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# Clinical Evaluation of Hard and Soft Tissue Parameters around Implant Surfaces Bio –Modified with Alendronate

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## Abstract

***Objective*:** The present study was to evaluate clinical parameters around implant surface modified with alendronate. ***Materials and Methods*:** 20 patients were randomly divided into two groups (Group I-test and Group II- control). In the test group the osteotomy site was irrigated with bisphosphonate solution and the implant was dipped in the solution and placed in the osteotomy site. In the control group implant the implant was placed as such in the osteotomy site. Soft tissue and hard tissue parameter were recorded at 1st week, 3 months and 6months. Statistical analysis was done. ***Results:*** Crestal bone level was evaluated showed no statistically result when observed on mesial and distal aspect at 6 months. ***Conclusion*:** Although implant site treated with amino bisphosphonate (local application) showed reduction in the crestal bone loss but it is not statistically significant when compared with control group. Keywords: Osseointegration, Aminobisphosphonate, Bhisphosphonate, Crestal bone loss, Alendronate, Dental implant.

**Keywords:** Alendronate, Tissue Parameters, bisphosphonate solution, osteotomy site



## INTRODUCTION

Loss of tooth causes disharmony in dynamic occlusal equilibrium and also is intriguing and psychologically disturbing on part of patient, because it compromises both esthetic and masticatory or functional component of occlusion. Since the early 1980s, implant surface is considered as one of the six important factors for successful Osseointegration. Implant surface can be modified by various method like physical modification, mechanical modification, biological modification, chemical modification and nano technology. It has been showed that bio-modification of implant surface have shown better implant-to-bone contact. A comprehensive codification system has been developed where surface characterization, made with standard analytical tools, describes the chemical composition and physical characteristics of the surface [1].

Local factors influence the overall success and survival of implants which include primary stability at the time of implant placement, the formation of a direct bone to implant contact (BIC), and the quantity and/or quality of the residual bone. Substantial efforts have been made to accelerate healing around implants. In this regard, adjunct therapies such as the placement of osteogenic coatings on implant surfaces have been proposed in an attempt to enhance BIC and new bone formation (NBF) around implant surfaces. Modifications in implant surface chemistry have also been reported to enhance the proliferation and differentiation of osteoprogenitor cells and to increase alkaline phosphatase (ALP) activity and the expression of osteogenic genes (which helps to enhance BIC and promote Osseointegration) [2]. Such implant surface modifications have been shown to improve Osseointegration in systemically healthy as well as

immunosuppressed patients, such as those with osteoporosis or poorly controlled diabetes mellitus [3, 4].

Over 200 million prescriptions have been dispensed worldwide for oral bisphosphonate since their introduction and as aging population continue to become more susceptible to bone disease. In an osteoporotic population, oral bisphosphonate improves bone quality and decrease the incidence of skeletal fracture. Alendronate and risedronate are currently the main medication used in the United States to treat the age-related bone condition osteopenia and osteoporosis. Once incorporated into mineralized bone, these drugs persist for a long time and have a terminal half-life of many years [5].

In the literature there are only few studies which include comparative evaluation of peri-implant soft tissue with and without application of bisphosphonate on implant surface and osteotomy site [6, 7]. Therefore, the current study was undertaken to evaluate the hard and soft tissue parameters around implant surface bio-modified with alendronate.

## MARERIALS AND METHODS

Randomised control trial was conducted in Himachal Institute of Dental Sciences, Paonta sahib, Himachal Pradesh, India. Total 10 patients with bilateral tooth loss in the mandible were included in the study (both male and female). Patient who were willing to comply with all the study related procedures after signing an informed consent form, patient with good oral hygiene, patient who were non-smokers patient with adequate amount of bone for implant placement and with bilateral edentulous space in mandible were included in the study. Patient with poor oral hygiene, patient with bruxism habit and with insufficient platelet count were excluded from the study.

### GROUPING OF PARTICIPANTS

Participants were divided into two by using simple randomization of tossing the coin.

