Original Research

Dentomaxillofacial Radiographic Changes in a Group of Iranian Patients with End Stage Renal Disease Undergoing Hemodialysis

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Abstract

Introduction: This study aims to evaluate the dentomaxillofacial radiographic changes in end stage renal disease (ESRD) patients who were on hemodialysis. **Methods:** Parathyroid hormone (PTH), calcium, phosphorus and alkaline phosphatase (ALP) measurements, as well as Panoramic and periapical radiographs were obtained from seventy four patients with a history of end stage renal disease (ESRD). **Results:** 74 patients examined with age range of 15 to 68 years, and a mean age of 41.4±14.6 years. The duration of dialysis ranged between 3 to 156 months with a mean duration of 40.4 months. Thinning or loss of lamina dura was observed in 16 patients (51.4%) and calcification of the pulp in 28 patients (40%). Changes in trabecular pattern was observed in 30 patients (40.6%), alterations in jaw bone density in 29 patients (39.2%) and bilateral calcification of stylohyoid ligaments in 13 patients (17.6%). We did not notice any non periapical origin radiolucent lesion. There was a significant relationship between bone trabecular pattern with P level, age and duration of dialysis. Changes in bone density showed significant relationship with frequency and hours of dialysis per week. **Conclusion:** No correlation was found between the radiographic changes and Ca level. Although changes in trabecular pattern and density were observed mostly in those who were on hemodialysis for a relatively long time, but we could not establish a definitive relation of radiographic manifestations in ESRD patients with the duration and frequency of dialysis.

Key words: Bone density, dentomaxillofacial radiography, end stage renal disease, hemodialysis patients, trabecular pattern.

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Introduction

End-stage renal disease (ESRD) is the final common pathway which numerous renal diseases lead to. These patients have to undergo dialysis or a kidney transplant to survive (1). The number of dialysis patients in Iran is 13000 people and the number of renal transplant patients is 17,000, also 1,500 people are added to the number of dialysis patients yearly in this country (2).End-stage renal disease shows the pathological changes in several organs. Among them, especially, bone changes are striking, described collectively as renal osteodystrophy (3). The primary retention of phosphate by abnormal kidneys results in

hyperphosphatemia, which causes hypocalcemia, resulting in secondary hyperparathyroidism which is the most problematic consequence of chronic renal failure in patients treated with long-term dialysis (4). Renal osteodystrophy, characterized by bone mineralization deficiency, and formation of brown tumors in the more advanced stages which histologically similar to those seen in primary hyperparathyroidism. Patients with ESRD show a broad spectrum of oral manifestations that affect the soft or hard tissues,including xerostomia, uremic breath, uremic stomatitis, calculus accumulation, and periodontitis (5). Today, with advances in diet and long term hemodialysis techniques, the human lifespan has been increased and secondary hyperparathyroidism subsequent to renal failure occurs with higher frequency. As a result, we can expect that the prevalence of oral manifestations, induced by calcium and phosphate metabolic disorders, equally increases in these patients, which can lead to enamel opacity, loss of lamina dura, loosening of teeth, change in trabecular pattern, bone fractures and brown tumors (6-8). Furthermore, some studies revealed that the duration of dialysis can also influence the prevalence of oral abnormalities (9).

According to the variety of maxillofacial changes and the probable relation between calcium level and non-apical originating lucent bone lesions in these patients and the preventability of the complications that can affect patients' quality of life, moral justification and necessity of this study is determine.

So, the aim of this study was to evaluate the dentomaxillofacial radiographic alterations especially loss of lamina dura, changes in bone density and trabecular pattern and the presence of non periapical radiolucent lesions and pulpal calcifications in a group of ESRD patients on maintenance hemodialysis, and to determine the frequency of these abnormality and the relation of hemodialysis duration and serum parameters with these manifestations.

