 30 participants with no implant treatment as controls (Control Group). 1.5 ml of unstimulated saliva was obtained for all participants. The quantitative enzyme-linked immunosorbent assay (ELISA) technique was used for the measurement of salivary IgA levels.

Results: The age range of the participants in the implant group was 38-62 years, with a mean age of 47.9 years; 18 (60%) were males and 12 (40%) were females. The age range of the study's controls was 38-59 years, with a mean age \pm SD of 45.2 ± 5.2 years for 18 (60%) males and 12 (40%) females. The mean number of implants was 2.7 ± 0.83 , and the mean period after implant placement was 19.2 ± 8.2 months. A low sIgA level ($< 250 \mu\text{g/mL}$) was present in 10% of implant patients, but not in any cases in the control group. In contrast, only 6.7% of implant patients had this amount at a level greater than $351 \mu\text{g/mL}$, compared to 53.3% in the control group. The mean \pm SD for cases was $302.7 \pm 36.8 \mu\text{g/mL}$ versus $370.8 \pm 59.2 \mu\text{g/mL}$ for controls, indicating that all normal distribution values were significantly lower in the implant patient group compared to higher values in healthy controls. Males had higher normal values across the board in both groups (cases and controls). Male dental implant patients' mean and standard deviation (312.2 ± 38.3 vs. $408.2 \pm 42.2 \mu\text{g/mL}$) showed a statistically significant decrease. Female dental implant patients' mean and standard deviation (287.3 ± 30.6 vs. $314.7 \pm 27.6 \mu\text{g/mL}$) showed a statistically significant decrease. Overall, there was a significant decrease in the mean \pm SD of dental implant patients ($302.7 \pm 36.8 \mu\text{g/mL}$) versus the rising level in the total healthy control group ($370.8 \pm 36.8 \mu\text{g/mL}$). The observed averages of sIgA for the presence of peri-implant mucositis in the two independent samples (yes, no) differed significantly by 60.7, with a 95% confidence interval of 41.1-80.3, and this finding is very significant ($p < 0.0001$).

Conclusion: Salivary immunoglobulin A level values were significantly lower statistically in implant patients compared to the control group. The results, however, showed that there is a connection between lower sIgA levels in saliva and the development of pre-implant mucositis, meaning that low sIgA levels are risk factors for peri-implant mucositis or that peri-implant mucositis causes lower sIgA levels to be produced in mouth saliva.

Keywords: Dental immunity; Dental implants; Pre-implant mucositis; Saliva; Secretory IgA (s-IgA)

Introduction

White blood cells (B lymphocytes), secrete proteins (immunoglobulins (Ig) or antibodies), which circulate throughout the body and bind, eliminate, and/or neutralize pathogens such as bacteria and viruses. Opsonizing or coating foreign materials to designate them for elimination or neutralization is how this is accomplished [1]. Saliva can be used to assess secretory IgA (sIgA),

which is secreted at mucosal surfaces (such as the mouth, nose, and gastrointestinal system) [2]. The first line of defense against infection at these surfaces is sIgA, which works to stop microbial colonization [3,4]. It is thought to be especially important in the fight against upper respiratory tract infections (URTIs), which include the flu and colds, caused by bacteria and viruses [5]. However, the relationship between sIgA and health is complex and subject to both confounding and reverse causality. For example, in the case of oral health, low levels

of sIgA are a risk marker for dental caries, decay, and gingivitis [6] but elevated levels for a short period at the onset of infection are an indicator of current oral infection [7-9]. It has also previously been proven that low levels of sIgA in saliva may be a sign of illness and/or a sign of stress due to muscle stress or stress on the immune system due to chronic infections [10].

Salivary immunoglobulins provide good protection for the oral environment [11]. The most common secretory immunoglobulin in mixed saliva is immunoglobulin A (IgA). This secretory Ig guarantees the host's acquired immunity. This salivary antibody helps to keep oral surfaces intact. Mucous membranes and enamel are examples of these surfaces, which act as the body's first line of defense. S-IgA actively contributes to the inhibition of microbial attachment to the previously stated surfaces as well as any entrance into the deeper tissues. Furthermore, because this IgA is crucial for Ag-Ab responses, it keeps bacterial toxins such as lipopolysaccharide from penetrating deeper tissues [12,13].