- Test group: After osteotomy, site was irrigated with bisphosphonate solution (sodium alendronate) and the implant was dipped in the bisphosphonate solution and then implant was inserted into the bone.
- Control group: After osteotomy, the implant was inserted as such in the prepared osteotomy site.

Alendronate, which belongs to the bisphosphonate class of drugs, is an anticatabolic agent that inhibits bone resorption and is therefore widely used for the treatment of skeletal disorders such as osteoporosis, bone metastases, and Paget's disease. It has been suggested that alendronate influences the three phases of bone remodeling, which are microinjury, osteoclastogenesis, and osteogenesis, thereby stimulating new bone formation by enhancing the proliferation and differentiation of osteoblasts and inhibiting osteoclast function [6].

### PREPARATION OF BISPHOSPHONATE SOLUTION

Second generation amino bisphosphonate sodium alendronate was used in the study as modified bisphosphonate solution. A dosage of 20 mg (10 mg two tablets) sodium alendronate tablet (Oateofos®) was crushed into powder and mixed with normal saline solution in a dappen dish. The concentration of solution was 20mg/ml.

### SURGICAL PROCEDURE

After anaesthesia crestal incision was given and Full thickness flap was raised. Osteotomy site preparation for implant placement was done. The osteotomy was generously irrigated with sterile saline to ensure debris free site. The implant was removed under aseptic condition from its sterile package and then dipped into prepared modified bisphosphonate solution and then the same solution was taken in the syringe and irrigation was done in the osteotomy site. For group II the implant was placed as such and the osteotomy site was irrigated with sterile saline.

All implants were placed with primary stability and were completely housed within the implant osteotomy, and the cover screw was placed. The flap margin was then repositioned and sutured by applying simple interrupted e with a 3.0 braided silk suture.

Patients was asked to follow postoperative instruction, which included ice pack, soft high nutritious diet, postoperative medication

- Antibiotic: Amoxicillin 500 mg 3times for 7 days.
- Analgesic: Ibuprofen 400 mg 3times a day as needed for pain.

Patient was instructed not to brush the surgical site, but to rinse with chlorhexidine gluconate mouthwash. After 7-10 days; sutures were removed. Three to four months after implant placement second-stage surgery was initiated. After giving mid crestal incision, the flap was reflected. Cover screw was removed and gingival former was placed over a period of 15 days. After 15 days gingival former was removed with 0.05 hex driver, copping was placed over the implant and screw was tightened and impression was made for the prosthesis. Porcelain fused metal crown was cemented over the abutment. Patients was reviewed at 1$^{st}$ week, 3$^{rd}$ month and 6$^{th}$ month with all clinical and radiographic parameters.

### CLINICAL AND RADIOGRAPHIC ASSESSMENT

The assessment of soft and hard tissue changes was done at 1$^{st}$ week, 3 months and 6 months. The following parameters- Mombelli plaque index [8],

Modified sulcular bleeding index by Mombelli [9], simplified gingival index by Apse [10] and associate and crestal bone loss was recorded. The mesial and distal crestal bone loss was evaluated using radiograph along with radiographic grid [11].