Materials and Methods

This cross-sectional study was conducted on 74 patients with documented ESRD, undergoing hemodialysis for at least 3 months, from the Shahid Beheshti Hospital in Hamadan (5). Since trabecular and lamina dura changes may occur in some other conditions such as fibrous dysplasia, Paget's disease, Addison's, Cushing's syndrome, and osteomalacia, the ESRD patients with the history of these conditions were excluded from the study (10). Other exclusion criteria included ESRD patients with the history of jaw trauma, patients diagnosed with acute renal failure and Patients who had undergone renal transplantation (11). The study design was reviewed and approved by the hospital ethical committee. Written informed consent was obtained from the patients after explaining the purpose and methodology of the study. In this study, patients were evaluated in terms of age, gender, etiology of renal failure, duration of dialysis and weekly frequency of hemodialysis. Serum calcium, phosphorus, iPTH (intact parathyroid hormone), and ALP (alkaline phosphatase) were measured. Data were collected in separate checklists which was confidential. Patients were evaluated radiographically in the Department of Oral and Maxillofacial Radiology, Faculty of Dentistry, Hamadan University of Medical Sciences. Individuals included in the study were subjected to digital panoramic radiography with the same machine (Planmeca Promax, Helsinki, Finland).

In complete edentulous patients or those whose number of verifiable teeth were minimal, only a panoramic radiograph was taken and for the remaining patients regional periapical radiographs were taken depending on the necessity and clinical conditions. According to the consensus of the evaluators, if digital panoramic image was proper to judge about the lamina dura and pulp stones, there was no need for taking additional periapical radiography.

The intraoral periapical radiographs were taken by standard exposure with an intraoral radiography device (Minray, Soredex manufactured by Finland) with parallel technique, and 0.1 second exposure time. All radiographs were evaluated independently by two oral and maxillofacial radiologists who did not know the history of the patients.

Radiographs were assessed for changes in the lamina dura, trabecular pattern, overall density of radiographs, the presence of radiolucent lesions not associated with root, pulpal calcifications and both-sided calcification of stylohyoid ligaments. Radiographs were graded according to the criteria mentioned in Table 1 (Modified from the criteria given by Vidyullatha et al. (11). Classification in the range of + 1 or -1 indicates clear and significant deviations from the normal. Score of +2 or -2 is a gross deviation. Furthermore, the relationship between selected indices of patients and scores of radiographic parameters of lamina dura, trabecular pattern and changes in density and total calcium, phosphate, parathyroid hormone and alkaline phosphatase were evaluated and rated. The data were analyzed using descriptive statistics and chi-square tests. To find out the relation, correlation coefficient was determined. P value less than 0.05 was considered statistically significant.

Table 1. Criteria for radiographic assessment- Modified from the criteria given by Vidyullatha et al. (11)

Parameters	Radiographic appearance	Scoring
Lamina dura	Entire lamina dura substantially thickened	+2
	Portions of Lamina dura thickened; milder degrees	+1
	Within normal limits	0
	Lamina dura substantially thinned; missing in some areas	-1
	Lamina dura essentially absent; may be present in isolated area	-2
Trabecular pattern	All trabeculae substantially coarser	+2
	Some coarser trabeculae; milder degrees	+1
	Within normal limits	0
	Delicate finely meshed trabeculations	-1
	Granular, nearly homogenous patterns; individual trabeculations essentially absent	-2
Overall density	Severe increase in radiographic density	+2
	Mild to moderate increase in radiographic density	+1
	Normal density	0
	Mild to moderate decrease in radiographic density	-1
	Severe decrease in radiographic density	-2
Radiolucent lesions (not associated with teeth)	Present	1
	Absent	0
Pulpal calcifications	Present	1
	Absent	0
both-sided calcification of stylohyoid ligaments	Present	1
	Absent	0

Results

A total of 74 patients (34 male and 40 female) with ESRD undergoing maintenance hemodialysis, were selected. The Patients ranged in age from 15 to 68 years old, with a mean age of 41.4 ± 14.6 years. The duration of dialysis ranged between 3 months to 156 months with a median duration of 40.4 months. Descriptive statistics for each of the variables in this study and causes of ESRD in these patients are presented in Table 2 and 3 respectively.

