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ORIGINAL RESEARCH

TO EVALUATE RISK MARKERS OF CARDIOVASCULAR DISEASE AND IT'S ASSOCIATION WITH PERI IMPLANT DISEASE- A CLINICAL STUDY.

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Abstract

Background: The goal of this research was to determine whether measures used to assess a person's overall cardiovascular health, known as cardiovascular risk markers, are associated with peri-implant disorders in patients with dental implants.

Methods: This clinical study was conducted on 40 subjects having peri-implantitis and peri-implant mucositis. Clinical examination was carried out to record the peri-implant probing pocket depths. Serum biochemical risk factors such as low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, triglycerides, total cholesterol, vitamin D, and uric acid, which are considered as Cardiovascular risk indicators were assessed.

Results: The peri-implantitis group had the lowest KMW (keratinized mucosa width). The peri-implantitis groups had considerably higher triglyceride and uric acid levels than the other groups. In the group with peri-implantitis, the lowest amounts of vitamin D were found. A positive correlation was discovered between triglyceride and uric acid levels and peri-implant disorders.

Conclusion: The risk for peri-implant and cardiovascular disease is elevated in people with high triglyceride and uric acid levels. Patients' serum biomarkers should be examined before undergoing dental implant surgery.

Keywords: Peri-implantitis, Risk factors, Triglycerides, Uric acid, Vitamin D

Introduction

The different ways in which individuals with missing teeth might benefit from dental implants include partial and total edentulism. While implants are rather successful, the incidence of peri-implant diseases is on the rise. [1] These two infectious peri-implant illnesses

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are referred to as peri-implant mucositis and peri-implantitis. Reversible infection of soft tissues around an implant is referred to as "implanted gingivitis" (or sometimes as "peri-implantitis"), whereas bone loss around the implant is called "periodontitis."[2] Treatment for peri-implant diseases has not yet been discovered. Peri-implant infections are unavoidable; hence it is necessary to take prevention measures before to their development. As a result, the first stage in the development of efficient preventative techniques is the identification of risk variables.[3] According to certain studies, the presence of several risk factors/indicators raises the risk of peri-implant mucositis and peri-implantitis. [4]There are a number of risk factors that may contribute to peri-implant disease, including smoking, periodontitis, poor dental hygiene, diabetes, alcohol usage, heredity, and other relevant risks for prosthetic and implant surface features. [5,6]

Over the years, certain studies have examined the occurrence of both medical conditions and peri-implantitis together.[7,8,9] In addition to the high triglycerides and cholesterol and cardiovascular sickness, research shows that bone cells are adversely affected by high triglycerides and cholesterol and cardiovascular disorders. Dyslipidemia has been associated with reduced bone metabolism and osseointegration of dental implants.[10] Hyperlipidemia and bone tissue metabolism have been shown to be associated with the processes that lead to low bone mineral density, increased osteoclast count, and reduced osteoblastic activity.[11,12] Because cholesterol, vitamin D, and statins are all connected, we can expect to see a significant correlation between them. As is the case with cholesterol, 7-dehydrocholesterol is a precursor to vitamin D, also known as the "sunshine vitamin."[13] Osteoblasts create more extracellular matrix proteins in the bone when activated by vitamin D, which activates osteoclasts to synthesize it.[14] All of these risk factors for peri-implantitis are connected, including hypertension, dyslipidemia with high LDL and triglyceride levels, low HDL levels, and vitamin D deficiency. An increased risk of atherosclerosis is also associated with changes in lipoprotein levels, such as reduced HDL and greater LDL and triglyceride levels.[15,16,17] An enhanced risk of cardiovascular disease and death has also been found in trials with subjects with insufficient levels of vitamin D.[18,19,20] Periodontal disease and cardiovascular disease have been connected to elevated serum lipid levels and lower serum 25-hydroxyvitamin D levels. [21,22,23,24]

As a result, greater blood uric acid levels have been connected to increased oxidative stress and inflammation. [25, 26] Elevated blood uric acid levels have been connected to hypertension, atherosclerosis, renal illness, obesity, insulin resistance, and dyslipidemia in various investigations. [27] We are not aware of any investigations on uric acid levels in patients with peri-implant diseases in the literature.