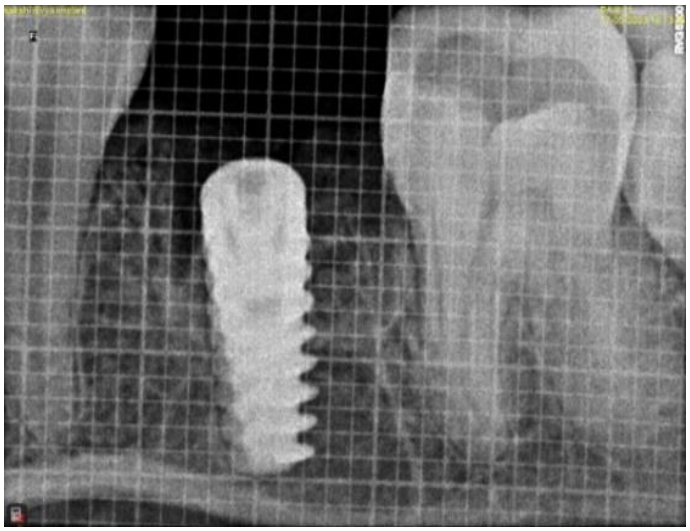

**Fig 1: Radiographic finding at 1st week**

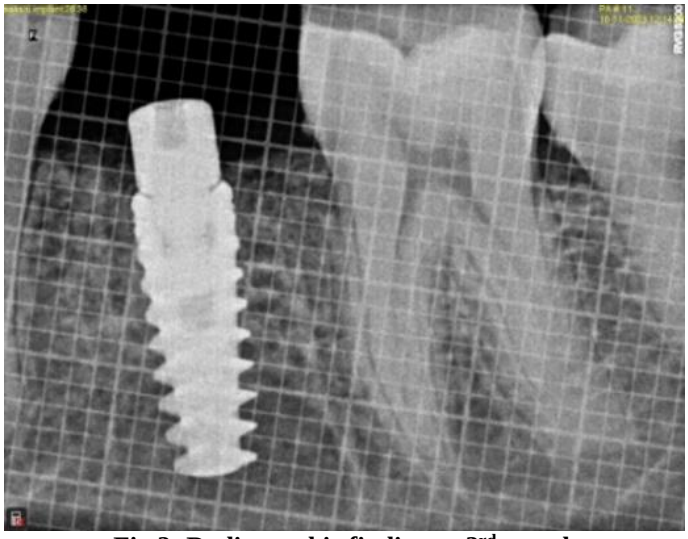

**Fig 2: Radiographic finding at 3rd month**

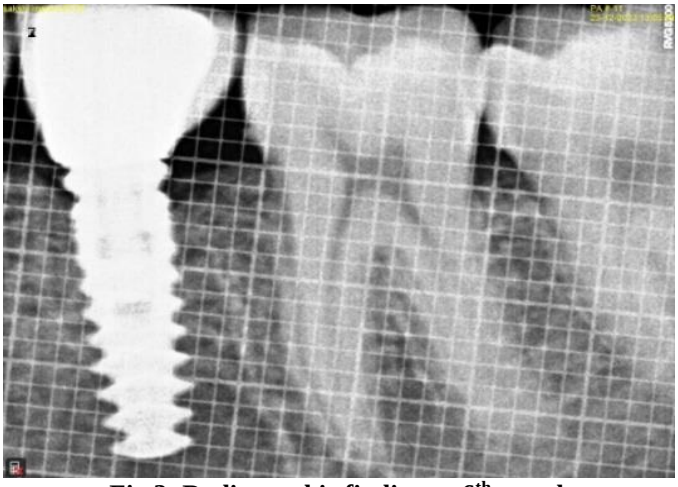

**Fig 3: Radiographic finding at 6th month**

**Statistical Analysis**

The statistical analysis was done using Statistical Package for Social Sciences (SPSS for Windows, Version 19.0). Descriptive statistics were calculated as mean and standard deviation. Prior to analysis, normality testing of the data was done using Shapiro-Wilk test which showed that the data deviated from normal distribution (P<0.05). Thereafter, comparison of study parameters between the two groups at various time intervals was done using Mann-Whitney U test. The level of significance for the present study was fixed at a p-value of less than 0.05.

## RESULTS

The comparison of plaque index between the study groups was done using Mann-Whitney U test which showed that there was no statistically significant difference in plaque index between the two groups (Table 1).

The comparison of gingival index, between the study groups at various time periods was done using Mann-Whitney U test which showed that there was no statistically significant difference in gingival index between the two groups at 1 week (P=0.089), at 3 months (P=0.146) and at 6 months (P=0.146) (Table 2).

Comparison of sulcular bleeding index was done using Mann-Whitney U test which showed that there was no statistically significant difference in bleeding index between the two groups at 1 week (P=0.089), at 3 months (P=0.146) and at 6 months (P=0.317) (Table 3).