The highest amount of salivary IgA (90%) is produced by the parotid and submandibular salivary glands, and the plasma cells found in these glands synthesize the antibody's dimeric form. The acini's epithelial cells release this IgA-dimer after it has been attached to a secretory particle and undergone proteolysis [14]. Serum and saliva create varying quantities of immunoglobulins. When there is an active disease or inflammation, these dynamics shift. Saliva is therefore a biomarker with diagnostic significance. In other circumstances, changes in oral immunity may result in a decrease in IgA production and this could be the cause of several oral pathologies [15].

A dental implant, often referred to as an endosseous implant or fixture, is a prosthesis that integrates with the jaw or skull's bone to support and function as an orthodontic anchor for dental prostheses such as crowns, bridges, dentures, and facial prostheses. The biological process of osseointegration, in which materials like titanium or zirconia develop a close link with the bone, is the foundation of contemporary dental implants. After positioning the implant fixture to maximize osseointegration, a dental prosthesis is affixed. Before the dental prosthetic (a tooth, bridge, or denture) is affixed to the implant or an abutment is positioned to support a dental prosthetic/crown, osseointegration must take a varied period of healing time [16,17].

It was reported that during the healing period needed for osseointegration, there was a variable degree of change in the oral conditions, such as changes in the colonization of oral microorganisms and oral s-IgA level, before either the dental prosthetic (a tooth, bridge, or denture) is attached to the implant or an abutment is placed to hold a dental prosthetic/crown [16,17]. Implant success or failure is largely determined by the thickness and condition of the bone and gingival tissues surrounding the implant, as well as by factors such as serum immunoglobulin A (sIgA), gingival sulcus cytokines, oral microbial balance, patient health, and medications that alter the likelihood of osseointegration [18-20]. It is also affected by how much stress the fixture and implant will experience during function. Given the potential for considerable biomechanical forces during chewing, carefully considering the location and quantity of implants is essential to the prosthetic device's long-term viability [21]. Healthy gingiva and bone are necessary for the long-term viability of osseointegrated dental implants [22].

There are three categories of risks and complications associated with implant therapy: those that arise during surgery (like excessive bleeding or nerve injury), those that arise within the first six months (like infection and osseointegration failure), and those that arise over

an extended period (like peri-implantitis and mechanical failures) [22]. A well-integrated implant with suitable biomechanical stresses can have survival rates of 93% to 98% for more than five years in the presence of healthy tissues [22-24]. Prosthetic teeth can also have life spans of 10 to 15 years. In 16 to 20 years, 52% to 76% of implants survive without issues or revisions, according to long-term studies; difficulties can arise as much as 48% of the time [25,26]. This study was conducted to evaluate differences in salivary IgA (S-IgA) levels in individuals who underwent dental implant surgery and compare them to individuals who were not exposed to dental treatments. S-IgA levels were determined at least 3 months after implant installation.

Materials and Methods

Study design

This is a cross-sectional clinical study comparing S-IgA levels in healthy adults who were treated with dental implants 3 months or more ago; and healthy adults who did not undergo any dental treatment. A total of 30 healthy subjects (aged 38-62 years) were recruited as transplant cases in this study. The comparison group contained 30 people who were similar in gender and age group to the cases. Group A (fixed dental implant group) and Group B (group without dental treatments). 2 ml of saliva was obtained from both groups. Enzyme-linked immunosorbent assay (ELISA) technology was used to measure IgA levels in saliva.

Ethical consideration: The Medical Ethics and Research Committee of Sana'a University's Faculty of Medicine and Health Sciences approved this study under number 2988, dated October 23, 2022. Every process followed the ethical guidelines set forth by the review committee. Written informed consent was given by the selected individuals.

Participants were included based on the following criteria: free from any systemic diseases, free from any apparent genetic disorders or dental anomalies, their age ranged between 38 to 62 years, as this is the main target group for dental implants in Yemen, caries-free and those who were able to maintain good oral hygiene. For the implant group, participants who had placed their implants at least 3 months ago were included. Individuals, who were below the age of 38, those who were undergoing any other dental treatment during the study period, or those with bad oral hygiene were excluded.

