

The Evaluation of Correlation Between Serum PTH and Dentoskeletal Changes in Panoramic Imaging of Hemodialysis Patients

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Introduction. This study aimed to investigate the relationship between serum levels of PTH and dental and bone changes in the panoramic view of hemodialysis patients.

Methods. Out of 236 patients with end-stage kidney disease (ESKD) who were hospitalized in two hemodialysis centers, 68 ones were selected and concerning their PTH serum levels, they were assigned to case group (PTH > 300 pg/mL) and control group (150 < PTH < 300 pg/mL). Patients in both groups had undergone dialysis for at least 6 months. After intraoral and extraoral examinations, panoramic radiography was performed for patients who hadn't taken any panoramic radiograph within 6 months prior to our study. All radiographs were evaluated for DMFT (decayed, missing and filled teeth) index, bone resorption, periodontal ligament (PDL), lamina dura, mandibular cortical thickness, bone granular pattern, pulp and periapical lesion and giant cell (brown) tumor. The results were analyzed by Chi square statistical tests. Significant level (*P* value) of test was considered less than .05.

Results. Among the eight variables, there was only a significant statistical difference between the case and control groups in the granular bone pattern and inferior mandibular cortex thickness.

Conclusion. High levels of PTH in hemodialysis patients with secondary hyperparathyroidism can significantly change the trabecular alveolar bone pattern to a granular bone pattern. It also dramatically decreases the thickness of the inferior mandibular cortex. The findings of this study could influence the dental treatment plans for ESKD patients and help in early diagnosis of osteoporosis in patients on dialysis with secondary hyperparathyroidism.

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INTRODUCTION

Chronic kidney disease (CKD) is a common disease all around the world, with increasing prevalence and massive health burden. In new guidelines, CKD is defined as abnormalities of kidney structure or function, present for more

than 3 months, with implications on health, which requires either GFR < 60 mL/min/ 1.73m² or markers of kidney damage, i.e albuminuria and hematuria.¹⁻³

Diabetes mellitus and hypertension are two main causes of CKD. Familial history, diet, toxicity with

heavy metals and other risk factors could also lead to loss of kidney function over time.⁴ According to the National Kidney Foundation (NFK)-Kidney Disease Outcomes Quality Initiative (KDOQI) in 2012, CKD can be divided into five stages based on GFR, and the last stage (stage 5) is known as end stage kidney disease (ESKD), in which, GFR is less than 15 mL/min/ 1.73m² and therefore, kidney replacement therapy would become necessary.⁵ Secondary hyperparathyroidism (sHPT) is a common finding in CKD patients.⁶ The KDOQI guidelines on bone and mineral metabolism, recommend serum PTH levels of 35 to 70 pg/mL for stage 3 CKD, 70 to 110 pg/mL for stage 4 and 150 to 300 pg/mL for stage 5 and dialysis.⁷

Skeletal resistance to parathyroid hormone in the context of decreased kidney function, causes decreased tubular phosphate excretion and elevated plasma phosphate level, leading to a decreased calcium and calcitriol in blood circulation. High levels of PTH leads to proliferation of osteoblasts, osteoclasts and osteocytes and several skeletal manifestations such as: bone resorption, reduced bone trabeculation, cortex thinning, fractures, brown tumors, periosteal reactions, sclerosis of dental root apices, decrease in volume of pulp chamber, increased tooth loss and caries secondary to xerostomia, caused by a variety of drugs (Figure 1).⁸⁻¹⁰ Indeed, it is better to prevent very high and very low PTH concentrations in patients with CKD, as recommended by experts. The recommended target range for serum PTH in dialysis patients has changed from 150 to 300 pg/mL in the KDOQI guidelines to two to nine times the upper limit of normal people.⁷

Panoramic radiography is a suitable modality for screening and primary diagnosis of dental disorders.¹¹ Due to its low cost, easy availability

and non-invasiveness, it is a good choice for tracing bone and dental changes in developmental problems and skeletal manifestations of systemic diseases such as ESKD and CKD. Approximately all patients who received dental care have a recent panoramic image; thus it is a cheap and common screening tool for tracing dental and skeletal changes. General practitioners and even dentists might be the first clinicians who discover these complications, with using these radiographs during the routine dental care.

