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Are Bone Turnover Markers and Vitamin D levels associated with Frequency of Complete Denture Relines?

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Are Bone Turnover Markers and Vitamin D levels associated with Frequency of Complete Denture Relines?

by

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A thesis submitted in partial fulfillment
of the requirements for the degree
Master of Science in Prosthodontics

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Each person whose signature appears below certifies that this thesis in his opinion is adequate, in scope and quality, as a thesis for the degree Master of Science.

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ABSTRACT OF THE THESIS

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Loma Linda University, September 2015
Dr. Mathew Kattadiyil, Chairperson

PURPOSE: To compare groups of subjects with varying frequencies of complete denture relines in terms of their bone turnover markers; C-terminal Telopeptide (C-Tx), Osteocalcin (OCN) and Vitamin D (25 OH- Vit D) levels to determine the presence of and the degree of association between them.

METHODS: This study was designed as a cross sectional study wherein a retrospective chart review of three hundred twenty four edentulous subjects with history of complete denture use for at least a year was performed to determine history and frequency of their complete denture relines. A total of 100 patients were enrolled. After consent was obtained, each subject was interviewed with a questionnaire for his or her updated medical and dental history, and medication/supplement use. A blood sample was obtained to measure 25-OH Vitamin D, Osteocalcin and C-terminal Telopeptide levels. Statistical comparison was done between the results obtained to determine the presence of an association between the frequency of relines and the bone turnover markers (OCN, CTx) and Vitamin D.

RESULTS: Significant correlations were found between the bone turnover markers, C-terminal telopeptide (C-Tx) (Pearson correlation coefficient 0.538, $p<0.001$) and

osteocalcin (OCN) (Pearson correlation coefficient 0.434,) and frequency of relines ($p<0.001$). The other variables like age, gender, race, diabetes, calcium and vitamin D supplements did not reveal any statistically significant effect on the frequency of complete denture relines.

CONCLUSION: The results of our study indicate that edentulous patients with elevated bone turnover markers, C-Tx and OCN, reveal increased frequency of denture relines.

CLINICAL IMPLICATIONS**:** Association between the frequency of complete denture relines and bone turnover markers can serve as an early predictor for rapid alveolar bone resorption and can assist in identifying patients at risk for frequent relines.

CHAPTER ONE

INTRODUCTION

The number of people in the United States requiring removable prosthodontic therapy has increased dramatically over the past 20 years (1). Current predictions for the next two decades suggest that the declining incidence of edentulism seen over the past two decades (2) will be more than compensated by an estimated 79% increase in adults over 55 years of age (3). There are multiple factors leading to complete edentulism, such as caries, periodontal disease, trauma or just plain neglect. Of the available rehabilitation options, most people opt for conventional complete dentures. These dentures, however, have to be relined at regular intervals as alveolar bone resorption continues to progress. Without relining, ill-fitting dentures lead to significant soft tissue morbidity and affects masticatory function, phonetics and confidence of the patient negatively. In addition, they can lead to temporomandibular joint disorders. The degree of resorption and the frequency of relines vary widely among the denture patients; and there is no predictor for rate of resorption. To date, there are no guidelines on the frequency of denture relines required for an edentulous patient. The lack of literature in this context has been acknowledged in the American College of Prosthodontics guidelines on the care and maintenance of complete dentures (4).

Alveolar bone loss precedes skeletal bone loss (5,6) and has been linked to osteoporosis and osteopenia. Bone mineral density measured at the hip and the spine by either dual absorptiometry x-ray or quantative computerized tomography

is the gold standard for diagnosing osteoporosis but may have false negatives due to conditions like osteoarthritis. Bone is maintained in the body by a balance in "bone turnover" which involves the processes of bone resorption (i.e. removal of existing bone by osteoclasts) and bone formation (i.e. deposition of new bone by osteoblasts). Alveolar bone has a relatively high turnover, thus, small imbalance between resorption and formation could manifest as increased rate of alveolar bone loss. Therefore, a patient may have substantial alveolar bone loss without evident generalized osteoporosis (7).

Bone turnover markers are elevated in patients undergoing bone loss (8). These bone turnover markers include both enzymes and non-enzymatic peptides derived from cellular and non-cellular compartments of bone. Most common markers are bone-specific alkaline phosphatase, hydroxyproline, hydroxylysine, pyridinoline, bone sialoprotein, C terminal telopeptide, N terminal telopeptide etc. to name a few.

Serum osteocalcin (OCN) and C-terminal telopeptide (C-Tx) are among the most sensitive markers of bone turnover and are easily obtained via blood draw (13). Vitamin D deficiency is also known to exacerbate and contribute to bone loss and osteoporosis (9). In fact, bone resorption has been reported to decrease when vitamin D is supplemented orally (10).