Collection of saliva

All participants were asked not to eat or drink 1 hour before unstimulated saliva was collected. To prevent any variation in saliva concentrations due to the influence of circadian rhythm, a morning appointment was scheduled (10-11 a.m.) [27]. All saliva samples were collected in sterile containers, and saliva was collected by the passive saliva method; the participant was asked to collect saliva on the floor of the mouth and then spit it into a pre-labeled bag Sterile container. Then 1.5 ml of saliva was taken with a dropper and stored in test tubes. Saliva samples were stored on dry ice and immediately transported to the immunology department laboratory at the National Public Health Laboratories in Sana'a where they were kept frozen in a deep freezer at -20°C.

Method of detection of S-IgA in saliva

The S-IgA levels in saliva were measured by ELISA (Enzyme-Linked Immunosorbent Assay) Kit in the immunology department laboratory at the National Public Health Laboratories in Sana'a.

Statistical analysis: The data analysis program utilized was Epi-info Statistics version 7. For quantitative data, descriptive statistics

were shown as mean \pm (standard deviation SD), minimum, maximum, and range; for qualitative data, they were shown as number and percentage. For quantitative variables, inferential analyses were performed using the paired t-test when there were two dependent groups with parametric data and the independent t-test when there were two independent groups with parametric data. The Chi square test was used to perform inferential analysis for independent variables in qualitative data that involved differences in proportions. P values less than 0.050 are considered significant, whereas values more than 0.050 are considered non-significant.

Results

The general characteristics of the study participants implant group and control group are shown in table 1. The age range of participants in the implant group was 38-62 years, with a mean age \pm SD of 47.9 ± 7.2 years, 18 (60%) were males and 12 (40%) were females. The age range of participants in the control group was 38-59 years, with a mean age \pm SD of 45.2 ± 5.2 years, 18 (60%) were males and 12 (40%) were females. The mean number of implants was 2.7 ± 0.83 , and the mean period after implant placement was 19.2 ± 8.2 months. Table 2 displays secretory IgA concentrations in unstimulated saliva for both implant and control groups. A low sIg A level ($<250 \mu\text{g/mL}$) was present in 10% of the participants in the implant group only ($p<0.0001$). The percentage of participants that showed sIgA levels between 250 and $300 \mu\text{g/mL}$ were 16.7% and 36.7% in the control and implant groups respectively and this variation was significant ($p=0.003$). sIgA levels greater than $351 \mu\text{g/mL}$ were found in only 6.7% of implant participants compared to 53.3% in the control group ($p<0.0001$). The mean sIgA concentrations were $302.7 \pm 36.8 \text{ g/mL}$ for the implant group and $370.8 \pm 59.2 \mu\text{g/mL}$ for the control group and the variation was statistically significant ($p<0.0001$), indicating that

sIgA concentrations were always significantly lower in the implant group compared to the control group.

Table 3 displays the influence of gender on the mean concentrations of s IgA in the unstimulated saliva in both implant and control groups. In general, and for both groups, males showed higher sIgA concentrations (levels) than in females. Similarly, for both genders, sIgA concentrations were higher in the control group than in the implant group ($p<0.0001$).

The impact of pre-implant mucositis on sIgA concentrations ($\mu\text{g/mL}$) in the unstimulated saliva of implanted patients is shown in Table 4. The observed averages of sIgA for the presence of peri-implant mucositis in the two independent samples (Yes, No) differed significantly by 60.7, with a 95% confidence interval of 41.1-80.3, and this finding is very significant ($p<0.0001$). This shows a connection between lower sIgA levels in saliva and the development of pre-implant mucositis (low sIgA levels are risk factors for peri-implant mucositis), or that peri-implant mucositis causes lower sIgA levels to be produced in mouth saliva.