Considering the conflicting results of older and newer studies and lack of adequate number publications about dental and bone changes in jaws in CKD, this study aimed to investigate the relationship between serum levels of PTH and dental and bony changes in the panoramic view of hemodialysis patients.

MATERIALS AND METHODS

In this descriptive, cross-sectional study, data from 236 patients who had been under maintenance hemodialysis for the past 6 months in Shahid Beheshti hemodialysis center of Bandar Anzali, Iran; were collected. The exclusion criteria were those PTH levels below 150 mL/min/ 1.73m² patient unwillingness to participate in the study, and absence of qualified radiographs.

Finally, 68 patients were selected according to their serum PTH levels and were assigned into two groups (Table 1). According to KDOQI guidelines, those with serum PTH levels > 300 pg/mL were included in the case and those with serum PTH levels between 150 to 300 pg/mL were included in the control group.²² After taking informed consent, intra- and extra-oral examinations were done for



Apparent Bone Changes in a Patient of the Case Group

Table 1. Demographic Data and Serum PTH Level of the Patients in Case and Control Groups

	Control Group		Case Group	
	Number	%	Number	%
Gender				
Male	22	67.7	20	58.8
Female	12	32.3	14	41.2
Total	34	100	34	100
Age, y				
Mean	59.2		58.7	
SD	12.6		14.1	
Serum PTH Level, pg/mL				
Mean	228		742	
SD	42.2		40.1	

each patient and the need for dental radiography was considered according to the patient condition. Panoramic radiography was prescribed for patients who did not have any panoramic radiograph within 6 months prior to our study.

Seven radiographic parameters were checked: 1) Periodontal ligament width, which increases in inflammatory conditions and systemic disorders, 2) The lamina dura width, i.e. the thin cortical socket of teeth that may disappear in these situations, 3) DMFT index (decayed, missing due to caries, and filled teeth in the permanent teeth), 4) Presence of periapical lesions, 5) Presence of giant cell lesions (brown tumors) as a characteristic finding of hyperparathyroidism, 6) Jaw bone trabecular pattern, which can change into a very fine “granular” appearance, and 7) The thickness of the inferior cortical border of the mandible at the angle area in millimeters, which would become thinner in hyperparathyroidism condition, measured by a ruler.

The first six parameters were investigated by a trained dentist. All the above-mentioned measurements were recorded, in addition to the age, sex and PTH level.

Personal patient information was concealed due to ethical considerations. The study was approved by the Research Ethics Committee of Guilan University of Medical Sciences (Code No: IR.GUMS.REC.1398.450).

Quantitative data were presented as mean \pm standard deviation (SD) for each variant were collected. Student's t-test and Chi-square were used were appropriate SPSS version 21.

RESULTS

In 68 patients with ESKD enrolled in this study, 22 ones (67.7%) were male and 12 ones (32.3%) were female with a mean age of 59.9 ± 12.2 .

After confirmation by the radiologist of the team, no patient in the control group showed granular pattern, however, 26.5% of the patients in the case group showed that with a significantly different prevalence ($P < .05$).

Periapical lesions were detected in 36.7% of the patients in the case and 51.7% of those in the control group, although the difference was not significant ($P > .05$). None of the patients in this study had brown tumors.

The mean thickness of the inferior cortical border

of the mandible was 2.27 ± 0.32 mm in the control and 1.65 ± 0.46 mm in the case group, with no statistically significant difference ($P < .05$).

The mean score of DMFT was 20 ± 7.59 for the control and 20.18 ± 8.7 for the case group, which were not significantly different ($P > .05$).

The lamina dura was found to be partially absorbed in 56.7% of the control group and 34.5% of the case group. Complete resorption was observed in 43.3% of the control group and 65.5% of the case group, with no significant difference ($P > .05$).