The comparison of bone loss (mesial and distal) between the study groups at various time periods. Statistical analysis was done using Mann-Whitney U test which showed that there was no statistically significant difference in bone loss (mesial and distal) between the two groups (mesial) at 1 week (P=0.734), at 3 months (P=0.762) and at 6 months (P=0.820) and (distal) at 1 week (P=0.791), at 3 months (P=0.880) and at 6 months (P=0.820) (Table 4).

**Table 1: Intergroup Comparison of Plaque Index at Various Time Periods**

| | Group | N | Mean | Std. Deviation | Mean Rank | P value |
|---|---|---|---|---|---|---|
| Plaque Score (1 Week) | Group 1 | 10 | 1.0000 | 0.66667 | 11.30 | 0.453 |
| | Group 2 | 10 | 0.8000 | 0.42164 | 9.70 | |
| Plaque Score (3 Months) | Group 1 | 10 | 0.4000 | 0.84327 | 11.50 | 0.146 |
| | Group 2 | 10 | .0000 | 0.00000 | 9.50 | |
| Plaque Score (6 Months) | Group 1 | 10 | 0.7000 | 0.48305 | 13.00 | 0.028* |
| | Group 2 | 10 | 0.2000 | 0.42164 | 8.00 | |

*Statistically significant (P<0.05, Mann-Whitney U test)

**Table 2: Intergroup Comparison of Gingival Index at Various Time Periods**

| | Group | N | Mean | Std. Deviation | Mean Rank | P value |
|---|---|---|---|---|---|---|
| Gingival Score (1 Week) | Group 1 | 10 | 1.0000 | 0.66667 | 12.50 | 0.089 |
| | Group 2 | 10 | 0.5000 | 0.52705 | 8.50 | |
| Gingival Score (3 Months) | Group 1 | 10 | 0.4000 | 0.84327 | 11.50 | 0.146 |
| | Group 2 | 10 | 0.0000 | 0.00000 | 9.50 | |
| Gingival Score (6 Months) | Group 1 | 10 | 0.2000 | 0.42164 | 11.50 | 0.146 |
| | Group 2 | 10 | 0.0000 | 0.00000 | 9.50 | |

**Table 3: Intergroup Comparison Sulcular Bleeding Index at Various Time Periods**

| | Group | N | Mean | Std. Deviation | Mean Rank | P value |
|---|---|---|---|---|---|---|
| Sulcus Bleeding (1 Week) | Group 1 | 10 | 1.0000 | 0.66667 | 12.50 | 0.089 |
| | Group 2 | 10 | 0.5000 | 0.52705 | 8.50 | |
| Sulcus Bleeding (3 Months) | Group 1 | 10 | 0.4000 | 0.84327 | 11.50 | 0.146 |
| | Group 2 | 10 | 0.0000 | 0.00000 | 9.50 | |
| Sulcus Bleeding (6 Months) | Group 1 | 10 | 0.1000 | 0.31623 | 11.00 | 0.317 |
| | Group 2 | 10 | 0.0000 | 0.00000 | 10.00 | |

**Table 4: Intergroup Comparison of Bone Loss (Mesial and Distal) at Various Time Periods**

| Group | N | Mean | Std. Deviation | Mean Rank | P value |
|---|---|---|---|---|---|
| Bone Loss Mesial Group 1 | 10 | 11.210 | 2.22583 | 10.95 | 0.734 |
| (1 Week) Group 2 | 10 | 11.0400 | 2.50564 | 10.05 | |
| Bone Loss Mesial Group 1 | 10 | 10.2900 | 1.80521 | 10.10 | 0.762 |
| (3 months) Group 2 | 10 | 10.7900 | 2.66560 | 10.90 | |
| Bone Loss Mesial Group 1 | 10 | 10.1300 | 1.76387 | 10.20 | 0.820 |