The primary hypothesis of this cross sectional pilot clinical study was that there would be a significant correlation between serum levels of bone turnover markers such as C-Tx and OCN and increased frequency of relines. The secondary hypothesis was that

there might be a negative correlation between serum Vitamin D levels and frequency of relines.

CHAPTER TWO

MATERIALS AND METHODS

This study was funded by an intramural grant, Grants for Research and School Partnerships (GRASP), from the Loma Linda University. After Institutional Review Board (IRB) approval was obtained, the electronic dental record system (axiUm, Coquitlam, BC, Canada) of the university dental school clinic was queried from Jan 2006 to Dec 2013 for patients aged 45 or older who had worn complete dentures for at least one year. A total of three hundred and twenty four subjects were identified. The charts of these subjects were searched for treatment codes of denture relines. All subjects who had conventional complete dentures, either maxillary, mandibular or both, were then screened for exclusion criteria which were: use of bisphosphonates or oral glucocorticoids (≥5mg/day of prednisone for ≥3months); history of metastases to bone, multiple myeloma, Paget's disease within the last 10 years; diseases affecting bone metabolism like chronic kidney disease, chronic liver disease, hyperparathyroidism, inflammatory bowel disease, rheumatoid arthritis, uncontrolled Diabetes Mellitus, and post menopausal women on hormone replacement therapy.

A sample size calculation was done based on published reports which have indicated a difference of approximately 21% between osteocalcin values in individuals with low bone turnover compared to those with higher levels of bone turnover and that are associated with bone loss. Poisson regression analysis of the dependent variable (reline counts) on the normally distributed independent

variable (serum OCN) was selected as the *apriori* statistical methodology to test the primary hypothesis. OCN was chosen because of the higher precision and repeatability of the assay compared to that of CTX (interassay coefficient of variations ranges: 2.6 to 3.9 vs. 7.7 to 8.5, respectively. To detect a response odds ratio of at least 1.25 due to a one-unit change in the serum OCN (mean =6.2ng/mL and standard deviation of 2.3) (11) requires a sample of 100 observations to achieve 80% power at 0.05 significance. The baseline reline rate is 20% and the mean exposure time is 3 years (12). The sample size was adjusted since a multiple regression of the covariate of interest on the other covariates in the Poisson regression is expected to have an R-Squared of 0.4. The sample size was adjusted for an over-dispersion parameter of 1.7. From this anaysis, a total of 100 patients was confirmed to be an adequate sample size. One hundred subjects were planned to be enrolled between April 2014 to October 2014.

After applying the inclusion and exclusion criteria, eligible subjects were contacted by phone for prescreening. Subjects who were willing to be considered for the study were scheduled for an appointment. At the appointment, the dental research personnel met with the subjects, explained the study in detail, including the need for a blood sample, and obtained informed consent. The research personnel then administered a questionnaire (see appendix A) regarding medical history and current medications/supplements, dental health, denture timeline and denture-care practices of the subject. The subjects were asked about bisphosphonate use, but none reported taking bisphosphonates. Subjects were asked about their history of dental relines. Denture reline frequency was calculated

by asking the subjects when they had the first denture and how many subsequent dentures/ relines they have had due to the dentures losing retention. Frequency of reline was defined as the average number of reline per year and was calculated as the ratio of # of relines/# years since first reline. (e.g. if a subject had 5 dentures over last 30 years due to loss of retention, the reline frequency was calculated to be 0.167. For subjects who had all of their relining performed at the Loma Linda University School of Dentistry clinic, the frequency of relining was confirmed by review of their dental records. If a new denture was fabricated because of need for reline, it was counted as a reline occurrence. A dental exam was done to assess the condition of the present dentures to determine if they needed another reline or denture. To minimize the risk of loss of subject privacy, a data log was created that contained an assigned subject code number and the collected data variables, but which did not contain personal identifiers. The first 100 subjects were enrolled and at the end of study enrollment, a total of 50 males and 50 females were selected.

Serum OCN and C-Tx have diurnal variations and can be influenced by food, therefore require fasting morning blood samples (14). Studies linking these markers to osteoporosis recommend drawing these samples in the morning hours. The subjects selected for the study were given a morning appointment for blood sample collection at the university medical office laboratory, with appointments scheduled between 8am and 10 am to eliminate inconsistencies in test results based on the diurnal variation of the serum markers. Two 5 ml vacutainers were collected and the samples processed for 25-OH Vitamin D, serum OCN and C-Tx.

After the lab results were obtained, subjects with abnormal lab values were re-

contacted, informed of the results and advised to discuss the abnormal results with their primary care provider.