The goal of this study was to determine if there were any risk factors for peri-implant problems based on serum biochemical parameters in persons who received dental implants, which are cardiovascular disease risk markers.

Materials and Methods

This cross-sectional study was conducted following all the ethical principles. The study adheres to the Declaration of Helsinki's Ethical guidelines. The study contained 40 persons with peri-implantitis, 45 people with peri-implant mucositis, and 40 healthy adults as a control group. Everyone signed an informed consent form.

The 2017 World Workshop Classification of Periodontal and Peri-Implant Diseases and Conditions [28] was used to diagnose peri-implant diseases.

Peri-implant health was ascertained by a procedure that could be described as “mild probing” with the goal of assessing clinical inflammation, haemorrhage, and/or suppuration as well as the absence of bone loss on radiography. To assess for peri-implant mucositis, the examiner found that when bleeding and/or suppuration were present with gentle probing and that there

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was no bone loss detected on the radiographs. This procedure may reveal persons with peri-implantitis due to the presence of bleeding and/or suppuration, as well as intra-osseous bone levels of at least 3 mm apical of the most coronal component of the implant. In order to participate in the trial, all patients had to have at least one dental implant in situ for at least 36 months. Histories of cancer, radiation, chemotherapy, or immunodeficiency within the previous four years were all exclusion factors to be included in this study.

Clinical and radiological examination of the peri-implant tissues

The same blinded examiner performed all clinical and radiographic examinations. Clinical examination was done with a standardized plastic periodontal probe (Colorvue: Hu-Friedy, Chicago, IL, USA). Patients were frequently examined, monitored and screened by clinical and radiological means. Diagnostic images were obtained, using digital periapical radiography, in order to reveal any possible dangers. Record of clinical parameters for peri-implant were as follows: probing depth (PD) at 6 sites per teeth and implant, gingival index (GI), plaque index (PI), bleeding on probing (BOP) and if bleeding is present and GI equal to BOP if no bleeding is seen (KMW). To calibrate the procedure, the researcher did the calibrating. The examiner was calibrated using ten peri-implantitis patients who were not included in this study. This was done over two days and at least 60 minutes in between probing measurements were maintained to ensure dependability, and the kappa value used to evaluate examiners' consistency was 0.89, showing a good degree of agreement.

Medical Examination

After having fasted for 12 hours, subjects' blood was collected and the levels of HDL, LDL cholesterol, total cholesterol, triglycerides, vitamin D, and uric acid were determined. We also analyzed components such as WBC, Hb, neutrophil, MCV, MPV and PCT in the complete blood count.

Statistical analysis

All data analyses were completed using SPSS 18.0 Statistical Package Software for Windows OS (SPSS Inc., Chicago, Illinois, USA). In order to compare data at $\alpha = 0.05$ with an 85% power value, at least 30 samples were necessary per group.

A common measure of quantity, the mean, the standard deviation (SD), and the median were employed to express quantitative amounts (IQR). One-way ANOVA was used on normally distributed variables, whereas Kruskal-Wallis test was used on non-normally distributed variables. The Chi-squared test was used on qualitative variables. Age was controlled while comparing the biochemical indicators of the three groups, and ANCOVA was utilized for that comparison.

To investigate the link between triglycerides, vitamin D, uric acid, GI, PD, and BOP, Spearman's correlation analysis was employed. When the level of significance was set at 0.05, all of the data was considered significant.

Results

The study enrolled a total of 125 patients. The distribution of peri-implant parameters by age, gender, medical history, implant number, implant position, prosthesis type, and antagonists is shown in Table1. Table 1 shows that there was no difference in the frequency of smoking and alcohol consumption between the three groups. The group with peri-implantitis had the lowest KMW (p 0.001).

