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# JAWBONE CHANGES IN CHRONIC KIDNEY DISEASE PATIENTS IN PRETRANSPLANT STAGE: A RADIOMORPHOMETRIC ANALYSIS USING PANORAMIC RADIOGRAPHY

## Cambios en la mandíbula en pacientes con enfermedad renal crónica en etapa pretrasplante: Un análisis radiomorfométrico mediante radiografía panorámica

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## ABSTRACT

**Aim:** Chronic kidney disease is characterized by several systemic complications that result from a profound hydroelectrolytic, metabolic, and immunological imbalance. Abnormalities in the calcium and phosphorus metabolism are highly prevalent among renal patients and increase the systemic complications. This study aimed to assess the risk of low bone density in renal patients through evaluation of panoramic radiographic exams by radiomorphometric indices: mandibular cortical width (MCW), panoramic mandibular index (PMI), and mandibular alveolar bone reabsorption degree (M/M Ratio).

**Material and Methods:** A sample of 60 panoramic radiographs: 20 adult pre-transplant renal patients, case group (G1) and 40 controls, paired by sex and age (G2) were evaluated. The morphometric measurements MCW, PMI and M/M ratio were measured. The radiographs were analyzed regarding dental absence, calcification of the style-hyoid ligament (CSHL), and idiopathic radiopaque areas.

**Results:** Radiomorphometric indices were significantly lower among pre-transplant females ($p<0.05$) and no significant difference was observed between males in the test and control group. A higher frequency of enostoses was observed among females and of CSHC calcification among males was observed in the pre-transplant patients ($p>0.05$).

**Conclusions:** These results suggest that pre-transplant females may present with more pronounced jawbone osteopenia.

**Keywords:** *Kidney disease; Chronic kidney disease-mineral and bone disorder; Panoramic radiography; Retrospective study; Bone density; Transplants.*

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## RESUMEN

**Objetivos:** La enfermedad renal crónica se caracteriza por diversas complicaciones sistémicas derivadas de un profundo desequilibrio hidroelectrolítico, metabólico e inmunológico. Las anomalías en el metabolismo del calcio y el fósforo son muy prevalentes en pacientes renales y aumentan las complicaciones sistémicas. Este estudio tuvo como objetivo evaluar el riesgo de baja densidad ósea en pacientes renales mediante la evaluación de radiografías panorámicas mediante índices radiomorfométricos: ancho cortical mandibular (ACM), índice mandibular panorámico (IMP) y grado de reabsorción ósea alveolar mandibular (cociente M/M).

**Material y Metodos:** Se evaluó una muestra de 60 radiografías panorámicas: 20 pacientes renales adultos pretrasplante, grupo de casos (G1) y 40 controles, pareados por sexo y edad (G2). Se midieron las medidas morfométricas de peso corporal medio (MCW), índice de masa corporal (PMI) y relación M/M. Las radiografías se analizaron en cuanto a ausencia dentaria, calcificación del ligamento estilohioideo (CSHL) y áreas radiopacas idiopáticas.

**Resultados:** Los índices radiomorfométricos fueron significativamente menores en las mujeres antes del trasplante ($p$<0,05) y no se observaron diferencias significativas entre los hombres del grupo de prueba y del grupo control. Se observó una mayor frecuencia de enostosis en las mujeres y de calcificación de CSHC en los hombres en los pacientes antes del trasplante ($p$>0,05).

**Conclusiones:** Estos resultados sugieren que las mujeres antes del trasplante pueden presentar osteopenia mandibular más pronunciada.

**Palabras clave:** *Enfermedad renal; Trastorno mineral y óseo asociado a la enfermedad renal crónica; Radiografía panorámica; Estudio retrospectivo; Densidad ósea; Trasplantes.*

## INTRODUCTION

Chronic kidney disease (CKD) is characterized by several systemic complications that result from a profound hydroelectrolytic, metabolic, and immunological imbalance. Abnormalities in the calcium and phosphorus metabolism are highly prevalent in the renal patients and increase the systemic complications.[1,2]