25-OH Vit D

Normal range: 30-100 ng/mL

The two major physiologically relevant forms of Vitamin D are Vitamin D2 (ergocalciferol) and Vitamin D3 (cholecalciferol). Vitamin D3 is derived mainly from actions of ultraviolet light on the skin while D2 is derived solely from dietary sources. As Vitamin D enters the circulation, it is metabolized to several forms, the majority of these being 25-hydroxycalciferol (25-OH-D). The first step in the metabolism of Vitamin D, 25-hydroxylation, occurs mainly in the liver. Only a small amount of 25-OH-D is metabolized in the kidney to other dihydroxyvitamin D metabolites. Since 25-OH-D is the predominant circulating form of Vitamin D in the population, it is considered to be the most reliable index of Vitamin D status. Its assay is a competitive radioimmunoassay with sample extraction.

Osteocalcin

Normal range:

Males: 3.2-39.6 ng/mL

Premenopausal females: 4.9-30.9 ng/mL

Postmenopausal females: 9.4-47.4 ng/mL

Osteocalcin, a 49 amino acid peptide is the major non-collagen protein of bone. Vitamin K is essential for the biosynthesis of osteocalcin, which is stimulated

by 1, 25-dihydroxyvitamin D. Osteocalcin is synthesized by osteoblasts during the process of bone formation and then incorporated into the bone matrix. During the process of bone resorption, it is released into the circulation from the matrix and hence, is considered a marker of bone turnover, rather than a specific marker of bone formation. It is immunoassayed using electrochemiluminescent detection.

C-Telopeptide

Normal range:

Males: 115-748 pg/mL

Premenopausal females: 112-738 pg/mL

Postmenopausal females: 142-1351 pg/mL

Beta C-terminal telopeptide (β-CTX) is a specific resorption marker for degradation of bone type I collagen by osteoclasts. More than 90% of organic bone matrix consists of type I collagen, which is primarily synthesized in bone. Bone constantly undergoes remodeling which includes bone resorption mediated by the action of osteoclasts. In abnormal states of bone metabolism, this process becomes imbalanced. When the rate of resorption exceeds formation (such as in osteoporosis), loss of bone mass occurs with a consequent increase in susceptibility to fractures. Resorption leads to an increase in the circulation of type I collagen fragments. Especially relevant collagen type I fragments are the C-terminal telopeptides (CTX). As bone ages, the a-aspartic acid that is present in C-terminal telopeptides converts to the β-form of aspartic acid (β-CTX). These isomerized telopeptides are specific for the degradation of type I collagen dominant in bone.

Elevated serum concentrations of isomerized C-terminal telopeptides of type I collagen have been reported for patients with increased bone resorption and serum levels return to normal during resorption-inhibiting therapy. It is immunoassayed using electrochemiluminescent detection.

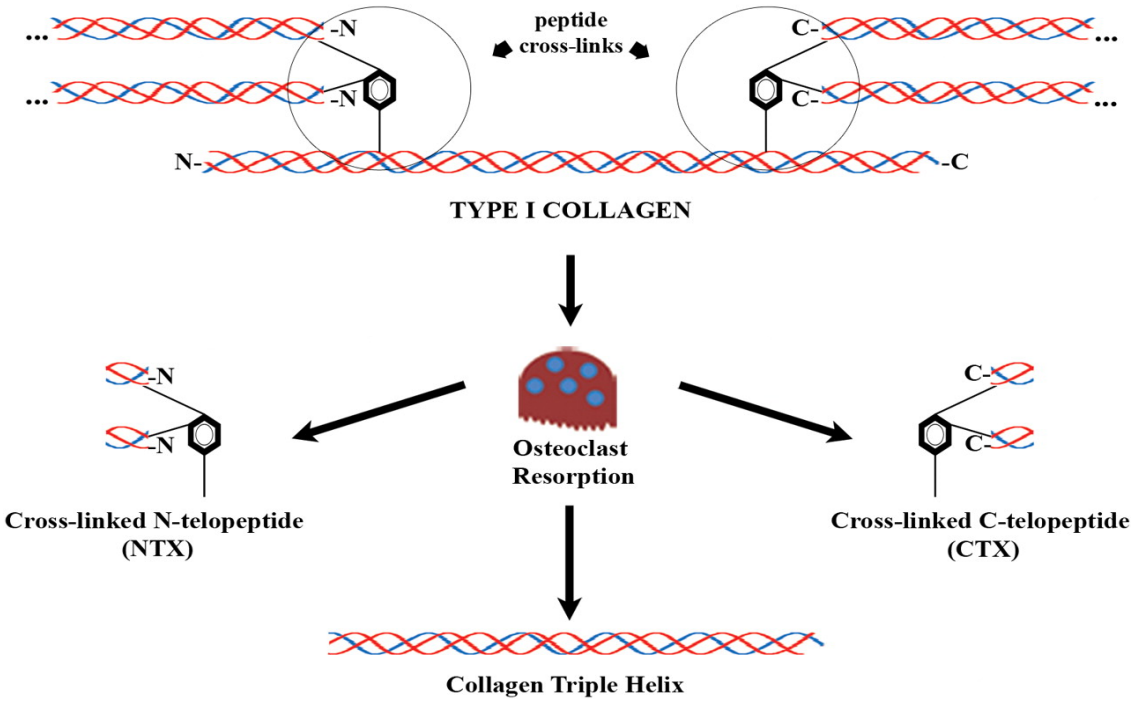

Figure 1. Structure of collagen with its terminal telopeptides.

