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Evaluation of Titanium Ions Levels in Blood in Patients with Endosseous Titanium Dental Implants using Inductively Coupled Plasma Mass Spectrometry - A Retrospective Study

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Abstract: ***The present study investigates the amount of titanium (Ti) released in blood of patients after implant and crown placement in a period ranging from 1 to 5 years. Over the years of a functional implant, it has been conceptualized that titanium di oxide layer can be destroyed during the micro-mechanical movement between the implant and bone and cause corrosion which leaks out small metallic particles or ions to leak into living tissues. This leak of metal ions may happen in relatively large concentrations into adjacent tissues and these can be present as nanoparticle debris or as organometallic complexes (bound to tissue proteins). In this study, the quantity of Ti present in the blood of patients who received implants was measured using a wide range of atomic analytical techniques such as Inductively Coupled plasma mass spectrometer (ICP-MS) which detects the lowest limit of Titanium levels in blood.***

1. Introduction

Titanium is the most widely used material for oral implants and is considered to be highly biocompatible.[1] After the discovery of osseointegration by a Swedish orthopedic surgeon, Per-Ingvar Branemark(1957), titanium was considered as a good biomaterial, with corrosion resistance without cytotoxicity, together with high material strength with excellent fatigue and wear resistance.[1] The interactions of dental implants with biological tissues are characterized by means of titanium dioxide (TiO2) layer.

When the stable oxide layer is broken down or removed and is unable to reform on parts of the surface, titanium can be as corrosive as many other base metals.[8] TiO_2 layer can be destroyed during movements between implant and bone tissue under loading conditions[5-7]. This destruction causes corrosion of the implant, thus, weakening it; and can induce the leak of small metallic particles or ions into living tissues.

Early reports by Ferguson[8] showed that ionization of all metal occurs to some extent and titanium may be released in relatively large concentrations into adjacent tissues. The ionization of metals leads to formation of corrosive products which can be present in blood and enter the systemic circulation and spread to all organs in our body in the form of nano-sized particles, ionic, colloidal, organic and inorganic forms. For the above reasons, many questions about the biocompatibility of Ti implants have lately been raised[9].

The aim of this study is to test the level of titanium ions released in blood of patients after implant and crown placement ranging from 1 to 5 years and to correlate it with the clinical probing depth, peri-implant mucosal conditions, levels of the peri-implant bone height and the levels of titanium ions present in blood.

2. Materials and methods

Patients who had undergone complete dental implant therapy before January 2015 in Department of Periodontics and Implantology, The Oxford Dental College and Research center were included in the study (Table 1).

Table 1: Patient selection criteria

Inclusion Criteria	Exclusion Criteria
• Male and female subjects of age 18-65yrs • Systemically healthy subjects • Subjects who had received dental implants with crown (1 year from placement of crown)	• Subjects who have other metal implants in the body • Subjects who are smokers and alcoholics • Acute infection at the implant site • Lactating and Pregnant women

The subjects were asked to fill up the consent form and thorough information about the study was given. Institutional ethical committee clearance was obtained prior to the start of the study

Table 2: Number of patients and implants according to groups

Groups	Subjects	Duration after Implant Placement
Group 1	15 Subjects following dental implant therapy	12 months to 24 months
Group 2	15 Subjects following dental implant therapy	24 months to 36 months
Group 3	15 Subjects following dental implant therapy	36 months to 48 months
Group 4	15 Subjects following dental implant therapy	48 months to 60 months

Clinical and Radiographic parameters[10] :-

1) Peri-Implant Probing depth
2) Plaque index(Mombelli et al, 1987)

3) Modified Gingival index (Mombelli et al, 1987)
4) Radiovisio graphs to assess the peri-implant bone level.

All these parameters were assessed before the blood sample collection.

For each patient, 10 ml of blood was drawn from the patient's antecubital vein in individual polypropylene syringes.. For all procedures a twenty-two gauge stainless steel needle (BD Vialon Biomaterial IV catheter, 0.9 × 25 mm, 35 cc/min; Beckton Dickinson, Mississauga, Ontario) was used to cannulate the vein. The blood samples analyzed in this study were collected and sent to Ramaiah Advanced testing laboratory, mathikere, Bangalore for testing the concentrations of Ti ions by Inductively Coupled Plasma Mass Spectrophotometer [11, 12].(Thermo Fisher Scientific GmBH, Bremen, Germany). The detection limits was 0.2 mg /L for Ti.