The periodontal ligament width was reduced in all of the patients of both groups. Crestal bone loss, was absent in 2.9% of the control and 5.9% of the case group ($P < .05$). Mild bone loss was observed in 5.9% of the patients in the control and none of the patients in the case group. Moderate bone loss, moderate to severe bone loss and severe bone loss were observed in 23.5% and 23.5%, 20.6% and 14.7%, and 47.1% and 52.9 of the control and case groups; respectively. None of these frequencies were significantly different ($P > .05$) (Tables 2 and 3).

Table 2. Comparison of the Results of Analyzable Variants in Case and Control Groups

Variant	Group	Measurement (unit)	P
Granular Bone Pattern, %	Case	26.5	.001
	Control	0	
Pulp and Periapical Lesions, %	Case	51.7	> .05
	Control	36.7	
Thickness of Inferior Border of Mandible, mm	Case	1.65	.00001
	Control	2.27	
DMFT	Case	20.18	> .05
	Control	20	
Loss of Lamina Dura, %	Case	65.5	> .05
	Control	43.3	

Table 3. Comparison of the Results of Analyzable Variants in Case and Control Groups (Cont.)

Vertical Bone Loss	Group	Presence in Each Group (%)	P
Absent	Case	5.9	> .05
	Control	2.9	
Mild	Case	0	> .05
	Control	5.9	
Moderate	Case	23.5	> .05
	Control	23.5	
Moderate to Severe	Case	14.7	> .05
	Control	20.6	
Severe	Case	52.7	> .05
	Control	47.1	

DISCUSSION

Chronic kidney disease is the sixteenth cause of death all around the world; therefore, early and accurate diagnosis, screening and monitoring are essential to reduce the burden of the disease.¹²

Changes in teeth and osseous structures, patterns are observed in 90% of cases of CKD, due to abnormal mineralization, including demineralization and decreased size and number of trabeculae, causing a granular pattern, ground glass appearance in jaws, loss of lamina dura, radiolucent lesions (brown tumors) and periodontal defects.¹³ Panoramic radiography is a routine procedure for diagnosis of dental problems and represents an overall view of both jaws and their structural condition. Its availability, low cost and non-invasiveness makes the panoramic radiography a suitable imaging for tracking of the changes in mineral pattern, especially in ESKD patients.¹¹

Till now, several cross-sectional studies and case reports have provided information on this subject. Most of them had small sample sizes, unisexual distribution of cases or limited age range and lacked proper surveillance. On the other hand, many of these studies have used cone-beam computed tomography (CBCT), which is an expensive and high-dose radiographic technique, to monitor osseous changes. In the present study, we collected information from two hemodialysis centers, including a wide age range of adult maintenance hemodialysis patients. We considered several items in the panoramic study to reveal different aspects of the disease. Among all, only trabecular pattern and thickness of the inferior border of mandible were significantly different between the control and case groups.

In this study, the prevalence of granular trabecular pattern in the case group was 26.5%, compared to 0% in the control group, which was significantly different. Massahud BC *et al.* reported quite similar findings in the prevalence of granular pattern, which was 25% in the case group and 0% in the control group. However, they enrolled 12 patients in each group and also the PTH cut-off level was 500 pg/mL in their study,

In another study by Dagistan *et al.*, the prevalence of granular bone pattern was reported to be 30% in the case group and 0% in controls. However, they have only included male patients and bony patterns were examined without considering PTH levels.

In previous studies, it was reported that medications and hyperparathyroidism in CKD patients, lead to an increased rate of dental caries, early tooth loss and consequently increase in DMFT.⁸⁻¹⁰ In the present study, the mean of DMFT values was not significantly different between the case and control groups. Hisestin *et al.* also did not find significant difference in DMFT value in CKD patients.¹⁴ Of note their patients were in different stages of CKD, while we only included patients on maintenance hemodialysis with high serum PTH levels.

