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Comparative analysis of serum titanium level in patient with healthy dental implant and patients with peri-implantitis- A cross sectional prospective study

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Abstract

Objectives: Titanium dental implants can last for more than two decades in the oral environment. Corrosion of the implant surface can release metallic particles or ions into surrounding tissue. The metallic constituents like titanium in human blood serum have not been fully studied. The study compares titanium serum levels before and after dental implant placement and compares levels in patients with healthy implants and those with per-implantitis.

Methods: The study comprised 2groups of Group 1 patient observing implant surgery and group 2 patients with diagnosed peri-implantitis. Each group comprised of 60 patients. Serum titanium level was measured from blood obtained from Group 1 at three different intervals (one month prior to implant surgery, 4th and 8th month after successful loading) and from Group 2 during the course of peri-implantitis by inductively coupled plasma–mass spectroscopy. The statistical analysis was done for the obtained data.

Results: Analysis showed a raised level of serum titanium at 4th month of post implant placement (2.39 mg/dl) and in patient with peri-implantitis(2.94 mg/dl) and both levels are significantly differ (ANOVA test) from pre-surgical estimation of serum titanium level (1.79 mg/dl).

Conclusions: Understanding the correlation between titanium corrosion and peri-implantitis is vital for enhancing the long-term success and safety of dental implants. Additional research is required to investigate these links and potential strategies to protect the well-being of implant patients.

Keywords: Dental implants; Serum titanium; Peri-implantitis; Inductivelycoupled plasma–mass spectroscopy; Titanium alloys.

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INTRODUCTION

Titanium implants have gained substantial usage in dentistry to supplant natural teeth because of their high biocompatibility. Titanium or titanium admixtures are the usual constituents of titanium implants, given their mechanical properties and biocompatibility. There is evidence indicating that titanium dental implants can endure exposure to the oral environment for more than two decades [1]. The biocompatibility exhibited by dental implants can be attributed to the formation of a titanium dioxide layer that prevents direct contact between the implant and the biological environment. This, in turn, reduces the potential for metal reactivity [2].

Currently, scholars are focusing on diverse approaches to expedite the process of osseointegration of dental implants and to augment the surface area of implant-bone contact. To this end, the osseointegration surface areas are enlarged by creating irregularities on the surfaces of materials used for dental implants [3]. The examination of dental implants' interactions with biological tissues involves the use of a titanium dioxide (TiO2) layer. When subjected to loading conditions, the TiO2 layer is susceptible to damage during movement between the implant and bone tissue, resulting in implant

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corrosion and consequential weakening. Furthermore, corrosion can trigger the release of minute metallic particles or ions into the surrounding living tissues [4].

A recent investigation revealed that the micromotion of the abutment under cyclic loading may produce wear particles of varying sizes between 2 and 80 nm in conical dental implant systems. Wear debris comprises titanium particles that are recognized to elicit a macrophage response [5]. Metal nanoparticles have been widely acknowledged for their ability to trigger an inflammatory response through their immunomodulatory potential. This potential is primarily exerted at the macrophage level and is characterized by an escalation in DNA damage, protein carbonylation, lipid per-oxidation, oxidative stress, and a reduction in superoxide dismutase activity, total glutathione levels, and total antioxidant capacity catalase [3].

Since Ferguson's seminal study, the generation of metal debris from joint replacement surgeries has been a significant concern within the field of orthopedic surgery. The surface oxide film layer of a metallic object implanted within the human body may undergo disruption or degradation over time due to spontaneous mechanical or electrochemical corrosion. This particular interaction can yield chemically reactive metallic byproducts, which may prompt the discharge of metal into the systemic circulation [6]. Bianco et al. investigated the dissimilarity between the levels of titanium in the serum and urine of rabbits before and following implant insertion. Their findings suggest that there was no noteworthy elevation observed [7].

A comprehensive examination of the metallic constituents in human blood serum has yet to be fully explored. It is uncertain whether the discharge of titanium or titanium particles from dental implants could have an impact locally or systemically. The present study aimed to compare the titanium serum level before and after the placement of dental implants and to compare the level of serum titanium in patients with healthy dental implants with per-implantitis.

MATERIALS AND METHODS

Study Design

A null hypothesis was developed for a prospective quasi-experimental study stating that there would be no alteration in the serum titanium level of patients before and after implant placement either in health or disease. This study was carried out in the Department of Periodontics from 2019 to 2022 and was permitted by the institutional ethical review committee [EC-19/12-F-FDS]. The study design consisted of 2 groups of 60 patients each. Group 1 comprising healthy patients seeking implant placement, Group 2 included patients with peri-implantitis who had implants placed more than 6 months.