Despite the improvements in patient care and renal replacement therapy, the impact of CKD on patient's morbidity and mortality is extremely relevant.[3] CKD patients are at high risk to develop oral health complications,[4] such as narrowing of pulp chamber,[5] enamel abnormalities[5,6] xerostomia and hypo-salivation,[6] premature tooth loss,[6] increased plaque index[7] and periodontal disease, when compared to the general population.[4,7-9] Panoramic radiographies are commonly performed in general dental practice. They have been proposed as a useful screening tool for osteoporosis because of their wide availability, practicality and low cost.[10,12]

Several panoramic radiography radiomorphometric indices have been investigated for the detection of low bone mineral density and osteoporotic changes in the maxillofacial region. These indices include mandibular cortical width (MCW), panoramic mandibular index (PMI), and mandibular alveolar bone reabsorption degree (M/M Ratio).[10,12]

Their main contribution lies in the fact that it is conducted among individuals seeking dental care for reasons other than bone mineral density assessment,[10] contributing

to determine the necessity of further investigations that could guide adequate therapeutic and preventive actions.[10-12]

In addition to the established radiomorphometric indices, panoramic radiographs can reveal other bone-related changes that may be associated with systemic bone disorders. Trabecular bone alterations,[13] enostoses, which are benign sclerotic bone lesions,[14] and calcification of the stylohyoid complex (CSHC) have been reported to show increased prevalence in patients with CTK.[14,15] These radiographic findings may serve as additional indicators of altered mineral homeostasis, complementing the traditional morphometric assessments.

Although many aspects of oral health in CKD patients have been explored[16-18] there are few studies about the effect of the end-stage renal disease in the jaw bones.[19,20] Therefore, this study aimed to assess the bony changes by means of panoramic radiography morphometric indices in chronic kidney disease in pretransplant stage patients (CKDPS) in comparison to healthy individuals. As a subobjective, findings in the CKDPS group in relation to the time of diagnosis and patients' sex were investigated.

## MATERIALS AND METHODS

### Study sample

This retrospective case-control study is in accordance with the Declaration of Helsinki and was approved by the Institutional Ethics Committee on Human Research (protocol n 753.254/2014).

The study follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement.[21] A total of 60 panoramic radiographies were selected from the archives of a private hospital in São Paulo, Brazil. This study employed a convenience sampling methodology. All chronic kidney disease patients in the pretransplant stage who were consecutively attended at the reference service between 2009 and 2013 and met the inclusion and exclusion criteria were enrolled as the case group (n=20). The control group (n=40) was subsequently selected from healthy individuals to match the case group by age (±2 years) and sex, as these demographic factors are known to influence radiomorphometric indices. A 2:1 control-to-case ratio was adopted to increase statistical power.

As inclusion criteria, all patients aged 40 years or older who had been diagnosed with kidney disease for more than two years were included. Patients with chronic kidney disease frequently present with associated systemic conditions, mainly systemic arterial hypertension and diabetes mellitus, which were not considered exclusion criteria in this study. Forty panoramic radiographies from healthy patients were selected as the control group. All information regarding patients' medical history was retrieved from their clinical records. The groups were paired by sex and age (± two years). Panoramic radiographs of low image quality or with incomplete visualization of the mandibular cortex at the mental foramen region were excluded. Data regarding patients' health status, sex and age were obtained from the charts.

### Panoramic Radiographs Evaluation

Panoramic radiographs were acquired with KODAK 8000 Digital Panoramic System Radiographic. Evaluation was performed under dim light conditions by one single examiner blinded to the patients' age, sex, and health status. A 2x magnifier and a negative viewer with a fixed light and masking with black paper that covered the surface area

beyond the edges of the radiograph were used. Data regarding the number of absent teeth, presence of enostosis and presence of calcification of the style-hyoid complex (CSHC) were analyzed.

Prior to the study measurements, examiners calibration was performed to ensure measurement reliability and consistency. One experienced dental radiology professional was trained and supervised in radiographic interpretation by a radiology professor, who reviewed all the images that were analyzed.

## Radiomorphometric analysis

The linear measurements were performed in millimeters with a plastic millimeter-scale ruler using the same negative viewer and magnifier ($x^2$). When the mental foramen was visible bilaterally, measurements were performed bilaterally, and the mean values of bilateral measurements were used for analysis. However, in four cases only one foramen was visible. In such cases, only unilateral measurements were considered.