Statistics

Proportion tests were performed with a Chi-square test. Statistical significance was set at 0.05. One way analysis of variance (ANOVA) will be used to analyze the difference among mean ion concentrations in the 4 groups. The Duncan multiple range test was applied to show the differences between groups.

3. Results and Tables

Intra-Group Comparison:-

Table 1: Comparison of mean titanium ions across the four groups

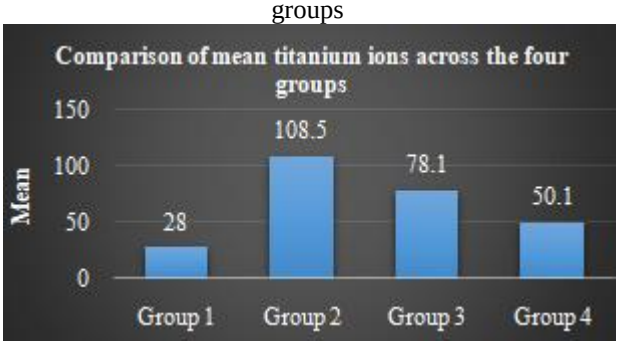
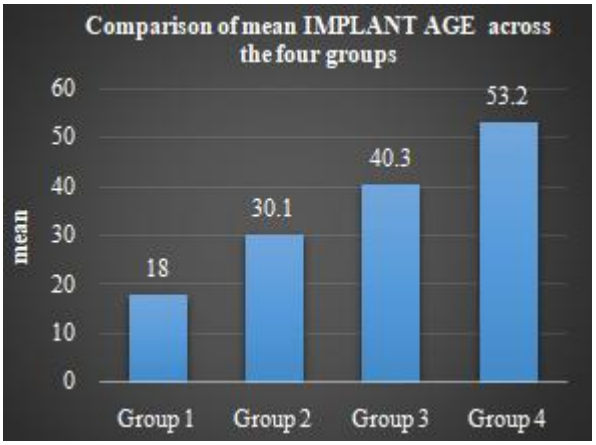


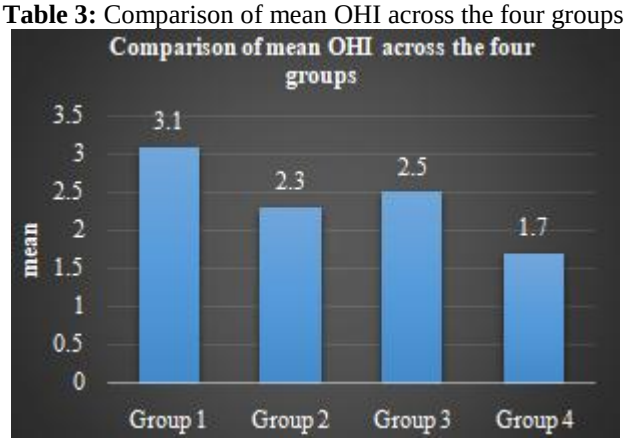
Table 2: Comparison of mean Implant Age across the four groups

	Mean	SD	F	p
Group 1 12 to 24 months	28.0	11.03	53.88	.000*
Group 2 24 to 36 months	108.5	24.07		
Group 3 36 to 48 months	78.1	21.23		
Group 4 48 to 60 months	50.1	13.04		



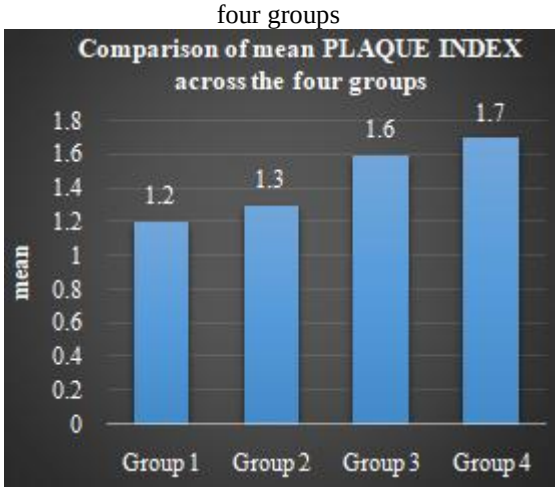
	Mean	SD	F	p
Group 1 12 to 24 months	18.0	3.32	269.6	.000*
Group 2 24 to 36 months	30.1	3.52		
Group 3 36 to 48 months	40.3	3.11		
Group 4 48 to 60 months	53.2	3.78		