Sample size calculation

The statistical software GPOWER (version 3.1) developed by Franz Faul at the University of Kiel in Germany was employed to determine the appropriate sample size for this study, with a type 1α error rate of 0.05 and a power of 95% with effect size of 0.5[7]. Ultimately, a sample size of 53 was selected; however, in anticipation of potential sample attrition, the sample size was increased to 60. As per the sample size calculation each group of the study comprises of 60 patients contributing to total population of 120.

Inclusion criteria

Group 1- (Healthy patients)

- Partially edentulous patients.
- Periodontally healthy patients.
- Patients with appropriate inter-occlusal distance for the placement of the implants
- Patients with no history of metal allergy.

Group 2 (Peri-implantitis)

- Post implant period should be more than 6 months but less than 2 years
- Implants having probing depths ≥ 5mm.

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- Bleeding on probing and/or suppuration.
- Bone loss ≥ 2mm were considered in the peri-implantitis group.

Exclusion criteria

- Patients using systemic or local antibiotics in the last 3 months.
- Immuno-compromised patients, who have received chemotherapy or radiotherapy.
- Pregnant and lactating women.

Method of assessment of peri-implantitis

The determination of peri-implantitis diagnosis was established through the evaluation of clinical and radiologic criteria, in accordance with existing recommendations. Specifically, implants with probing depths equal to or greater than 5mm, accompanied by bleeding upon probing and/or suppuration, as well as bone loss of 2mm or more, were diagnosed as peri-implantitis (Figure 1, 2).

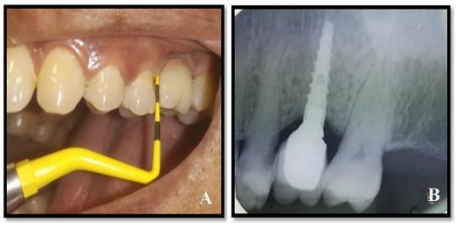
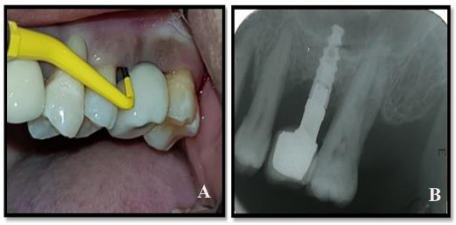


Figure 1: Clinical and radiological assessment of healthy implant patient [A] Periodontal pocket depth less than 2 mm [B] Absence of bone loss

In order to determine the diagnoses, it was necessary to obtain a consensus from three reviewers (MS, VS, KK) who worked independently. Furthermore, supplementary information regarding the subjects' age, gender, smoking habits, and diabetes status was also documented.



Methodology

Figure 2: Clinical and radiological assessment of peri-implantitis patient [A] Periodontal pocket depth more than 5 mm [B] Radiographic bone loss more than 2 mm

Blood serum was collected from patients of Group 1 at 3 different intervals, one month prior to implant placement, 4th month after surgical phase (loading of implant) and 8th month after surgical phase (loading of implant), and from the study Group 2, at the course time of peri-implantitis. 2 ml of blood was withdrawn from the anterior cubital fossa of the patients. Blood samples were stored at -20° C. After collection of the whole blood, it was left undisturbed in the vacutainer, allowing it to clot at room temperature. Centrifugation was performed at 1000–2000 rpm for 20 min in a refrigerated centrifuge. The resultant serum samples were obtained and analysis for titanium was performed using inductively coupled plasma mass spectrometry (ICP-MS), with a detection limit of 0.5 nanograms at the Ramaiah Advanced Drug Testing Laboratory, Bangalore.

Statistical analysis

The normality of the obtained dataset was checked using the Shapiro Wilk test. After stating the descriptive analysis for all the groups, Multiple group comparison was done with ANOVA test. The level of significance was set at alpha value 0.05. All statistical analyzes were performed using SPSS software version 22

Table (1). Descriptive analysis of estimated serum titanium values in study groups

Study Groups	Sample size	Subgroup	Mean±SD	95% Confidence Interval Mean		Coefficient of variation
				Upper	Lower	
Group 1	60	Pre-surgical	1.736±0.318	1.817	1.655	0.183
		At 4th month	2.390±0.208	2.443	2.337	0.087
		At 8th month	2.357±0.148	2.395	2.320	0.063
Group 2	60	Peri-implantitis	2.943±0.177	2.988	2.898	0.060