| Group | N | Mean | Std. Deviation | Mean Rank | P value |
|---|---|---|---|---|---|
| (6 months) Group 2 | 10 | 10.7800 | 2.54593 | 10.80 | |
| Bone Loss Distal Group 1<br>(1 Week) Group 2 | 10<br>10 | 11,1700<br>10.9900 | 2.29882<br>2.31586 | 10.85<br>10.15 | 0.791 |
| Bone Loss Distal Group 1<br>(3 months) Group 2 | 10<br>10 | 10.5800<br>10.7600 | 2.11440<br>2.47575 | 10.30<br>10.70 | 0.880 |
| Bone Loss Distal Group 1<br>(6 months) Group 2 | 10<br>10 | 10.2700<br>9.7700 | 2.13752<br>4.02549 | 10.20<br>10.80 | 0.820 |

## DISCUSSION

Dental implant has been deemed as one of the disciplines in dentistry and are amongst the most researched topics in our field. Wide variety of implant system are available depending upon the shape, size, surface topography and coating each with its own advantage and limitation.

Recently bio-modification of implant surface have shown better implant-to-bone contact. Various studies have been conducted by modifying the implant surface showing hard and soft tissue changes clinically and radiographically.

Implant surface can be modified by various method like physical modification, mechanical modification, biological modification, chemical modification and nano technology. In the present study the implant surface was modified by chemical method. The drug used was alendronate. Alendronate belongs to the bisphosphonate (BP) class of drugs that are commonly used to treat osteoporosis. It is a second generation BP which has a tenfold increased efficacy over the first-generation bisphosphonates like etidronate. In a study by Zuffetti *et al.*, [12], clodronate solution- a second generation BP was used to irrigate the osteotomy site. Their study showed bisphosphonate-treated implant had more contact with newly formed bone than the control implant. There are three generations of BPs but the third- generation bisphosphonate are not easily available though they may be more potent than the previous generations.

The ability of Alendronate to increase osteoblastic differentiation and inhibit osteoclast recruitment and activity has been documented [6]. It was also found to stimulate osteogenesis in conjunction with regenerative materials around osseous defects and promote bone formation around endosseous implants. Moon *et al*., [13] also studied the effect of heparin and alendronate coating on titanium surfaces on inhibition of osteoclast and enhancement of osteoblast function, and suggested that alendronate-immobilized titanium implant enhances activation of osteoblast differentiation and inhibits osteoclast differentiation.

In the present study, a total of 20 patients (both males and females) were randomly divided into two groups- group I (Test group) and group II (control group). In test group, alendronate tablet was crushed into powder and mixed with 1ml saline solution in a dappen dish. The implant was then coated with the solution and the osteotomy site was irrigated with the prepared solution.

Local application of alendronate was employed in the present study since the use of long- term systemic BPs may lead to osteonecrosis of jaw which is also called as bisphosphonate-related osteonecrosis of jaw (BRONJ) [12]. In our study Alendronate dosage 20mg (10mg two tablet) was crushed into powder and then mixed in normal saline in a dappen dish. The concentration of the final solution obtained was 20mg/ml. In a previous study, alendronate at a concentration of 25mg was used and was applied using surgical foam pellets by Yaffe *et al*., [14]. It was demonstrated in their study that local application of this concentration resulted in a 10% absorption at the surgical site.

Another study done by StephenJ Meraw *et al*., [15], where hydroxyapatite implants were loaded with BPs, it was observed that hydroxyapatite had a high affinity to bind with bisphosphonate thus being absorbed on hydroxyapatite surface. However, no sustained release of the drug at the target site was seen even after being absorbed on the hydroxyapatite implant. In the present study irrigation in the osteotomy site was done with alendronate solution which may have not led to sustained release of the drug since no signs of osteoradionecrosis was observed during the study period.