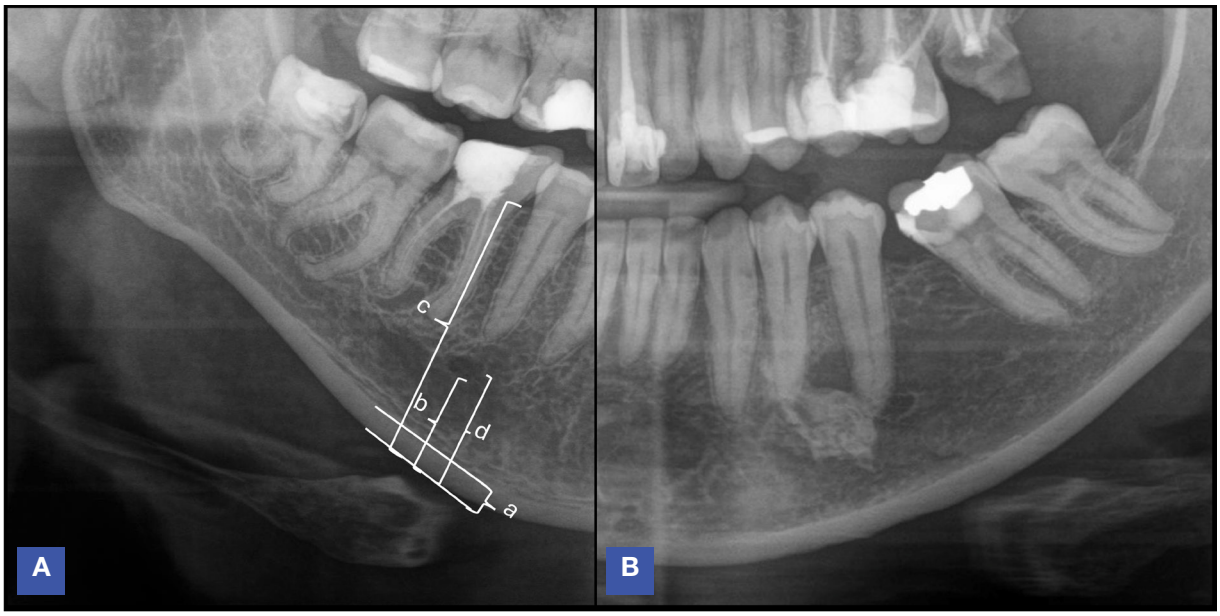
The inferior edge of the mental foramen was traced, and a line parallel to the long axis of the mandible and tangential to the inferior border of the mandible was drawn. A line perpendicular to this tangent intersecting the inferior border of the mental foramen was constructed. Taking these lines as reference, three linear measurements were performed (Figure 1):

1. **Mandibular Cortical Width (MCW):** the thickness of the mandibular cortex at the region of the mental foramen (a)[22] ;

2. **PMI:** the MCW divided by the distance between the inferior cortical of the mental foramen and the inferior mandibular cortex (a/b)[22] ;

3. **Mandibular alveolar bone resorption index (M/M):** the total mandibular height was divided by the height from the center of the mental foramen(c) to the inferior border of the mandible (d; c/d).[22]

**Figure 1**
Three linear measurements as reference




**A:** Measurement of MCW. **B:** Example of an enostosis located near the tooth apice. (**a-b:** PMI. **c - d:** M/M ratio).

### Data analysis

Fisher's exact test and Chi-square test were used to evaluate the presence of enostosis and CSHC, respectively in the case and control group. The morphometric measurements and the mean number of missing teeth were statistically compared between the case and control groups using the Student's t-test. To evaluate possible relationships between the time of diagnosis, number of lost teeth, and the radiomorphometric indices, Pearson's correlation test was performed. The Stata software (StataCorp, College Station, USA) was used to process and analyze the data. A sig-nificance level of α = 0.05 was adopted.

## RESULTS

The case group comprised 10 females and 10 males with mean age of 50 (±8.1; min.: 40; max.: 63) and 50.3 (±8.3; min.: 40; max.: 65) years, respectively. The control group was divided into 20 females and 20 males with mean age of 50.9 (±7.6; min.: 40; max.: 66) and 50 (±7.3; min.: 40; max.: 65) years, respectively. The mean time of diagnosis of renal disease in the case group was 79.7 (± 46.7; min.: 25; max.: 152) months among females and 67.2 (± 40; min.: 25; max.: 142) among males ($p$>0.05). No significant differences were observed between groups regarding the number of missing teeth ($p$>0.05).