Table 3: Comparison of mean OHI across the four groups



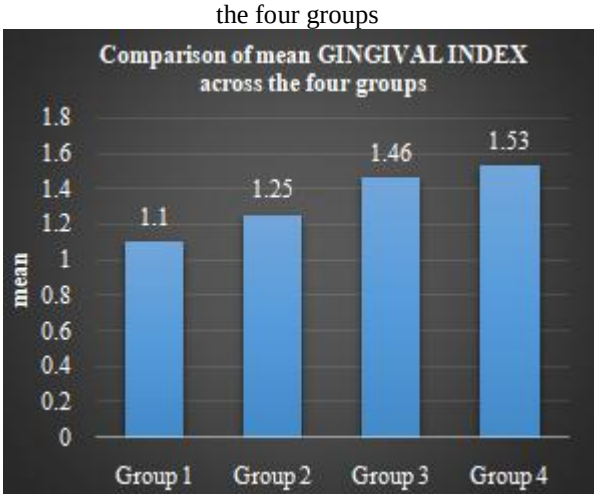
	Mean	SD	F	p
Group 1 12 to 24 months	3.1	1.73	2.6	.05*
Group 2 24 to 36 months	2.3	1.31		
Group 3 36 to 48 months	2.5	1.00		
Group 4 48 to 60 months	1.7	1.29		

Table 4: Comparison of mean PLAQUE INDEX across the four groups



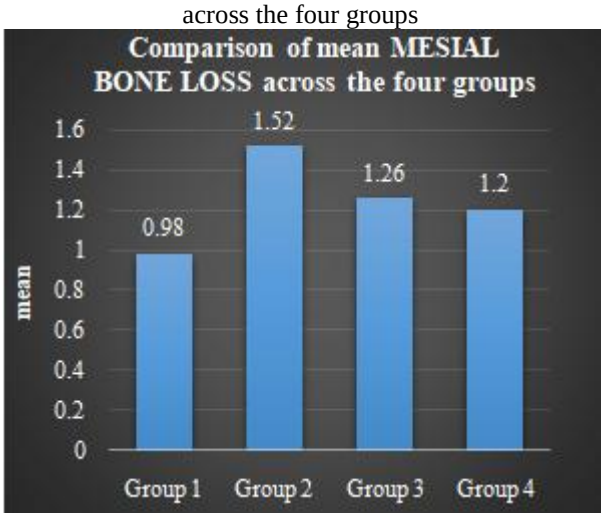
	Mean	SD	F	p
Group 1 12 to 24 months	1.2	1.03	.664	.578
Group 2 24 to 36 months	1.3	.84		
Group 3 36 to 48 months	1.6	.98		
Group 4 48 to 60 months	1.7	1.09		

Table 5: Comparison of mean GINGIVAL INDEX across the four groups



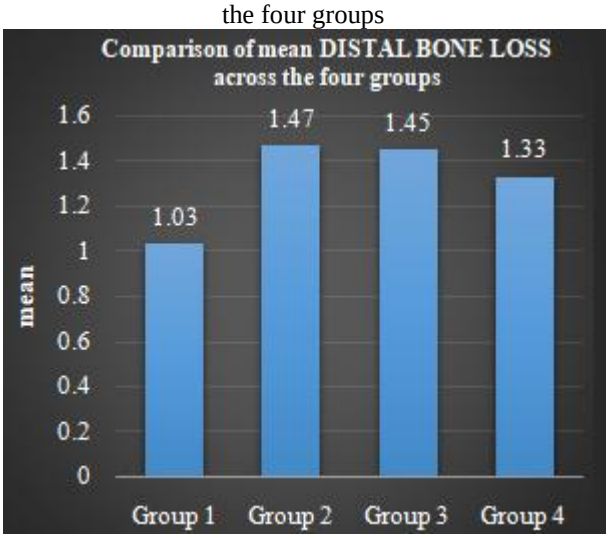
	Mean	SD	F	p
Group 1 12 to 24 months	1.10	.73	.784	.508
Group 2 24 to 36 months	1.25	.64		
Group 3 36 to 48 months	1.46	.89		
Group 4 48 to 60 months	1.53	1.09		