Evaluation of hard and soft tissue parameters around the implant surfaces of both groups (test and control) was done. For soft tissue parameters, Plaque index, Gingival index and Sulcular bleeding index were evaluated. No statistically significant differences in plaque index between test and control groups at 1$^{st}$ week, 3 months and 6 months were seen (Table 1). Similar results were noted in a study Rajpal J *et al*., [16]. Gingival index recorded at 1$^{st}$ week, 3 months and 6 months between the two groups showed no statistically significant result at 1 week (P=0.089), at 3 months (P=0.146) and at 6 months (P=0.146) (Table 2). Sulcular bleeding index was also recorded at 1$^{st}$ week, 3 months and 6 months and no statistically significant difference in sulcular bleeding index when intergroup comparison was done at 1$^{st}$ week (P=0.089), at 3 months (P=0.146) and at 6 months (P=0.317) (Table 3). Similar results were also seen in the study done by Rajpal J *et al.*, [16].

For the hard tissue parameter, crestal bone level was evaluated with a radiographic grid placed on a IOPA by standardized paralleling technique with the help of XCP tool. Bhardwaj I *et al.,* [11] in their study also utilized a radiographic grid to evaluate marginal bone levels. The mesial and distal marginal bone levels were evaluated at 1 week, 3months and 6months post implant placement. No statistically significant difference in bone loss (mesial) between the two groups at 1 week (P=0.734), at 3 months (P=0.762) and at 6 months (P=0.820) (Table 4) was observed. Similarly, no statistically significant difference in bone loss (distal) between the two groups at 1 week (P=0.791), at 3 months (P=0.880) and at 6 months (P=0.820) (Table 5) was observed. The results obtained in the present study with regard to changes in marginal bone level is contrary to the study conducted by Sharma *et al.,* [17]. In their study, 1% alendronate gel applied in the surgical site showed a better bone fill when compared to placebo gel. The difference in the outcome can be attributed to the use of a gel in their study as against the solution used in the present study.

Biomodification of implant surface was done in the present study to reduce the amount of peripheral peri-implant bone loss and to improve the fixation of an implant to the bone. No statistically significant difference was observed in plaque score, gingival score, sulcus bleeding score and crestal bone loss. Similar observations were also seen in the study done by Aggarwal R *et al.,* [6] and Jahan S *et al.,* [7]. This might be due to the limitation of short follow-up and less sample size to establish the effectiveness of alendronate in implant osseointergration. Further studies with histochemical analysis should be done to know the amount of drug incorporated in the titanium surface of implant. Moreover, third generation bisphosphonate may also be used whenever available to see their efficacy as compared to second generation bisphosphonates used in the present study.

## CONCLUSION

Within the limitations of the present study, following conclusion can be made:

1) All the 20 implants placed in the patients, of both group demonstrated a 100% survival rate at the end of 6$^{th}$ month.
2) There was no statistically significant difference in reduction of crestal bone level, plaque score, gingival score and sulcus bleeding score in both test group and control group.