Discussion

One of the numerous secretions that is primarily high in the secretory immunoglobulin A isotype is saliva. Since saliva is continuously secreted by salivary glands to flush the oral cavity clean, S-IgA is thought to be the first line of defense against microorganisms. There is evidence that native oral microbiota pathogens have been found to coat S-IgA [15]. The current investigation is unique since there is currently little information on the assessment of S-IgA after the placement of dental implants. The fact that this is the first study to disclose s-IgA levels among Yemeni participants is another oddity.

In the current investigation, 10% of implant patients had a low sIg A level ($<250 \mu\text{g/mL}$), while the control group did not exhibit this condition in any cases. 36.7% of implant patients exhibited sIgA levels between 250 and $300 \mu\text{g/mL}$, compared to 16.7% of the control group. Compared to 53.3% in the control group, only 6.7% of implant patients had this quantity at a level of more than $351 \mu\text{g/mL}$. The average \pm standard deviation for the cases was $302.7 \pm 36.8 \text{ g/mL}$, while the controls had a mean of $370.8 \pm 59.2 \mu\text{g/mL}$. This suggests that the implant patient group had much lower normal distribution values than the healthy control group. These findings suggested that the immune system may be overworked throughout the implant process. This is explained by the fact that the mucosa-associated lymphoid tissue (MALT), which contains almost half of the body's lymphocyte population, forms the basis of the mucosal immune system, which is the largest immune system in the body [28]. Because MALT cells are constantly exposed to antigens, they are found strewn across the surfaces of all mucosal tissues and serve as the basis for several immune responses. Additionally, because the MALT structure circulates immune cells between the mucosa and glands, immune responses produced in one MALT structure will impact the immunity of the entire MALT [29]. MALT comprises, among others, the salivary duct-associated lymphoid tissue (DALT) and the gut-associated lymphoid tissue (GALT) [28]. Dental implants and its chronic stress on the bone and body in general due to implants might lead to adverse effects on health, such as oxidative stress [30], as well as immune stress, and mucus membrane alteration. This hypothesis could be proven by the results of the effect of intense exercises for long periods on the health of the secretory immune system by lowering the level of s-IgA in all secretory body fluid including saliva [31,32]. Focusing on mucosal humoral immunity, the effect of dental implant also depends on the number and period after implant placement, which reduces

Table 1: General characteristics of participants in the implant and control groups group.

Characters	Cases	Controls
	Number (%)	Number (%)
Sex		
Male	18 (60)	18 (60)
Female	12 (40)	12 (40)
Age group in Years		
≤ 45	9 (30)	16 (53.3)
46-55	16 (53.3)	12 (40)
≥ 56	5 (16.7)	2 (6.7)
Mean age	47.9 Years	45.2 Years
SD	7.2 Years	5.2 Years
Min-Max	38-62 Years	38-59 Years
Number of implants		
1 implant	1 (3.3)	
2 implants	12 (40)	
3 implants	13 (43.3)	
4 implants	3 (10)	
≥ 5 implants	1 (3.3)	
Mean \pm SD	2.7 ± 0.83 implants	
Period after implant placement		
≤ 12 months	7 (23.3)	
13-24 months	13 (43.3)	
≥ 25 months	10 (33.3)	
Mean \pm SD	19.2 ± 8.2 months	

Table 2: The concentrations of secretory IgA in the non-stimulated saliva of implanted patients compared with healthy controls.

Concentration	Implant group n=30		Control group n=30		Z-statistic	P
	No	%	No	%		
<250 µg/ml	3	10	0	0	4.9	<0.0001
250-300 µg/ml	11	36.7	5	16.7	2.9	0.003
301-351 µg/ml	14	46.7	9	30	1.9	0.045
>351 µg/ml	2	6.7	16	53.3	5.1	<0.0001
Mean	302.7 µg/ml		370.8 µg/ml		5.3*	<0.0001
SD	36.8 µg/ml		59.2 µg/ml			
SE	6.7 µg/ml		18.8 µg/ml			
Median	305.3 µg/ml		366.6 µg/ml			
Mode	312.2 µg/ml		439.9 µg/ml			
Min- Max	241.9-399.4 µg/ml		265.5-445.5 µg/ml			

*T-test

Table 3: Effect of gender on mean concentrations of secretory IgA in unstimulated saliva in both implant and control groups.