Table 6: Comparison of mean MESIAL BONE LOSS across the four groups



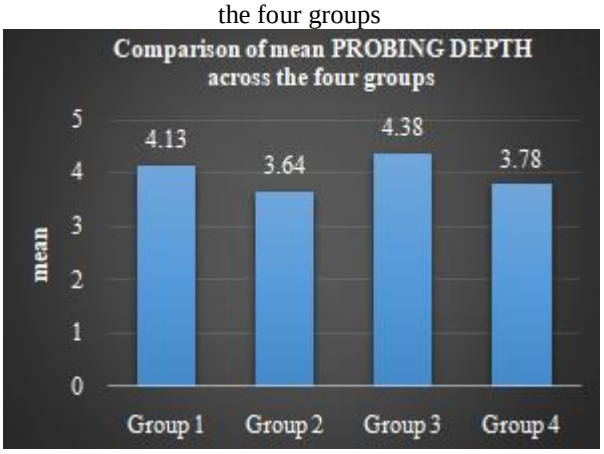
	Mean	SD	F	P
Group 1 12 to 24 months	.98	.62	1.444	.241
Group 2 24 to 36 months	1.52	.87		
Group 3 36 to 48 months	1.26	.59		
Group 4 48 to 60 months	1.20	.69		

Table 7: Comparison of mean DISTAL BONE LOSS across the four groups



	Mean	SD	F	P
Group 1 12 to 24 months	1.03	.61	1.132	.345
Group 2 24 to 36 months	1.47	.86		
Group 3 36 to 48 months	1.45	.77		
Group 4 48 to 60 months	1.33	.65		

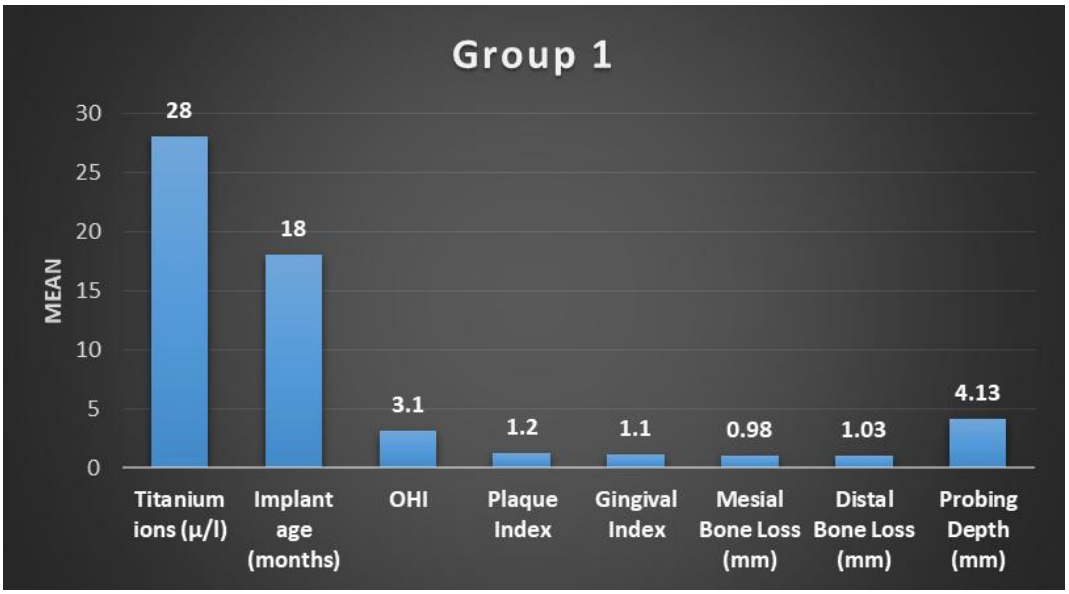
Table 8: Comparison of mean PROBING DEPTH across the four groups