Statistical Analysis

Data analysis was done using SPSS software (IBM, Armonk, NY, USA). Continuous variables were summarized using means and standard deviations for the data, which were normally distributed. Two-variable comparisons were performed by Independent t-test whereas analysis of variance (ANOVA) was used for comparisons between two or more groups. Pearson Correlation was used to assess the relationship between continuous variables. Results were considered significant at p-values of less than 0.05.

CHAPTER THREE

RESULTS

A total of 50 male and 50 females were included in the study. The mean age of males was 70.70 years and of females was 71.92 years. The males and females had a mean reline frequency of 0.11 and 0.10 over 15.48 and 19.73 years respectively. Baseline characteristics are detailed in Table 1.

Table 1. Baseline characteristics and demographics

Baseline Characteristics		Male	Female
Age (years) (mean ± SD)		70.70 ± 13.09	71.92 ± 10.30
Frequency of reline (mean ± SD)		0.11 ± .09	0.10 ± .10
Time (mean ± SD)		15.48 ± 12.44	19.73 ± 17.33
Race N (%)	Caucasian	42 (84%)	34 (68%)
	African American	2 (4%)	4 (8%)
	Asian	3 (6%)	5 (8%)
	Hispanic	4 (6%)	8 (16%)
Calcium Supplements N (%)	No	34 (68%)	27 (54%)
	Yes	16 (32%)	23 (46%)
Vit D supplements N (%)	No	22 (44%)	18 (36%)
	Yes	28 (56%)	32 (64%)
Diagnosis of Diabetes N (%)	No	41 (82%)	42 (84%)
	Yes	9 (18%)	8 (16%)

The mean value of Vitamin D levels, Osteocalcin levels and C-Telopeptide levels are provided in Table 2.

The frequency of relines in males was 0.11 per year and 0.10 in females. There was no statistical difference in the frequency of relines or levels of Vitamin D, Osteocalcin and C Telopeptide between males and females. (Table 2.)

Table 2. Effect of gender on variables

Independent Samples Test					
Gender		N	Mean	Std. Deviation	*P*-value
Vit D	Male	50	40.48	14.31	0.27
	Female	50	37.52	12.59	
C-Tx	Male	50	399.78	210.88	0.69
	Female	50	417.28	221.72	
OCN	Male	50	23.16	12.43	0.67
	Female	50	24.24	13.06	
Frequency of Reline	Male	50	0.11	0.09	0.56
	Female	50	0.10	0.10	

To assess for confounding variables, patients who reported use of calcium supplements were evaluated against the biomarkers, Vitamin D and frequency of reline. Mean Vitamin D levels were 45.36 ng/ml in those taking supplements and 34.93 ng/ml in those not taking supplements with a p value of <0.001 of the t-test. The *P* values for C-Tx, OCN and reline frequency were not significant. (Table 3.)

Table 3. Effect of calcium supplement intake on variables

Independent Samples Test					
Calcium Supplements		N	Mean	Std. Deviation	P-value
Vit D	No	61	34.93	12.76	<0.001*
	Yes	39	45.36	12.21	
C-Tx	No	61	418.26	221.57	0.58
	Yes	39	393.31	207.42	
OCN	No	61	23.36	12.41	0.74
	Yes	39	24.23	13.27	
Frequency of Reline	No	61	0.11	0.11	0.64
	Yes	39	0.11	0.08	
* Statistically significant at an alpha of 0.05					

Similarly, use of Vitamin D supplements was evaluated and patients using supplements had a mean Vitamin D level of 44.17ng/ml as compared to 31.25ng/ml in those not taking supplements ($p<0.001$). The *p* values for C-Tx, OCN and reline frequency were not significant. (Table 4.)