Sex	Implant group n=30		Control group n=30		P
	Mean ± SD µg/ml	Min-Max µg/ml	Mean ± SD µg/ml	Min-Max µg/ml	
Male	312.2 ± 38.3	255.5-399.4	408.2 ± 42.2	289.9-445.5	<0.0001
Female	288.3 ± 30.6	241.9-326.6	314.7 ± 27.6	265.5-345.5	0.0009
Average	302.7 ± 36.8	241.9-399.4	370.8 ± 36.8	265.5-445.5	<0.0001

Table 4: Concentrations of secretory IgA (µg/ml) in the unstimulated saliva of implant participants with and without peri-mucositis.

Peri-implant mucositis	Dental implant n=30				
	Mean ± SD	Min-Max	Difference	95%CI	p
Yes n=9	260.2 ± 13.2	241.9-280	60.7	41.1 -80.3	<0.0001
No n=21	320.9 ± 27.2	281.6-399.4			

host protection accordingly and leads to an increased risk of infection of the dental implant and the occurrence of oral and upper respiratory tract infections (URTIs).

Males in the current study showed generally higher normal values in both the case and control groups ($p < 0.0001$). The mean and standard deviation of male dental implant patients (312.2 ± 38.3 vs. 408.2 ± 42.2 µg/ml) decreased statistically significantly ($p < 0.0001$). The mean and standard deviation of female dental implant patients revealed a statistically significant decrease ($p = 0.0009$): 288.3 ± 30.6 vs. 314.7 ± 27.6 µg/ml. Overall, the mean ± SD of dental implant patients decreased significantly (302.7 ± 36.8 µg/ml) compared to the rising level in the entire healthy control group (370.8 ± 36.8 µg/ml) ($p < 0.0001$). In all the saliva sIgA tests, males were found to have greater levels of sIgA than females. This finding is in line with previous studies that found younger males to have significantly higher IgA mean values (p less than 0.05) than females [27,33,34].

Conversely, the current investigation revealed a highly significant ($p < 0.0001$) difference in the observed averages of sIgA for the presence of peri-implant mucositis between the two independent samples (Yes, No), with a 95% confidence interval of 41.1-80.3. This may suggest an association between pre-implant mucositis and low salivary sIgA levels

(low sIgA levels may be risk factors for peri-implant mucositis) or that low salivary sIgA levels may be a result of peri-implant mucositis, but a true association cannot be confirmed. Unless other parameters related to mucositis are evaluated. The direction of this potential association is consistent with the critical function of sIgA in defense of infection [3,4].

In the current investigation, participants (case and control) were told to collect saliva on the floor of their mouths and then spit it into sterile containers containing 1.5 ml of saliva, which was used for testing. An hour before saliva collection, volunteers were told not to eat or drink anything but water and to rinse their mouths only with water. By doing this, the likelihood of food particles or any other type of salivary stimulation was reduced. Since it is commonly known that the circadian rhythm affects both the flow rate and concentration of saliva, all samples were taken between 10 and 11 am to guarantee that there was no variation in the concentration of saliva [35].

The ELISA method was used to measure the levels of S-IgA. The following are some of the advantages of ELISA: 1. It is very sensitive; 2. It does not require radioisotopes (radioactive substances) [36]; and 3. It is specific to analyte detection.

The rationale for selecting a group of healthy adults with implants

was that their antigenic action had been shown to have a strong antigenic stimulus represented by dental implants which are a foreign part of the patient's body [37]. The focus of saliva studies globally has still been on evaluating the effect on salivary secretion rates and IgA levels caused by infections, systemic diseases, surgery, medications, sports, and various syndromes with gene mutation. Despite these studies, the mutual relationship between IgA and dental implants is the least researched among them, and therefore the relationship between IgA and dental implants must be studied extensively.

Limitations of the Study

The limitation of this study includes the small sample size, and that the collection of saliva was done only once with no follow-up periods. A prospective study involving a greater number of patients to investigate how implants affect the oral cavity's level of s-IgA and follow-up study should be conducted.