Among radiographic changes of the jaws, parameters such as loss of lamina dura and calcification of the pulp were not evaluable in 4 patients who were edentulous or have less than ten teeth from decay or severe periodontal problems. So of the 70 patients, thinning or loss of lamina dura was seen in 36 patients (51.4%) and calcification of the pulp in 28 patients (40%). Among the 74 patients, 30 patients (40%) showed changes in trabecular pattern 29 patients (39.2%) changes in bone density and bilateral calcification of stylohyoid ligaments were observed in 13 patients (17.6%). In evaluation of panoramic view, we did not notice any non-periapical radiolucent lesion. More detailed radiographic changes with frequency and percentage are shown in Table 4.

To determine the relationship between radiographic manifestations with serum parameters, spearman's rho correlation were used. There was statistically significant relationship between lamina dura changes and other variables, shown in Table 5. Changes in lamina dura, suggested a significant correlation with the levels of iPTH (P value<0.001, r=-0.74), P (P value=0.009, r=-0.46) and ALP (P value<0.001, r=-0.56), but not with Ca level (P value=0.111, r=-0.15). There was also a significant correlation between age and lamina dura changes but the relationship between lamina dura changes and other variables, including sex, duration of dialysis, and dialysis hours per week were not significant. The only biochemical parameter which showed a significant relation with bone trabecular pattern was serum P levels (P-value=0.014, r=-0.41). Also there is a significant relationship between the bone trabecular pattern with age, sex, and duration of dialysis (Table 5). According to the analysis, the changes in bone density was significantly associated with serum

ALP levels (P value=0.048 , r=-0.36) and other values of blood chemicals showed no significant relation. However, changes in bone density showed significant relationship with hours (P value= 0.043, r=-0.38) and frequency (P value=0.011, r=-0.47) of dialysis per week (Table 5).

Table 2. Descriptive statistics for each of the variables in this study

Variables	Minimum	Maximum	Mean	Standard deviation
Duration of dialysis(months)	3	156	40.4	34.4
Number of dialysis per week	2	4	2.8	0.5
Hours of dialysis per week	6	16	10.1	2.4
Ca	5	15	9.4	1.5
P	3	13	6.9	2
ALP	89	1848	330.1	293.3
iPTH	18	1816	296.5	178.5

Table 3. The underlying etiology of renal failure in studied hemodialysis patients

Etiology	Number	Percent
Diabetes	8	10.8
Hypertension	13	17.6
Glomerulonephritis	23	31.1
Polycystic kidney disease	3	4.1
Urologic Problems	1	1.3
Congenital	1	1.3
Unknown	25	33.8

Table 4. Radiographic changes in the jaws

Radiographic changes	Scoring	Number	Percent
Lamina dura changes	-2	18	25.7
(Evaluated in 70 patients)	-1	18	25.7
	0	34	48.6
	+1	0	0
	+2	0	0
Changes in trabecular pattern	-2	3	4.1
(Evaluated in 74 patients)	-1	6	8.1
	0	44	59.4
	+1	19	25.7
	+2	2	2.7
Overall bone density.	-2	1	1.4
(Assessed in 74 patients)	-1	۱۳	17.5
	0	45	60.8
	+1	5	6.8
	+2	10	13.5
Radiolucent lesions	0	74	100
(Assessed in 74 patients)	1	0	0
Pulp calcification	0	42	60
(Assessed in 70 patients)	1	28	40
Bilateral calcification of stylohyoid ligaments	0	61	82.4
(Assessed in 74 patients)	1	13	17.6

Table 5. Relation between radiographic changes and serum iPTH, calcium, phosphorus, and alkaline phosphatase, and age, sex, duration and frequency of dialysis

Variables	Lamina dura changes (P-value)	trabecular pattern changes (P-value)	bone density changes (P-value)
iPTH	<0.001	0.781	0.693
Ca	0.111	0.635	0.499
P	0.009	0.014	0.540
ALP	<0.001	0.054	0.048
Age	<0.001	0.012	0.689
Sex	0.78	0.03	0.070
Duration of dialysis	0.423	0.023	0.077
frequency of dialysis per week	0.229	0.154	0.011
hours of dialysis per week	0.592	0.395	0.043