Table 4. Effect of Vitamin D supplement intake on variables

Independent Samples Test					
Vit D supplements		N	Mean	Std. Deviation	*P*-value
Vit D	No	40	31.25	10.41	<0.001*
	Yes	60	44.17	12.88	
C-Tx	No	40	390.90	206.79	0.51
	Yes	60	420.28	221.96	
OCN	No	40	21.40	9.67	0.14
	Yes	60	25.23	14.24	
Frequency of Reline	No	40	0.11	0.11	0.73
	Yes	60	0.11	0.08	
* Statistically significant at an alpha of 0.05					

The effect of presence of diabetes was also evaluated and diabetic patients had a mean frequency of relines of 0.12 against non-diabetic who had a reline frequency 0.11, with p value of 0.50 (Table 5.). Similarly, there were no differences observed in levels of Vitamin D, C-TX or OCN between patients with or without a diagnosis of diabetes

Table 5. Effect of diabetes on variables

Independent Samples Test					
Diabetic		N	Mean	Std. Deviation	P-value
Vit D	No	83	39.18	13.92	0.77
	Yes	17	38.12	11.52	
C-Tx	No	83	412.07	222.22	0.71
	Yes	17	391.24	183.70	
OCN	No	83	23.63	12.19	0.90
	Yes	17	24.06	15.34	
Frequency of Reline	No	83	0.11	0.10	0.50
	Yes	17	0.12	0.05	

ANOVA was done to compare variables of interest based on the arch on which reline was done (maxilla, mandible or both) (Table 6.) and race (Caucasian, African-American, Asian and Hispanic) (Table 7.). No significant effect of arch type or race was found on biomarker or Vitamin D levels.

Table 6. Effect of reline arch on variables

Reline Arch		N	Mean	Std. Deviation	95% Confidence Interval for Mean		P-value
					Lower Bound	Upper Bound	
Vit D	Maxilla	12	39.67	21.99	25.69	53.64	0.48
	Mandible	9	33.78	13.08	23.72	43.84	
	Both	78	39.57	11.96	36.88	42.27	
C-Tx	Maxilla	12	368.50	249.25	210.13	526.87	0.60
	Mandible	9	362.33	109.63	278.07	446.60	
	Both	78	420.41	221.14	370.55	470.27	
OCN	Maxilla	12	22.25	15.17	12.61	31.89	0.59
	Mandible	9	20.22	7.97	14.10	26.34	
	Both	78	24.44	12.83	21.54	27.33	
Frequency of Reline	Maxilla	12	0.08	0.07	0.04	0.13	0.58
	Mandible	9	0.11	0.08	0.05	0.17	
	Both	78	0.11	0.10	0.09	0.14	

Table 7. Effect of race on variables

Race		N	Mean	Std. Dev.	95% Confidence Interval for Mean		P-value
					Lower Bound	Upper Bound	
Vit D	Caucasian	76	40.14	13.88	36.97	43.32	0.50
	African American	6	34.00	8.92	24.64	43.36	
	Asian	7	35.14	12.39	23.69	46.60	
	Hispanic	11	36.25	13.46	27.21	45.30	
C-Tx	Caucasian	76	415.95	208.06	368.40	463.49	0.47
	African American	6	334.33	115.77	212.84	455.83	
	Asian	7	318.29	118.79	208.42	428.15	
	Hispanic	11	455.18	328.44	234.53	675.83	
OCN	Caucasian	76	24.87	13.40	21.81	27.93	0.16
	African American	6	15.00	4.20	10.60	19.40	
	Asian	7	17.57	2.30	15.45	19.70	
	Hispanic	11	24.27	12.41	15.94	32.61	
Freq. of Reline	Caucasian	76	0.11	0.08	0.09	0.13	0.55
	African American	6	0.07	0.06	0.00	0.14	
	Asian	7	0.15	0.17	-0.01	0.30	
	Hispanic	11	0.12	0.14	0.03	0.21	

After evaluating for all confounding variables, Pearson correlation was used to assess the relationship between frequency of relines and biomarker/Vitamin D levels. (Table 8.) The Pearson correlation showed statistically significant (*P* value <0.001) values for C-terminal Telopeptide and Osteocalcin and no significant relationships were observed between frequency of reline and age (data not shown) or Vitamin D (Figure 1). In contrast, significant positive correlations were observed between the levels of bone resorption markers C-terminal Telopeptide and Osteocalcin and frequency of relines. (Figures 2 and 3, respectively)

Table 8. Correlation among the variables

Correlations		
Variable tested with frequency of relines	Pearson Correlation	P-value
Vit D	0.03	0.79
C-Telopeptide	0.54	<0.001*
Osteocalcin	0.43	<0.001*
Age (years)	0.01	0.93
* Statistically significant at an alpha of 0.05		