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(Developed by IBM Corporation, Armonk, N.Y., USA in 2013)

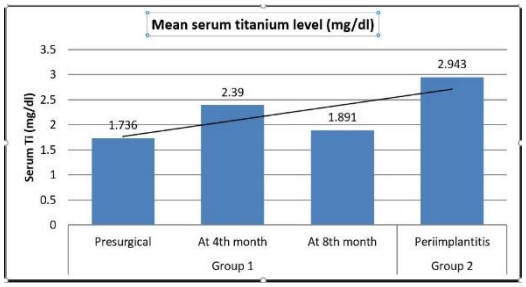

Figure 3: Graph showing the trend line for increasing serum titanium level in study groups

RESULTS

The present study included 120 patients, comprised of 53 females and 67 males. The age range was 23–47 years with an average value of 40±8 years. In the current investigation, no statistically meaningful variance was observed with regard to the demographic characteristics of the participants enlisted for the research, suggesting the absence of any bias in the selection process based on age and gender.

Table (2). Comparison of mean scores of subgroups by repeated ANOVA test

Group 1	F value	p value	Effect size
Pre-surgical			
At 4th month	227.399	< 0.0001*	0.794
At 8th month			

*p<0.05 significant

The analysis of aggregated data showed increasing trend line in serum titanium level in group 1 and group 2 patients (Figure 3). Patients with peri-implantitis showed higher mean serum value (2.94±0.17) comparing to group 1 patients. In the Group 1 patients highest mean serum titanium level (2.39±0.20) was observed at 4th month after loading procedure (Table 1). The comparative analysis of subgroups in Group 1 with repeated ANOVA test showed a significant difference (p=.001) and subgroups comparison with post hoc analysis with paired t test showed significant result except between the serum titanium level at 4th month and at 8th month (Table 2, 3). Significant results were obtained when Group 2 was submitted to paired analysis with Group 1 subgroups by using unpaired t test (Table 4).

Discussion:

Since approximately 1981, titanium has been utilized for the construction of dental implants. The primary alloys employed are commercially pure titanium (cpTi) and Ti-6Al-4V, both of which exhibit clinical success rates of up to 99% after a decade. These alloys possess biocompatibility when in contact with bone and gingival tissues, and have the ability to undergo osseointegration [7].

The corrosion behavior of metal implants is a crucial determinant of their biocompatibility. This is due to the potential detrimental effects resulting from the release of metal ions during the corrosion process. The tissue in the immediate vicinity of the implant, as well as the systemic environment, can be affected by these factors, potentially leading to allergic reactions. The presence of an oxide layer on the implant's surface significantly influences the outcome of osseointegration. The utilization of dental implants may result in elevated levels of titanium in both the bloodstream and serum [8].

Gopi G conducted an assessment on the liberation of titanium, aluminium, and vanadium from dental implants through a comparison of the serum concentrations of these ions prior to and following surgical procedures. Notably, a marginal variation was observed in the postoperative levels of titanium (2.31mg/dl) in relation to the preoperative levels (2.28 mg/dl), without any statistical significance (P > 0.5). [7] The current investigation assessed significant differences in the concentrations of titanium in the bloodstream before (1.79 mg/dl) and after (2.39 mg/dl) the 4th month of the loading of the implant, and the findings demonstrated an absence of agreement with the study conducted by Gopi et al.

Another study demonstrated a comparable lack of significance in the relationship between the average concentration of titanium in the serum at the beginning, after 8 weeks, and after 6 months, with values of 2.39 mg/dl, 2.35 mg/dl, and 2.38 mg/dl, respectively [9]. Our study also found lack of significance in titanium level at pre-surgical phase and at 8th month of post loading of the implant. This signifies that serum

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titanium levels significantly raises immediately after loading the implant but with due time the concentration lowered down by the macrophages.

The release of titanium particles from the surface of the implant has a detrimental impact on both the nearby and far-reaching tissue as it infiltrates the surrounding tissues and enters the bloodstream [10]. In the localized region of dental implant known as the peridontium, the presence of titanium particles can trigger an inflammatory condition called peri-implantitis, characterized by an escalation in inflammatory mediators such as macrophages, cytokines, TNF-alpha, and IL-6. Multiple investigations have been conducted in order to assess the concentration of titanium and inflammatory mediators in the serum; however, no substantial findings were attained [11, 12,13]. Our research, on the other hand, revealed a statistically significant variance in the serum concentration of titanium between individuals with uncompromised dental implants and those experiencing peri-implantitis.