P-value >0.05 is not significant

iPTH: intact Parathyroid hormone; Ca: calcium ; P: Phosphorus; ALP: Alkaline phosphatase

Discussion

A wide range of dentomaxillofacial complications have been reported as a result of chronic renal failure (CRF) or its treatment. Dental manifestations include delayed eruption of permanent teeth in children with CRF, enamel hypoplasia in primary and permanent teeth, loss of lamina dura, widening of periodontal ligament, severe periodontal destruction, tooth mobility, and calcification or narrowing of dental pulp. Oral malodor, dry mouth, taste change, increased caries incidence, calculus formation, and gingival bleeding are the common oral manifestations (12). A range of bony anomalies can develop in chronic renal disease, which reflects the defect in calcium metabolism including hyperphosphatemia, hypocalcemia and resultant secondary hyperparathyroidism. Up to 92% of patients receiving hemodialysis are involved with secondary hyperparathyroidism. Orofacial features of CRF due to hyperparathyroidism include bone demineralization, ground glass appearance of bone, decrease thickness of cortical bone, radiolucent giant cell lesions (brown tumours), abnormal bone healing after extraction, metastatic soft tissue calcifications, and jaw fracture (8). Very few studies have been done previously on the assessment of radiographic changes in the jawbones of ESRD patients and the data is limited (11).

Panoramic and/or periapical radiographs of seventy-four patients on permanent hemodialysis were evaluated in this study. The mandibular molar area was the best region for investigation of radiographic changes on panoramic radiograph, because of no superimposition of anatomic structures and more involvement of this area by osseous pathosis. Therefore, the three major changes including lamina dura, trabecular pattern and density changes were much more evident in the molar region, above the mandibular canal on panoramic image (3,10).

In the present study no brown tumor was found, which was similar to Rani's study (10). Medeiros Queiroz et al. also reported the brown tumor only in one of 154 hemodialysis patients (5).

In hemodialysis patients of this study, the frequency of pulpal calcifications was 40%. In the study of Galili et al. (13) a significant pulp narrowing was shown in chronic renal disease patients compared with healthy control group. There is conflicting literature regarding by the presence of pulpal calcification and systemic disturbance. In the study of Patil and Sinha, 33.92% of the ESRD patients had pulp stones, but no significant relationship was found between the presence of the pulpal calcification and carotid artery calcifications (CAC) in the ESRD patients who were on haemodialysis (14). Similar findings were observed in the Kansu et al. study (15). In fact, the diversity and complexity of etiological factors of pulpal calcification (like long-standing local irritants, aging, idiopathic factors, fluoride supplementation, hypervitaminosis D or a genetic predisposition) make it very difficult to determine the specific aetiology in any particular patient (15).

In this study, the frequency of partial loss of the lamina dura was 25.7 percent, and complete or nearly complete loss of lamina dura were observed in the 25.7 percent of reviewed cases (51.4% of patients revealed lamina dura changes). In a study by Kelly, 45% of people showed partial loss of lamina dura while a complete or nearly complete loss of lamina dura were observed in only 8% (53% of patients revealed lamina dura alterations) (3). However in Rani's study, these changes were seen in 70% of dialysis patients (10). Rivas in a study using 29 panoramic radiographs of dialysis patients stated that lamina dura completely disappeared in 74 percent (16). Amann and Uthman (18) in a review of 10 patients, reported the loss of

lamina dura, in 60% of patients. These differences in the prevalence may be due to differences in the number of patients, underlying etiologic condition of renal failure, treatment modalities and duration of their treatment. Pugh considered this phenomenon as a manifestation of subperiosteal resorption that is an indicator of hyperparathyroidism when it occurs in the last phalange (19). Some authors considered that loss of lamina dura is a first detectable finding (19) while the others reported this as a late finding in renal osteodystorphy (20).

However, since the loss of lamina dura may occur in Paget's disease, Cushing's syndrome fibrous dysplasia, rickets and osteomalacia, it should not be considered pathognomonic feature of this disease (10). A similar change to the loss of lamina dura, is radiographic cortical loss in the inferior border of the mandible, mandibular canal, alveolar crest, palatal suture, nasal floor and sinus wall (21,22). In this study, we were not looking specifically for these changes.