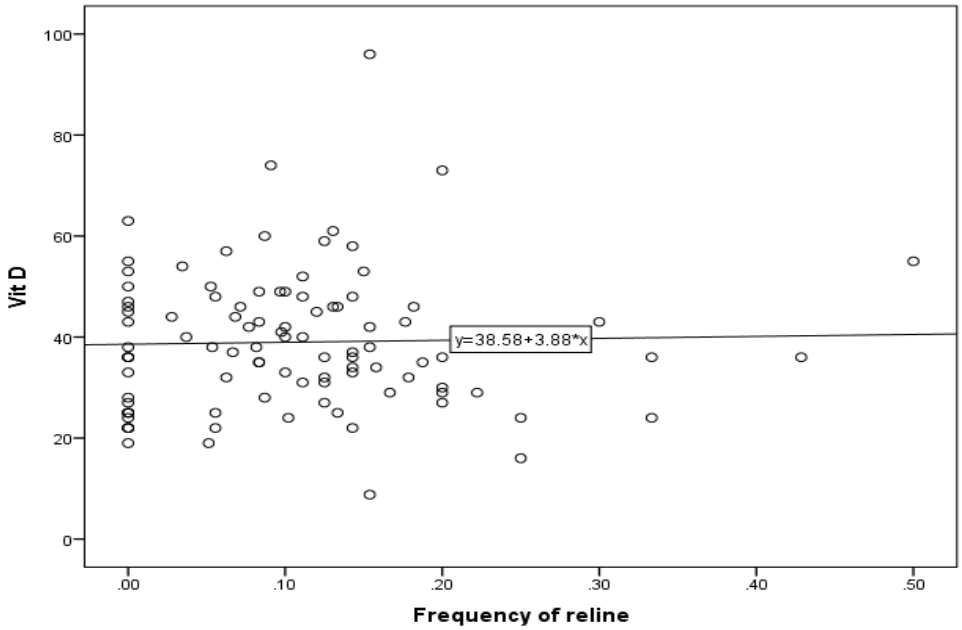

Figure 2. Scatter plot of correlation of Vitamin D and frequency of relines

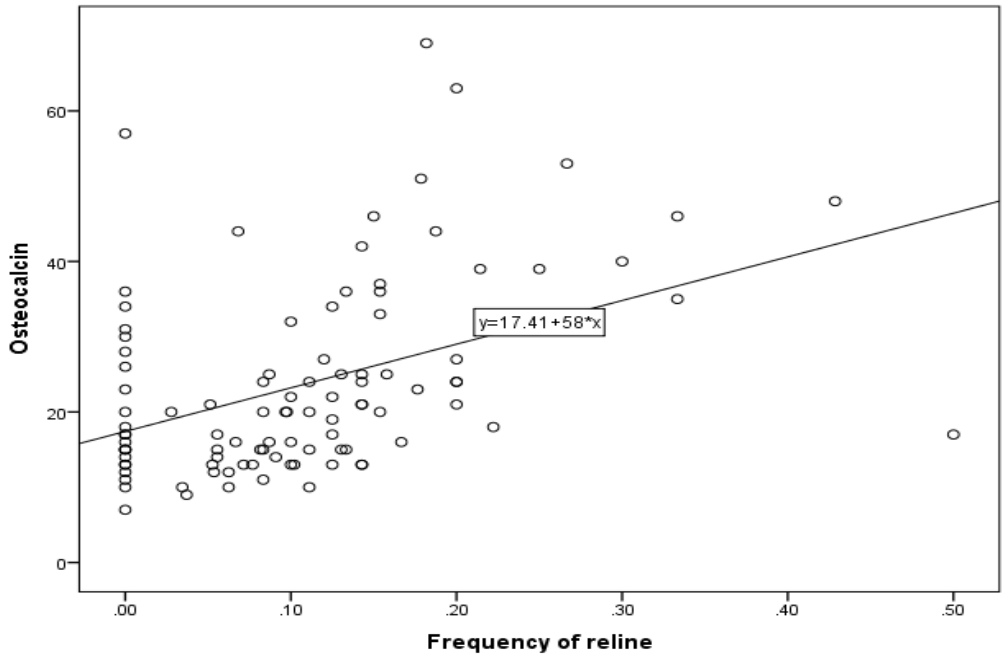

Figure 3. Scatter plot of correlation of Osteocalcin and frequency of relines

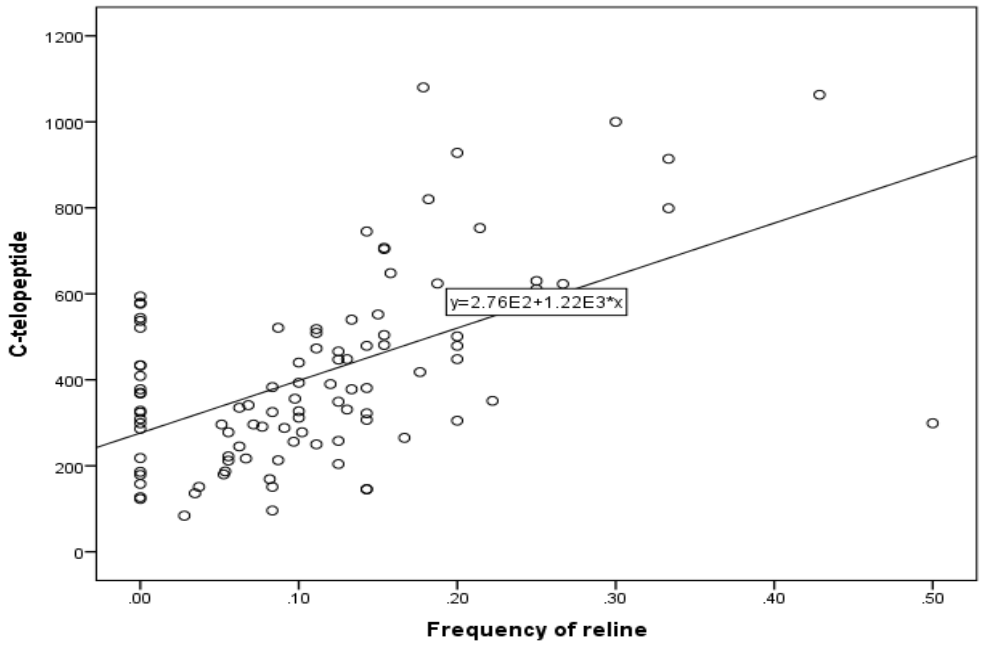

Figure 4. Scatter plot of correlation of C Telopeptide and frequency of relines

CHAPTER FOUR

DISCUSSION

Residual ridge resorption (RRR) (15), which is defined as diminishing quantity and quality of the residual ridge after teeth are removed, is a lifelong process, The rate of reduction in size of the residual ridge is maximum in the first 3-6 months and then gradually tapers off. (16). It has also been shown that the rate of RRR varies from one individual to another at different phases of life and even at different sites in the same person (17,18) . Additionally. the RRR is four times faster in the mandible as compared to the mandible (19,20). Over time various etiologic factors, both local and systemic, have been found to be responsible for this process (21, 22,23, 24) that contribute to this extremely dynamic physiologic process that causes changes in the architecture of the maxillary and mandibular ridges. To dental clinicians, this phenomenon has significance as this can lead to loss of support to the complete removable denture prosthesis making them unstable, inefficient and uncomfortable for the patient. This in turn calls for frequent relines/ remakes of these prostheses to make up for the resorption of bone. Since the rate at which these relines need to be done is unknown due to lack of any reliable predictors, the whole process continued to be an enigma that remained unsolved.

To the best of our knowledge, this report is the first to identify the relationship between biomarker levels and frequency of complete denture relines. With a paucity of studies on frequency of denture relines, our study provides much needed information on this topic and perhaps an innovative solution to this

important clinical scenario by identifying bone resorptive biomarkers as possible early predictors of alveolar bone resorption associated with denture reline frequency.