Table (3). Subgroup comparison by Post hoc analysis with paired t test

Paired subgroup	Difference of mean	t value	p value	Cl at 95%	Cohen's d Effect size
Pre-surgical vs 4th month	-0.654	16.374	< 0.0001*	0.5635 and 0.7565	2.53
Pre-surgical vs 8th month	-0.622	16.301	< 0.0001*	0.5307 and 0.7093	2.57
4th month vs 8th month	0.033	1.405	0.496	0.0224 and 0.1024	0.23

*p<0.05 significant

Previous research has demonstrated the existence of titanium particles in the tissues surrounding dental implants. Nevertheless, no conclusive statistical proof has been presented to establish a connection between dissolved titanium and peri-implantitis [14]. The current investigation assessed the levels of titanium in the serum of patients with both healthy implants and implants affected by peri-implantitis. The findings obtained from this study demonstrated statistical significance, which aligns with the research conducted by Olmedo et al [10].

Although the occurrence of inflammation is observed as a healing response promptly following the loading of an implant and is accompanied by heightened levels of titanium in the serum [9], a similar response can also manifest in cases of peri-implantitis. During peri-implantitis, macrophages that are recruited engulf wearable titanium particles, resulting in an elevation of titanium levels in the serum [10, 12]. The potential of titanium particles that have undergone corrosion to induce an immune response may result in inflammation of the periodontium and the subsequent degradation of bone tissue. The primary focus during the management of peri-implantitis was previously centered on mitigating inflammation. However, the emphasis should be on reducing the corrosion of titanium implants.

While the serum's titanium level does not reach toxic levels in instances of dental implants, it is important to note that these titanium particles have the potential to be transported through the bloodstream to various regions of the body, thereby inducing toxic consequences. The exposure of titanium in dental implants to fluoride ions can occur through mouth rinses, toothpastes, drinking water, or food. Consequently, the utilization of fluoride as a potential confounding factor should be taken into consideration in forthcoming confirmatory investigations that aim to evaluate the connection between titanium corrosion and peri-implantitis [16, 17]. In order to mitigate the leaching of titanium particles, an examination was conducted using an aqueous solution of lactic acid and phosphate-buffered saline. However, it was discovered that there was no discernible connection between the augmentation of surface roughness and the release of ions, both in experimental and biological circumstances [16].

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Table (4). Pair wise analysis of Group 2 and Group 1 by unpaired t test

	Mean ± SD	Difference of mean	t value	p value	CI at 95%	Cohen's d Effect size
Pre-surgical	1.736 ± 0.318	-1.207	25.646	< 0.0001*	1.119 and 1.300	4.84
Peri-implantitis	2.943 ± 0.177					
4th month	2.390 ± 0.208	-0.553	15.683	< 0.0001*	0.482 and 0.617	2.96
Peri-implantitis	2.943 ± 0.177					
8th month	2.358 ± 0.148	-0.586	19.622	< 0.0001*	0.533 and 0.646	3.78
Peri-implantitis	2.943 ± 0.177					

*p<0.05 significant

Themedicinal capability of neutralizing antibodies against IL1β, IL6, or TNFα in the prevention of osteolysis caused by Ti particles was also studied [13].

Limitations of the study

The current investigation utilizes the ICP-MS technique to evaluate the serum titanium level which present in minute amounts. Further investigations are required in order to assess the level of titanium and inflammatory components present in gingival tissues and blood serum, despite the observed significant correlation between healthy implants and those affected by peri-implantitis.

Conclusion

In summary, understanding the complex relationship between titanium corrosion and peri-implantitis is crucial for improving the long-term success and safety of dental implants. Further research is needed to explore these connections and potential mitigation strategies to ensure the continued well-being of dental implant patients.

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Conflict of interest

The authors declare no competing interest.

Ethical approval

The study was approved by Institutional Ethical Review Committee [EC-19/12-F-FDS].

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Author's contribution

Dr. Mahantesha S – Substantial contribution to concept and study design, Critical review of the manuscript

Dr.Vibha Shetty- Patient selection and study design, Analysis and interpretation of the data, Critical review of the manuscript

Dr. Kranti K- Analysis and interpretation of the data, Critical review of the manuscript

Dr.Shobhasubbaiah- Followed laboratory investigation and data segregation, Critical review of the manuscript

Dr. Greeshma C- Data analysis and critical review of the manuscript

Dr. Babashankar Alva- Critical review of the manuscript for important contents

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