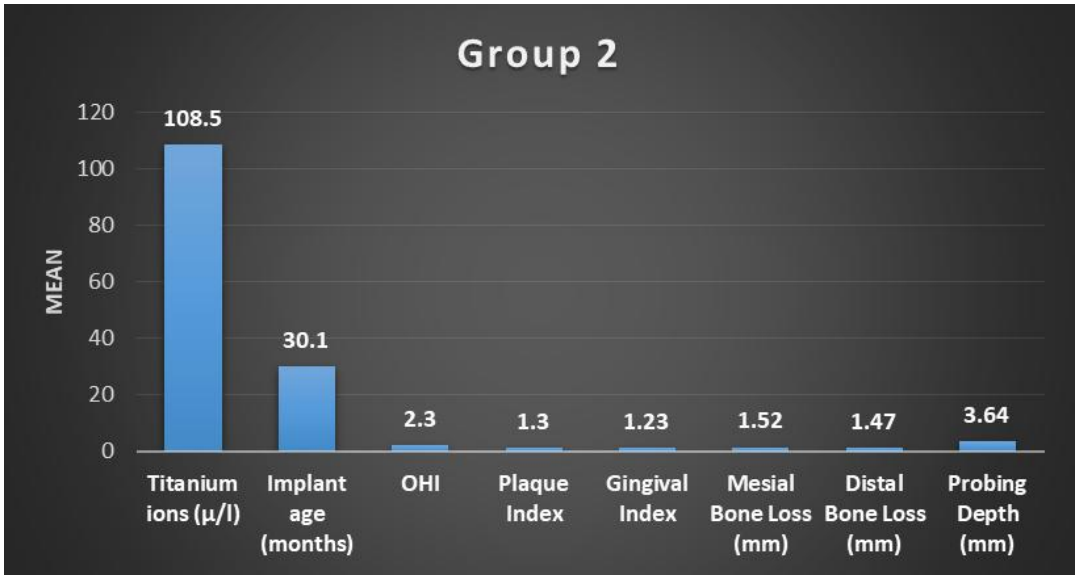
	Mean	SD	F	P
Group 1 12 to 24 months	4.13	2.03	.379	.768
Group 2 24 to 36 months	3.64	1.78		
Group 3 36 to 48 months	4.38	2.25		
Group 4 48 to 60 months	3.78	1.96		

Inter-Group Comparison

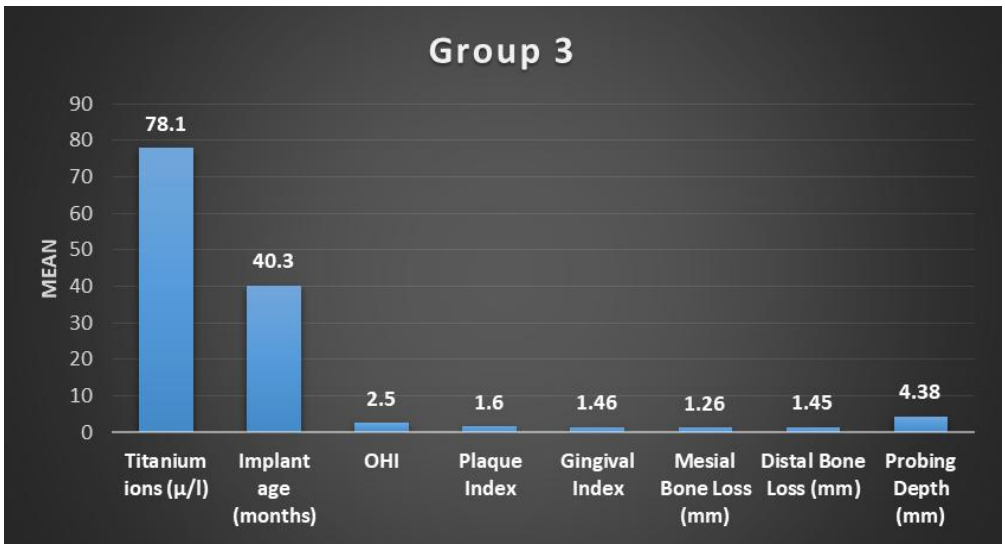
Group 1 (12 to 24 Months)	
Titanium ions (µ/l)	28
Implant age (months)	18
OHI	3.1
Plaque Index	1.2
Gingival Index	1.1
Mesial Bone Loss (mm)	0.98
Distal Bone Loss (mm)	1.03
Probing Depth (mm)	4.13