Results from this study show that the reline frequency is independent of gender. A one-year double-blinded study has shown that there is 36% reduction in mean alveolar bone loss of patients receiving calcium and Vitamin D supplements when compared to those receiving placebo (25). According to the results of our study, the use of calcium and Vitamin D supplements did not affect frequency of relines but did affect the Vitamin D levels. This is likely due to the fact that most marketed calcium supplements are supplied in combination with Vitamin D. Also, the race of the patient did not affect the reline frequency. Diabetic patients have low bone turnover that can affect the levels of bone turnover markers (26), however, our results show that there was no statistical difference between diabetics and non diabetics in terms of biomarker levels, Vitamin D levels or reline frequency. The reasons why our results differ from other published reports is unclear, but may be due to differences in study populations, study design, and/or the type of biomarker or the measurement assays performed.

Prior studies have shown that alveolar bone resorption can be faster in the mandible (19,20). Therefore a sub analysis was done to assess this as a confounding effect. However, our results did not show a statistical difference in the reline frequency of the biomarker levels among patients with maxillary denture, mandibular denture or complete dentures in both arches. This difference in results could be due to the fact that our study was a cross-sectional study and as such we

could not determine how much resorption had occurred already in each arch even in patients who had relines for both maxillary and mandibular dentures. In future prospective studies, this could be done by measuring the ridge height using standardized radiographs to compare the true amount of resorption in both the arches separately as demonstrated by Wical et al. (27)

According to our study, age did not affect the reline frequency, which suggests that any correlation found between biomarker levels and reline frequency seems to be independent of age as well. Bisphosphonate use can also slow down bone turnover and affect biomarker levels, but use of bisphosphonates was an exclusion criteria.