Three radiographic trabecular patterns of facial bone are attributed to hyperparathyroidism although these facial skeletal changes are uncommon. The classic form is termed “osteitis fibrosacystica” including increased bone cell activity, peritrabecular fibrosis, and brown tumors. Radiographically, this form appears with a combination of cortical thinning of multiple bones, coarsened trabecular patterns, osteolytic lesions, and “salt-and-pepper” appearance of the skull, which is the result of mixed osteolytic and sclerotic bone. The second form is a classic ground glass pattern, similar to fibrous dysplasia. But unlike true fibrous dysplasia, this finding can be diffuse and generalized, with poor corticomedullary distinction, an imaging finding not present in fibrous dysplasia. The third and the rarest form is uremic leontiasisossea which is characterized by significant hypertrophy of the jaws with serpiginous tunneling or channeling within the bone and poor visualization of the cortical bone. The cause of this unusual structure is not known; and the radiographic findings could not be explained with any specific microscopic changes (23).

In the present study, trabecular changes were revealed in 40.6% of patients. Among these, 8.1% (n=6) had delicate and finely intertwined trabecular pattern, 3 patients (4.1%) represented complete loss of normal trabeculation, granular or almost homogeneous pattern, 19 patients (25.7%) showed some mild coarse trabeculae, and 2.7% (n=2) showed coarse whole trabecular pattern. In the Kelly study (3), thin, delicate and finely intertwined trabeculation was seen in 37% of patients, Among these 8% revealed complete loss of normal trabeculation, granular or almost homogeneous pattern. Differences in the reported percentages could be due to variation in the number of subjects, observer disagreement, and the differences in the study design.

It is notable that renal osteodystrophy is a range between low turnover bone disease such as osteomalacia, and high turnover bone disease, like severe secondary hyperparathyroidism. Patients at both ends of the spectrum of bone turnover in renal osteodystrophy may represent the same bone mineral density on densitometry. Low bone mineral density may reflect inadequate mineralization as seen in osteomalacia or increased peritrabecular fibrosis as seen in secondary hyperparathyroidism. High bone mineral density readings on densitometry may capture extraosseous calcifications, which are frequently seen in chronic renal disease (24).

About the relation of radiographic changes with serum parameters in the present study, we revealed a relation between trabecular bone changes and serum P, and also bone density changes and ALP. Alteration in lamina dura showed a relation with iPTH, P and ALP, but not with Ca. However, in Rani's study, the relation between the radiographic changes and Ca, P, and ALP levels did not show significance (10). In the study of Medeiros Queiroz et al. (5), no significant correlation was observed between dialysis duration and also biochemical changes with radiographic bone alterations in the patients with chronic kidney disease undergoing dialysis (5). However, the radiographic alterations that were evaluated in this article were different from our study, and consisted of calculus, tooth decay, bone loss, residual roots, impacted teeth, diffuse or circumscribed bone rarefaction and bone sclerosis. Furthermore, the differences in the study design, the patients' medications, their clinical and paraclinical status, and ethnic variations could be the factors of discrepancy between studies.

Although, an appropriate sampling method was considered for this study, our findings may be limited because of the difference in etiologic underlying conditions of renal failure in our patients, and also impossibility to perform drug assessment accurately. Some of our patients were given supplements of calcium, but the majority of them were from a low economic background, so their supplements use was irregular. This might be also one of the contributing factors for lack of a correlation between calcium levels and bone changes in this study. According to our results, we could not establish a definitive relation of radiographic manifestations in ESRD patients with the duration and frequency of dialysis. We suggest further longitudinal studies to assess the influence of hemodialysis state on maxillofacial radiographic features along with the biochemical serum markers over duration of time so as to validate the influence of

duration of dialysis therapy on radiographic and dental health.

Conclusion

ESRD patients undergoing hemodialysis show various degrees of changes in jaw radiographic pattern. Nevertheless, none of these changes had relation with calcium level. Annual radiographic evaluation is recommended to assess the progress of the insufficiency or reversal of the changes after therapy.

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