Conclusion

Salivary immunoglobulin A level values were significantly lower statistically in implant patients compared to the control group. The results, however, showed that there is a connection between lower sIgA levels in saliva and the development of pre-implant mucositis, meaning that low sIgA levels are risk factors for peri-implant mucositis or that peri-implant mucositis causes lower sIgA levels to be produced in mouth saliva.

References

- Phillips AC, Carroll D, Drayson MT, Der G (2015) Salivary Immunoglobulin A Secretion Rate Is Negatively Associated with Cancer Mortality: The West of Scotland Twenty-07 Study. *PLoS ONE* 10: e0145083.
- Hood LE, Weissman IL, Wood WB (1978) *Immunology*. Menlo Park, CA: Benjamin/Cummings.
- Teeuw W, Bosch JA, Veerman EC, Amerongen AV (2004) Neuroendocrine regulation of salivary IgA synthesis and secretion: implications for oral health. *Biol Chem* 385: 1137-1146.
- Mestecky J (1993) Saliva as a manifestation of the common mucosal immune system. *Ann N Y Acad Sci* 694: 184-194.
- Gleeson M (2000) Mucosal immune responses and risk of respiratory illness in elite athletes. *Exerc Immunol Rev* 6: 5-42.
- Senpuku H, Miyazaki H, Yoneda S, Yoshihara A, Tada A (2010) A quick statistically accurate diagnosis for caries risk in the elderly. *Clin Lab* 56: 505-512.
- Rashkova MP, Toncheva AA (2010) Gingival disease and secretory immunoglobulin a in non-stimulated saliva in children. *Folia Med (Plovdiv)* 52: 48-55.
- Janket S, Meurman JH, Baird AE, Qvarnstrom M, Nuutinen P, et al. (2010) Salivary immunoglobulins and prevalent coronary artery disease. *J Dent Res* 89: 389-394.
- Walsh NP, Gleeson M, Shephard RJ, Woods JA, Bishop NC, et al. (2011) Position statement. Part one: Immune function and exercise. *Exerc Immunol Rev* 17: 6-63.
- Gallagher S, Phillips AC, Evans P, Der G, Hunt K, et al. (2008) Caregiving is associated with low secretion rates of immunoglobulin A in saliva. *Brain Behav Immun* 22: 565-572.
- Dawes C (1993) Considerations in the development of diagnostic tests on saliva. *Ann N Y Acad Sci* 694: 265-269.
- Bokor-Bratic M (2000) Clinical significance of analysis of immunoglobulin A levels in saliva. *Med Pregl* 53: 164-168.
- Dodds MW, Jonson DA, Yeh CK (2005) Health benefits of saliva: A review. *J Dent* 33: 223-233.
- Bernimoulin JP (2003) Recent concepts in plaque formation. *J Clin Periodontol* 30: 7-9.
- Marcotte H, Lavoie MC (1998) Oral microbial ecology and the role of salivary immunoglobulin A. *Microbiol Mol Biol Rev* 62: 71-109.
- Sharafuddin AH, Alshameri BH, AL-Haddad KA, Al-Najhi MMA, Al-Shamahy HA (2023) The effect of dental implants on increasing the colonization rate of aerobic bacteria in the oral cavity. *Universal Journal of Pharmaceutical Research* 8: 1-8.
- Al-Hamzi MA, Sharafuddin AH, Al-Shameri BHH, AL-Haddad KA, Al-Najhi MM, et al. (2023) The effect of dental implants on aerobic bacteria colonization in the oral cavity and the antibiotic profile of common isolated aerobic bacteria. *Universal Journal of Pharmaceutical Research* 8: 1-6.
- Al-dossary O A I, Al-Kholani ALM, AL-Haddad KA, Al-Najhi MM, Al-Shamahy HA, et al. (2022) Interleukin-1 β levels in the human gingival sulcus: rates and factors affecting its levels in healthy subjects. *Universal Journal of Pharmaceutical Research* 7: 1-6.
- Almotareb FL, Al-Shameri BHH, Al-Najhi MMA, Al-dossary OAI, Al-Shamahy HA (2023) Increase of Transforming Growth Factor-Beta 1 in Gingival Crevicular Fluid during Human Orthodontic Tooth Movement. *J Oral Med and Dent Res* 4:1-09.
- Al-Shamahy HA, Al-dossary OAI, Al-Adhami IAA, Al-dhorae K (2023) Tumor necrosis alpha (tnf- α) levels in the human gingival sulcus: rates and factors affecting its levels in healthy subjects.
- Papaspyridakos P, Mokti M, Chen CJ, Benic GI, Gallucci GO, et al. (2014) Implant and prosthodontic survival rates with implant fixed complete dental prostheses in the edentulous mandible after at least 5 years: a systematic review. *Clin Implant Dent Relat Res* 16: 705-717.
- Berglundh T, Persson L, Klinge B (2002) A systematic review of the incidence of biological and technical complications in implant dentistry reported in prospective longitudinal studies of at least 5 years. *J Clin Periodontol* 29: 197-212, Discussion 232-233.
- Pjetursson BE, Thoma D, Jung R, Zwahlen M, Zembic A (2012) A systematic review of the survival and complication rates of implant-supported fixed dental prostheses (FDPs) after a mean observation period of at least 5 years. *Clin Oral Implants Res* 23: 22-38.
- Bozini T, Petridis H, Garefis K, Garefis P (2011) A meta-analysis of prosthodontic complication rates of implant-supported fixed dental prostheses in edentulous patients after an observation period of at least 5 years. *Int J Oral Maxillofac Implants* 26: 304-318.
- Simonis P, Dufour T, Tenenbaum H (2010) Long-term implant survival and success: a 10-16-year follow-up of non-submerged dental implants. *Clin Oral Implants Res* 21: 772-777.
- Chappuis V, Buser R, Bragger U, Bornstein MM, Salvi GE, et al. (2013) Long-term outcomes of dental implants with a titanium plasma-sprayed surface: a 20-year prospective case series study in partially edentulous patients. *Clin Implant Dent Relat Res* 15: 780-790.
- Jha A, Singh R, Jha S, Singh S, Chawla R, et al. (2020) Comparative evaluation of salivary immunoglobulin A levels between pedodontic subjects. *J Family Med Prim Care* 9: 2052-2055.
- Cesta M F (2006) Normal structure, function, and histology of mucosa-associated lymphoid tissue. *Toxicol. Pathol* 34: 599-608.