## REFERENCES


1. Coelho, P. G., Marin, C., Granato, R., Giro, G., Suzuki, M., & Bonfante, E. A. (2012). Biomechanical and histologic evaluation of non-washed resorbable blasting media and alumina-blasted/acid-etched surfaces. *Clinical oral implants research*, *23*(1), 132-135.
2. Kellesarian, S. V., Abduljabbar, T., Vohra, F., Malignaggi, V. R., Malmstrom, H., Romanos, G. E., & Javed, F. (2017). Role of local alendronate delivery on the osseointegration of implants: a systematic review and meta-analysis. *International Journal of Oral and Maxillofacial Surgery*, *46*(7), 912-921.
3. Almagro, M. I., Roman-Blas, J. A., Bellido, M., Castañeda, S., Cortez, R., & Herrero-Beaumont, G. (2013). PTH [1-34] enhances bone response around titanium implants in a rabbit model of osteoporosis. *Clinical oral implants research*, *24*(9), 1027-1034.
4. Al Amri, M. D., Kellesarian, S. V., Al-Kheraif, A. A., Malmstrom, H., Javed, F., & Romanos, G. E. (2016). Effect of oral hygiene maintenance on HbA1c levels and peri-implant parameters around immediately-loaded dental implants placed in type-2 diabetic patients: 2 years follow-up. *Clinical Oral Implants Research*, *27*(11), 1439-1443.
5. Aggarwal, R., Babaji, P., Nathan, S. S., Attokaran, G., Kumar, S. S., & Sathnoorkar, S. (2016). Comparative clinicoradiographical evaluation of effect of aminobisphosphonate (sodium alendronate) on peri-implant bone status: Controlled clinical trial. *Journal of International Society of Preventive and Community Dentistry*, *6*(4), 285-290.
6. Veena, H. R., & Prasad, D. (2010). Evaluation of an aminobisphosphonate (alendronate) in the management of periodontal osseous defects. *Journal of Indian Society of Periodontology*, *14*(1), 40-45.
7. Jahan, S., Kaushik, M., & Wadhawan, A. (2019). Comparative evaluation of peri-implant soft and hard tissue with and without application of bisphosphonate on implant surface and osteotomy site–A clinico-radiographic, cone-beam computed tomographic study. *Contemporary Clinical Dentistry*, *10*(2), 208-213.
8. Mombelli, A., Van Oosten, M. A. C., Schürch Jr, E., & Lang, N. P. (1987). The microbiota associated with successful or failing osseointegrated titanium implants. *Oral microbiology and immunology*, *2*(4), 145-151.
9. Misch, C. E. (1993). Implant success or failure: Clinical assessment in implant dentistry. In: Misch, C. E, editor. *Contemporary Implant Dentistry*. St Louis: Mosby; pp. 29-42.
10. Apse, P., Zarb, G. A., Schmitt, A., & Lewis, D. W. (1991). The longitudinal effectiveness of osseointegrated dental implants. The Toronto Study: peri-implant mucosal response. *International Journal of Periodontics & Restorative Dentistry*, *11*(2), 95-111.
11. Bhardwaj, I., Bhushan, A., Baiju, C. S., Bali, S., & Joshi, V. (2016). Evaluation of peri-implant soft tissue and bone levels around early loaded implant in restoring single missing tooth: A clinico-

radiographic study. *Journal of Indian Society of Periodontology*, *20*(1), 36-41.

12. Zuffetti, F., Bianchi, F., Volpi, R., Trisi, P., Fabbro, M. D., Capelli, M., ... & Testori, T. (2009). Clinical application of bisphosphonates in implant dentistry: histomorphometric evaluation. *International Journal of Periodontics & Restorative Dentistry*, *29*(1), 31-39.
13. Moon, H. J., Yun, Y. P., Han, C. W., Kim, M. S., Kim, S. E., Bae, M. S., ... & Kwon, I. K. (2011). Effect of heparin and alendronate coating on titanium surfaces on inhibition of osteoclast and enhancement of osteoblast function. *Biochemical and Biophysical Research Communications*, *413*(2), 194-200.
14. Yaffe, A., Iztkovich, M., Earon, Y., Alt, I., Lilov, R., & Binderman, I. (1997). Local delivery of an amino bisphosphonate prevents the resorptive phase of alveolar bone following mucoperiosteal flap surgery in rats. *Journal of periodontology*, *68*(9), 884-889.
15. Meraw, S. J., Reeve, C. M., & Wollan, P. C. (1999). Use of alendronate in peri-implant defect regeneration. *Journal of periodontology*, *70*(2), 151-158.
16. Rajpal, J., Gupta, K. K., Tandon, P., Srivastava, A., & Chandra, C. (2014). Assessment of hard and soft tissue changes around Implants: A clinico-radiographic: in vivo: study. *Journal of Dental Implants*, *4*(2), 126-134.
17. Sharma, A., & Pradeep, A. R. (2012). Clinical efficacy of 1% alendronate gel as a local drug delivery system in the treatment of chronic periodontitis: a randomized, controlled clinical trial. *Journal of periodontology*, *83*(1), 11-18.