Madrois *et al.* classified their ESKD patients according to two factors: hemodialysis duration (less or more than 5 years) and PTH level.¹⁵ They observed no significant difference in DMFT between their case and control groups and concluded that dental and osseous changes were independent of on hemodialysis duration or serum PTH level, which supports the result of our study. According to both studies, it can be concluded that in secondary hyperparathyroidism the serum levels of PTH have no significant effect on DMFT, while other factors such as diet and oral hygiene have a positive impact on this index.¹⁵

Brown tumor is a type of giant cell lesion seen in primary and secondary hyperparathyroidism. Facial bones get involved in 2% of cases, mostly affecting the mandible.¹⁶ In the present study, none of our 68 patients showed giant cell lesions of jaws in panoramic radiography. In the study by Madrois *et al.*, which included patients with a history of CKD for at least three months, brown tumor was found in only one patient.¹⁵ Admassie *et al.* also detected seven patients with secondary hyperparathyroidism and brown tumor and concluded that these lesions might be a late manifestation of the disease.¹⁷ In our study, the mean disease duration was six months. Thus, longer follow-up may reveal more cases of brown tumor.

There is a controversial issue regarding the relationship between secondary hyperparathyroidism and inflammatory periapical lesions. In the present study, significant difference was not detected between serum PTH levels and periapical inflammation. Madrois *et al.*¹⁴ classified their patients into three groups of low, intermediate and high PTH levels. They found no significant relationship between PTH levels and periapical inflammation in different groups, which was

similar to the result of our study. Therefore, it can be suggested that osteolytic activity caused by increased parathyroid activity might not play an important role in periapical inflammation. Other systemic conditions such as diabetes mellitus and high blood pressure together with poor oral hygiene could predispose patients to periapical inflammation.¹⁸ We recommend more study on this issue.

Nowadays, the replacement of missing teeth with dental implants has attracted more attention, especially in CKD patients. One of the major prerequisites for successful implant treatment is the presence of sufficient alveolar bone height for primary stabilization.⁸ In the present study, we investigated the amount of vertical bone loss caused by calcium and phosphate imbalance. We found that 5.9% of the control group and 2.9% of the case group did not have vertical bone loss. We classified the patients according to the severity of bone loss into four groups and found no significant difference in bone loss between the case and control patients in any degree of bone loss. In another similar study, Frankenthal *et al.* declared that secondary hyperparathyroidism seems to have no obvious effect on alveolar bone loss.¹⁴ Osseous demineralization takes a long time to be detected on radiographs in CKD patients. In our study the mean duration of ESKD was six months and the mean age of our patients was 59.2 and 58.7 years in the case and control groups, respectively. The relatively short duration of CKD and mean age in our study may explain the non-significant difference in alveolar bone loss in various degrees of bone loss. Therefore, it seems that increasing age and poor oral hygiene are among important risk factors of bone loss beside metabolic imbalance in CKD and the effect of control of these factors should be studied in future.¹¹

Osteoporosis is an asymptomatic condition which can be complicated by bone fractures. Excessive secretion of PTH can also intensify this disorder. One of the diagnostic methods for early detection of osteoporosis, is measurement of the cortical layer thickness, especially in mandibular bone.¹⁴ In the present study, the average thickness of the mandibular cortex was significantly lower in the case than the control group. Furthermore, in one patient with a history of kidney transplant rejection, this cortex had completely faded in panoramic

radiography. Henriques *et al.*, investigated the mental index (the thickness of the mandibular cortex at the region of mental foramen) and found that 37% of their cases, and none of the controls had severe cortical thinning.¹⁹ These findings were compatible with the findings of our study. According to the two studies, maxillofacial radiologists and dentists might be the first clinicians to diagnose osteoporosis and refer such patients to specialists. At early stages of hyperparathyroidism, osseous changes can be more obvious as compared to dental changes. One of these changes is the loss of lamina dura, which is the cortical layer of the inner portion of the tooth socket. In our study the percentages of loss of lamina dura, were not significantly different between the case and control groups. Pudbury *et al.*²¹ showed that, the thickness of lamina dura noticeably decreases in hyperparathyroidism. Periodontal ligament (PDL) width was also narrowed in all of the patients in this study. Gradual thinning of PDL space would normally occur with increasing age, so such circumstances could be expected in these patients.

CONCLUSION

Early diagnosis of secondary hyperparathyroidism in CKD patients is possible by close monitoring of PTH level. It is recommended to study the patients with longer duration of the disease regarding osseous changes in detail.

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