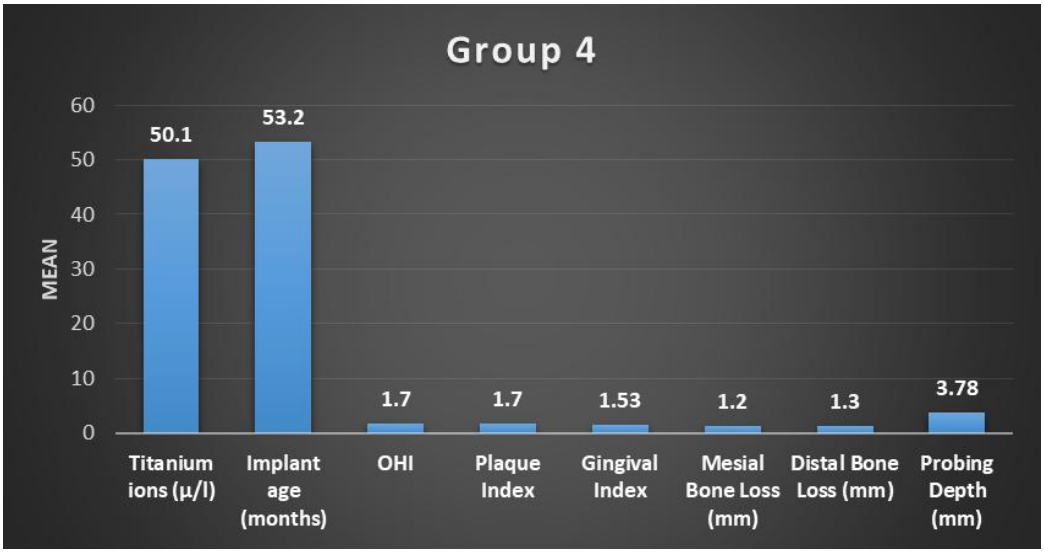
Group 2 (24 to 36 Months)	
Titanium ions (µ/l)	108.5
Implant age (months)	30.1
OHI	2.3
Plaque Index	1.3
Gingival Index	1.23
Mesial Bone Loss (mm)	1.52
Distal Bone Loss (mm)	1.47
Probing Depth (mm)	3.64



Group 3 (36 to 48 Months)	
Titanium ions (µ/l)	78.1
Implant age (months)	40.3
OHI	2.5
Plaque Index	1.6
Gingival Index	1.46
Mesial Bone Loss (mm)	1.26
Distal Bone Loss (mm)	1.45
Probing Depth (mm)	4.38



Group 4 (48 to 60 Months)	
Titanium ions (µ/l)	50.1
Implant age (months)	53.2
OHI	1.7
Plaque Index	1.7
Gingival Index	1.53
Mesial Bone Loss (mm)	1.2
Distal Bone Loss (mm)	1.3
Probing Depth (mm)	3.78



4. Discussion

Italian dentist Formiggini in 1947 putforth a "self-tapping screw" made of tantalium. As the material was pricey it was replaced by titanium and Branemark coined the term "osseointegration", terming the advent of modern implant dentistry. Presently, Titanium and titanium- based alloy $TiAl_6V_4$ are the most common materials used, having excellent biocompatibility, mechanical proprieties and better corrosion resistance[13].

Over the years, several reports have shown that titanium di-oxide layer can be destroyed over the years due to micro-mechanical movements between the implants and bone which causes corrosion products of titanium to enter in the blood.

Titanium toxicology is a subject currently under discussion. Persistent use of titanium-based materials is known to have systemic and local effects of titanium completely and lead to have more concentration studies on titanium.[8].According to epidemiological studies, inhalation of environmental dust containing titanium does not have a deleterious effect on lungsbut other studies have suggested the association of titanium particles with pleural pathologies, granulomatous diseases and malignant lung neoplasm. The International Agency for Research on Cancer (IARC), has classified TiO2 as "possibly carcinogenic to humans" (Group 2B), based on inhalation studies that induced lung tumors in rats.[8]

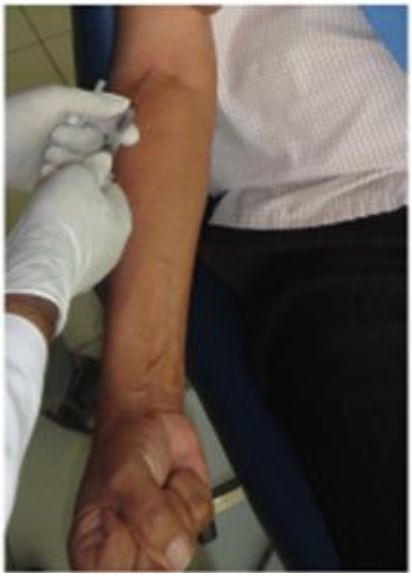
The results of my study showed that among the various groups, patient who had undergone implants from 24 to 48 months have the highest level of titanium levels (Avg108.5 microgram/litre) which is well within the safety limits[15, 16]