29. Brandtzaeg P (2013) Secretory immunity with special reference to the oral cavity. *J Oral Microbiol* 5: 1-24.
30. Pingitore A, Lima GP, Mastorci F, Quinones A, Iervasi G, et al. (2015) Exercise and oxidative stress: Potential effects of antioxidant dietary strategies in sports. *Nutrition* 31: 916-922.
31. Costa RJS, Snipe RMJ, Kitic CM, Gibson PR (2017) Systematic review: Exercise-induced gastrointestinal syndrome-implications for health and intestinal disease. *Aliment Pharmacol Ther* 46: 246-265.
32. Vitti A, Nikolaidis PT, Villiger E, Onywera V, Knechtel B (2020) The, "New York City Marathon": Participation and performance trends of 1.2M runners during half-century. *Res Sport Med* 28: 121-137.
33. Stoica GH, Samborschi C, Michiu V (1978) Influence of sex and age on serum immunoglobulin concentrations in healthy subjects. *Med Interne* 16: 23-31.
34. Corega C, Vaida L, Rigoni G, Albanese M, D'Agostino A, et al. (2013) Salivary level of IgA in healthy subjects undergoing active orthodontic treatment. *Minerva Stomatol* 62: 11-16.
35. Evans E, Hayes C, Palmer C, Bermudez O, Cohen S, et al. (2013) Dietary intake and severe early childhood caries in low income, young children. *J Acad Nutr Diet* 2: 119-124.
36. De La Rica R, Stevens M (2012) Plasmonic ELISA for the ultrasensitive detection of disease biomarkers with the naked eye. *Nat Nanotechnol* 7: 821-824.
37. Kasacka I, Szarmach IJ, Buczek P, Tankiewicz A, Pawlak D (2006) Preliminary evaluation of saliva composition in allergic patients subjected to orthodontic treatment, morphological examination. *Adv Med Sci* 51: 55-58.