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Table 1: Characteristics of the study groups

	Peri-implantitis group (*N* = 40)	**Peri-implant mucositis group (*N* = 45)**	**Healthy implant group (*N* = 40)**	***P* value**
Age (median (IQR)	50	54	49	0.18
Gender (female/male)	33/7	22/23	30/10	
Smoke	8	3	3	0.33
Alcohol	5	0	0	0.22
PD	5.3	3	2.6	< 0.01
PI	2 .2	2.1	0	< 0.01
GI	2.0	2.0	0	< 0.01
BOP	71.6	100	0	< 0.01
KMW	1.1	2.1	2.9	< 0.01
Number of implants	55	49	53	

N number of participants, *PD* probing depth, *PI* plaque index, *GI* gingival index, *BOP* bleeding on probing, *KMW* keratinized mucosa width, *IQR* interquartile range

Table 2 shows that the peri-implantitis patients showed significantly increased triglyceride as well as uric acid values than in the other groups. The P value in the peri-implantitis group was higher after age adjustment (Table 2). Vitamin D levels were observed to be lowest in the peri-implantitis group. It was discovered that triglyceride levels as well as clinical indications have a positive association. There was also a link between uric acid and the GI, PD, BOP, and KMW values (Table 3). Levels Of vitamin D were expected to have a strong connection (r = 0.191, p = 0.020) with GI readings.

Table 2: Biochemical parameters in the study groups

	Peri-implantitis (*N* = 40)	**Peri-implant mucositis (*N* = 45)**	**Healthy implant (*N* = 40)**	***P* value**	***P* value (age-adjusted)**
LDL-C (mean ± Sd)	128.2 ± 22.1	109.5 ± 22.5	112.1 ± 23.4	0.45	0.57
HDL-C	47	45	47	0.07	0.07
Triglyceride	122	115	85	< 0.01	< 0.01
TOTAL-C (mean ± Sd)	203.4 ± 29.1	178.6 ± 24.3	197 ± 31.3	0.15	0.32
Vitamin-D	13.8	13.5	16.9	0.04	0.04
Uric acid	6.1	4.1	3.0	< 0.01	< 0.01

N number of participants, *LDL-C* low-density lipoprotein cholesterol, *HDL-C* high-density lipoprotein cholesterol, *TOTAL-C* total cholesterol,

Table 3: Spearman correlation analysis among biochemical and peri-implant parameters

	GI	**PD**	**BOP**	**KMW**
Uric acid	$r = 0.23$, $p = 0.06$	$r = 0.46$, $p = < 0.01$	$r = 0.23$, $p = 0.08$	$r = -0.24$ $p = 0.06$
Vitamin D	$r = -0.19$, $p = 0.02$	$r = 0.06$, $p = 0.46$	$r = -0.13$, $p = 0.09$	$r = 0.04$ $p = 0.62$
Triglyceride	$r = 0.26$, $p = 0.01$	$r = 0.33$, $p = < 0.01$	$r = 0.22$, $p = 0.06$	$r = -0.21$ $p = 0.01$

GI gingival index, *PD* probing depth, *BOP* bleeding on probing, *KMW* keratinized mucosa width

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Discussion

Epidemiological and laboratory studies have established a connection between increased plasma concentrations of the cytokines TNF- and IL-1 and changes in lipid metabolism.[29,30,31] Once exposed to microbes/endotoxins, TNF- and IL-1 can trigger increases in triglycerides, LDL, and free fatty acids.[32] Periodontal and peri-implant disease also shows high levels of these cytokines.[33,34] A few researches have suggested that hypercholesterolemia may be connected to dental implant osseointegration.[35,36] The authors suggest that serum cholesterol levels be evaluated prior to any surgery for implant and bone graft failure, as hypercholesterolemia has been associated with an increased risk of failure. [10] Heterogeneous lipoprotein subclasses (low HDL, high LDL, and triglyceride levels) are all recognized risk factors for coronary artery disease.[37,38] Some research studies have claimed a connection between peri-implantitis and cardiovascular illness.[39, 40] however that claim has not been proven. To analyse these biochemical indicators as cardiovascular disease risk factors and probable risk factors in patients with peri-implant disorders, we carried out this study. In contrast to the claims made in the marketing materials, our research found no statistically significant variations in LDL-C, HDL-C, or TOTAL-C across the groups. We found that subjects in the peri-implantitis group had increased triglyceride and uric acid levels. In our investigation, we found that the levels of uric acid, triglycerides, and gastric inhibitory polypeptide, and GI, PD, BOP, and KMW values were all in a positive correlation.