5. Conclusion

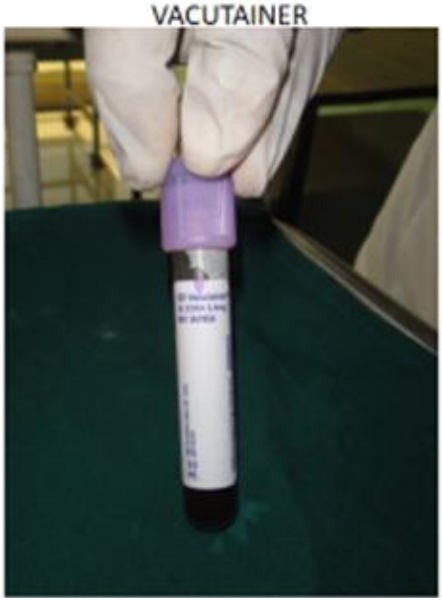
In this study, we have proved that corrosion products of titanium di oxide layer leaks in the form of titanium ions into the blood of patients who has undergone endosseous implants. However, further animal studies and in-vitro studies should be done to prove the mechanism of leaching and deposition of titanium ions in the blood

Photographs:

COLLECTION OF VENOUS BLOOD



STORAGE IN EDTA COATED VACUTAINER



INDUCTIVELY COUPLED PLASMA MASS SPECTROPHOTOMETER
(THERMO FISHER SCIENTIfiC GMBH, BREMEN, GERMANY)

SAMPLES KEPT FOR DIGESTION

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T +91 80 4091 8017
E info@ramaiahlab.com

TEST REPORT

Format No.: RATL/TR/01

Name and Address of Customer: Dr. Vinayak R, Senior Lecture, Dept. of Periodontics Oxford Dental College, Bangalore -68.

Test Report Ref. & Date: 1805073 to 1805089 & 06.06.2018 | **Date of Receipt:** 31.05.2018
Sample: Blood | **Sample ID:** Refer table | **Date of Analysis:** 06.06.2018
Sampling: Sample not drawn by us | **Description:** Red coloured liquid

#	JOB ORDER No.	SAMPLE ID	PARAMETER	RESULTS (µg/l)	TEST METHOD
01.	1805073	G II-7	Titanium (Ti)	89	ICP-MS
02.	1805074	G II-8	Titanium (Ti)	169	ICP-MS
03.	1805075	G II-9	Titanium (Ti)	89	ICP-MS
04.	1805076	G II-10	Titanium (Ti)	88	ICP-MS
05.	1805077	G II-11	Titanium (Ti)	91	ICP-MS
06.	1805078	G II-12	Titanium (Ti)	110	ICP-MS
07.	1805079	G II-13	Titanium (Ti)	73	ICP-MS
08.	1805080	G II-14	Titanium (Ti)	110	ICP-MS
09.	1805081	G III-1	Titanium (Ti)	83	ICP-MS
10.	1805082	G III-2	Titanium (Ti)	70	ICP-MS
11.	1805083	G III-3	Titanium (Ti)	103	ICP-MS
12.	1805084	G III-4	Titanium (Ti)	97	ICP-MS
13.	1805085	G III-5	Titanium (Ti)	82	ICP-MS
14.	1805086	G III-6	Titanium (Ti)	59	ICP-MS
15.	1805087	G III-7	Titanium (Ti)	65	ICP-MS
16	1805088	G III-8	Titanium (Ti)	68	ICP-MS
17	1805089	G III-9	Titanium (Ti)	128	ICP-MS

CONCLUSION AND REMARKS: NA
Parameter not in NABL scope

ANALYST

AUTHORIZED SIGNATORY
(Dr. P. Yuvaraj, TM)