We observed a strong positive and linear correlation between reline frequency and levels of OCN and C-Tx. Patients with higher frequency of relines had higher levels of these bone turnover markers circulating in their blood. Amongst C-Tx and OCN, the correlation was stronger with C-Tx. The significance of this is unclear but could be due to the fact that OCN because it is released by osteoblasts, it is reflective of the bone formation aspect of the bone turnover process. In contrast, C-Tx is released directly as a result of bone resorption. Clinically, the significance of our findings is the potential use of biomarkers to predict the pattern of bone resorption. This translates into the ability to predict risk of need for frequent relines, and thus, can help the patient and their treatment provider in making more informed decisions, and provide appropriate recommendations regarding the various treatment choices available. For instance, based on the values of the markers, subjects at higher risk of frequent relines could benefit from implants and

implant retained/supported prosthesis as opposed to conventional complete dentures. Early placement of implants would help preserve bone as well as reduce the need for relines especially in implant supported fixed prosthesis (28,29). However, a larger study would be needed to determine cutoff values of the markers that would define the risk status.

Since alveolar bone resorption may precede skeletal resorption, this could be a novel approach for early identification of potentially co-morbid conditions such as osteoporosis/osteopenia.

Bisphosphonates are effective antiresorptive agents successfully used to treat diseases characterized by osteoclast-mediated bone resorption, such as osteoporosis, Paget disease, and metastatic bone diseases (30). Our study suggests a new, intriguing area of exploration for future studies related to the possibility of using these medications to reduce the amount of RRR and eventually frequency of relines. For example, a limited course of bisphosphonate therapy soon after teeth removal, when RRR is greatest, could potentially attenuate residual ridge loss. However, this benefit would have to balanced against the risk of bisphosphonate-related osteonecrosis of the jaw, a serious and difficult to treat dental condition. At any rate, further clinical studies are required before such an approach can be recommended.

This study is the first to investigate the association of bone turnover markers and reline frequency. One of the limitations of the study is that the study population was mainly White and most of the patients wore dentures on both arches. Therefore, to answer the question whether race or denture arch truly affects

denture frequency, further investigations will be required. Another potential limitation of this study was that although the patient-reported number of relines was confirmed with the dental records when available, this was not possible for some patients who had relines done at another facility. These relines were documented based on self-reporting alone. Hence, a recall bias could have occurred leading to minor discrepancies. Also, the design of the study was cross sectional with only one value of the biomarker levels recorded at the time of the study. As we did not have any prior value to compare our levels with, fluctuations or over time could not be factored in the analysis. Whether these fluctuations, if any, would affect reline frequency is unknown and requires future prospective studies.

CHAPTER FIVE

CONCLUSIONS

This study identifies a significant linear correlation between frequency of complete denture reline and OCN and C-Tx levels, which appear to be independent of age, gender, race, use of calcium and Vitamin D supplements and denture arch. Future studies with increased number of subjects are needed to confirm this correlation and to determine a cutoff value of OCN or C-Tx level above which patients with higher risk of frequent relines due to rapid alveolar bone resorption can be identified and offered adjunctive treatment such as dental implants and bone augmentation techniques to preserve the remaining alveolar bone long term.

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APPENDIX A

QUESTIONNAIRE USED FOR DATA COLLECTION

Name____

- - - - - - - - --- - - - - --- --- - - - -

Patient ID no (for office use)____________________

Age____

Sex MALE FEMALE

Race Caucasian African-American Asian Hispanic

Native American /Pacific Islander Other

Dental History:

When was the first time you had dentures?

Where did you get your first denture?

What was the reason the teeth had to be extracted?

How many times have you had dentures since the first time?

How frequently have you had to replace dentures?

What problems have you had with your dentures?

Medical history:

Do you have Diabetes mellitus?

If yes, are your sugars well controlled?

If female, are you post menopausal?

If yes, have you ever been on hormone replacement therapy?

If yes, how long have you been on HRT?

Have you been diagnosed with:		How long?
- Chronic kidney disease	yes/no	_____
- Rheumatoid arthritis	yes/no	_____
- Bone cancer/cancers spreading to bone	yes/no	_____
- Multiple myeloma	yes/no	_____
- Paget's disease	yes/no	_____

Medication history

Are you on any of the following medications:		How long?
- Alendronate (Fosamax)	yes/no	_____
- Risedronate (Actonel/Atelvia)	yes/no	_____
- Ibandronate (Boniva)	yes/no	_____
- Zolindronate (Reclast)	yes/no	_____
- Raloxifene (Evista)	yes/no	_____
- Denosumab (Prolia)	yes/no	_____
- Calcitonin (Miacalcin, Fortical)	yes/no	_____
- Teriparatide (Forteo)	yes/no	_____

Do you take calcium and/or Vit D supplements?
If yes, how often do you take them?
How long have you been taking them?