The links between peri-implantitis and cardiovascular disease may be related to the fact that both peri-implantitis and cardiovascular disease are associated with higher plasma lipid levels. Peri-implant disease has been linked to elevated total cholesterol and triglyceride levels in a research by Vohra et al. [41] Researchers such as Alasqah et al. [42]found that levels of low-density lipoprotein and total cholesterol, as well as indications of peri-implant disease such as PI, BOP, and crestal bone loss, were higher in obese patients compared to those who were not fat. An additional investigation showed that, after adjusting for metabolic indicators such as total cholesterol and triglycerides, obese patients had statistically significant lower marginal bone loss.[43] Plasma lipid levels have been found to be strongly linked to periodontal disease severity in multiple investigations.[44,45] A positive association was found between triglyceride levels and GI, PD, and BOP levels in our experiment. Hyperlipidaemia and peri-implantitis have a bidirectional association. Lachmann et al. [40] discovered that persons with cardiovascular illness, implants, and other severe comorbidities have a high incidence of intermediate and advanced plaques and BOP. Previous research found an odds ratio of 8.7 for peri-implantitis and cardiovascular disease in participants who were additionally considering age, smoking, and gender [39].

Despite there being a small number of preclinical studies which show that vitamin D supplementation can successfully speed up the healing of peri-implant bone, it is not yet known if vitamin D supplementation can actually help with this process. [46,47,48] Peri-implantitis and peri-implant mucositis are two distinct conditions, but our study found that vitamin D levels were lower in the peri-implantitis group and peri-implant mucositis group than in the healthy implant group. In their paper, Mangano et al. [49] sought to discover whether low vitamin D levels in the blood would be linked to early implant failure. This research found that individuals with implants had a greater implant failure rate, but there was no connection between the two. Fibroblast growth factor (FGF)-23 and 25-hydroxyvitamin D3 (25(OH) D3) levels were measured in peri-implant sulcus fluid of both healthy and sick subjects by Acipinar et al. [17] Peri-implantitis patients' levels of 25(OH)D3 were found to be considerably lower than healthy peri-implant patients.

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Studies have shown that uric acid is associated with the development and progression of coronary artery disease, particularly hypertension and hyperuricemia.[50–52] An association between uric acid and inflammatory reactions has also been confirmed.[53] Uric acid increases the production of proinflammatory cytokines such as IL-1, IL-6, and TNF- in human mononuclear cells.[54] The peri-implantitis group showed considerably higher uric acid levels as compared to the other groups. Additionally, amounts of urinary acid were associated to scores on the GI, PD, BOB, and KMW. Our data indicate that high serum uric acid levels are correlated with inflammation.

According to previously conducted research, a significant connection exists between periodontitis and several systemic disorders, including cardiovascular disease and diabetes. However, no such relationship has been established between peri-implantitis and cardiovascular disease.[55,56] Thus, some studies found that there was no statistically significant relationship between peri-implantitis and cardiovascular diseases, with a result [8, 57, 58] concluding that "any cardiovascular disease occurred as a result of pre-existing peri-implantitis."

In our study, there were some limitations; Because we did not use coronary angiography to measure the presence of coronary artery disease, and we relied on radiographic methods to indicate the severity of the bone loss that surrounds dental implants, our findings may have been incomplete. Peri-implant crevicular fluid can disclose any localized damage surrounding dental implants and finding proinflammatory cytokines in that fluid can help. A further disadvantage of this study is the small sample size. These findings must be confirmed with additional study that includes a bigger sample size.

Conclusion

It was finally apparent that the peri-implantitis group had significantly higher triglyceride and uric acid levels (risk markers for cardiovascular disease). Longer-term, large-sized clinical investigations are required to confirm the connection of these risk variables with cardiovascular and peri-implant disorders.

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