THIS CERTIFICATE IS ISSUED SUBJECT TO THE FOLLOWINGCONDITIONS:
> TO BE UTILISED FOR Q.A. / Q.C. FUNCTIONS ONLY; ENDORSEMENT OF THE PRODUCT IS NEITHER SUGGESTED NOR INTENDED
> THE ABOVE RESULTS ARE VALID ONLY WITH RESPECT TO THE SAMPLE SUBMITTED FOR ANALYSIS
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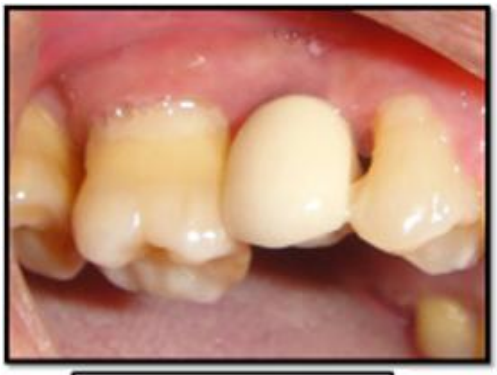
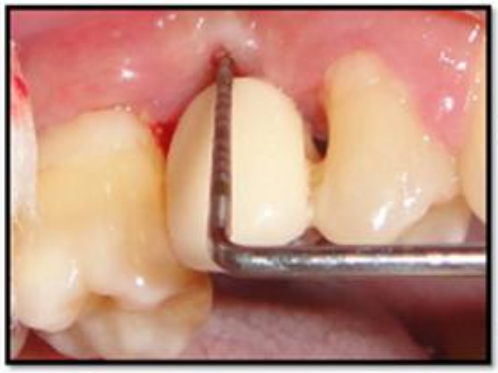
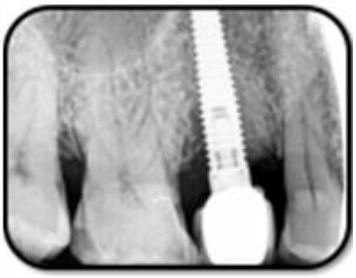
> SAMPLE WILL NOT BE RETAINED BEYOND THIRTY DAYS AFTER REPORT REF. DATE ABOVE EXCEPT PERISHABLE ITEMS



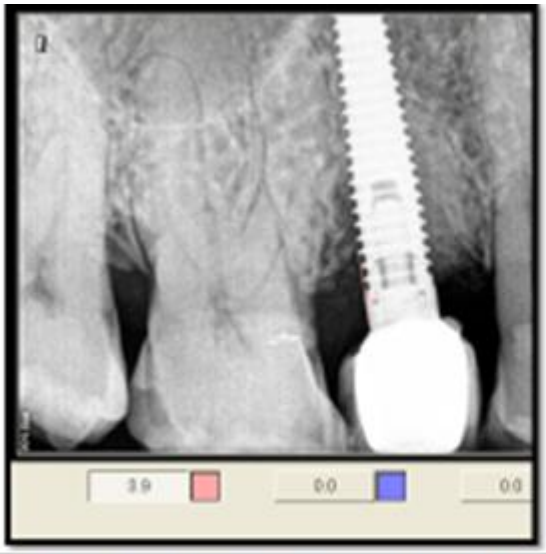
RESTORED IMPLANT IRT 15
(26 months- Group II)



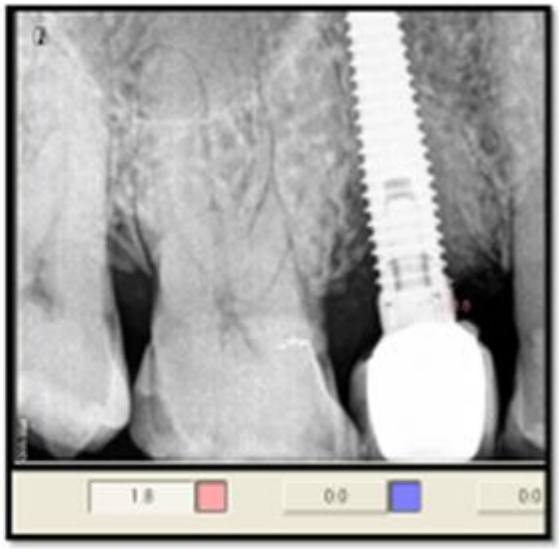
PROBING DEPTH OF 3 mm



RVG SHOWING PERI-IMPLANT BONE LOSS IRT 15



RVG SHOWING PERI-IMPLANT BONE LOSS = 3.9 mm ON THE DISTAL SIDE



RVG SHOWING PERI-IMPLANT BONE LOSS =1.8mm ON THE DISTAL SIDE

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