**Table 1**

Distribution of the occurrence of enostosis and CSHC between groups.

| | | Case group | | Control group | | |
|---|---|---|---|---|---|---|
| | | Present (%) | Absent (%) | Present (%) | Absent (%) | p-value |
| **Females** | Enostosis | 5 (50) | 5 (50) | 1 (5) | 19 (95) | 0.009* |
| | CSHC | 4 (40) | 6 (60) | 7 (35) | 13 (65) | 0.181* |
| **Males** | Enostosis | 0 | 10 (100) | 0 | 20 (100) | - |
| | CSHC | 5 (50) | 5 (50) | 5 (15) | 17 (85) | 0.04* |
| | | Mean (SD) | | Mean (SD) | | |
| **Teeth Loss** | Females | 14.1 (6.9) | | 8.6 (7.3) | | 0.02** |
| | Males | 14.8 (8.3) | | 11.5 (7.7) | | 0.14** |

***:** Fisher's exact test.

**Table 2**

Distribution of morphometric indices for the mandible in the case and control groups.

| | | Case group | | Control group | | |
|---|---|---|---|---|---|---|
| Sex | Index | Mean | SD | Mean | SD | p-value |
| | MCW | 4.70 | 0.67 | 5.50 | 0.60 | 0.003 |
| **Females** | PMI | 0.33 | 0.04 | 0.38 | 0.05 | 0.01 |
| | M/M | 1.89 | 0.26 | 2.09 | 0.23 | 0.04 |
| | MCW | 5.77 | 0.66 | 5.94 | 0.84 | 0.60 |
| **Males** | PMI | 0.39 | 0.04 | 0.36 | 0.06 | 0.28 |
| | M/M | 2.10 | 0.38 | 2.03 | 0.19 | 0.52 |

**SD:** Standard Deviation. **CM:** Cortical width. **PMI:** Panoramic mandibular index. **M/M:** Alveolar crest resorption degree ratio.

**Table 3**
Correlation analysis between time since diagnosis, tooth loss, and radiomorphometric indexes in CKDPS group

| Variables | Correlation Coefficient (r) | p-value |
|---|---|---|
| Time since diagnosis *versus* MCW | 0.081 | 0.63 |
| Time since diagnosis *versus*PMI | 0.127 | 0.43 |
| Time since diagnosis *versus* M/M Ratio | 0.06 | 0.72 |
| Number of teeth lost *versus* MCW | -0.268 | 0.26 |
| Number of teeth lost *versus* PMI | -0.141 | 0.56 |
| Number of teeth lost *versus* M/M Ratio | -0.016 | 0.94 |

The presence of enostosis and CSHC was significantly higher in the case group than in the control group among females ($p$<0.05; Table 1). When radiomorphometric indices were analyzed separately by sex, CKDPS patients showed significantly lower mean values of MCW, PMI, and M/M ratio compared to controls ($p$<0.05; Table 2). No significant correlations were found between the time since diagnosis, the number of missing teeth, and the morphometric índices ($p$>0.05), Table 3.

## DISCUSSION

Over the past decades, survival rates among end-stage renal disease patients have progressively improved.[23] Interdisciplinary treatment with dental support contributes to the improvement of a patient's overall health and quality of life.[13] Panoramic radiography is extensively used in routine dental examinations and has been widely validated to detect osteolytic changes in osteoporotic patients.[24-27] In this investigation, a significant reduction of the radiomorphometric indices was observed CKDPS females compared to controls, however no difference was observed between groups among males. Radiographic findings in the CKD patients were not correlated with the duration of the disease.

Among the most important complications of CKD one can cite osteodystrophy and secondary osteoporosis that can lead to bone fragility and increase incidence of bone fractures.[28] Bony alterations observed on panoramic radiographs may serve as early indicators of systemic bone changes, warranting further specific evaluations.

Reduction of jawbone cortical thickness is well described in postmenopausal women.[29] Hence, to diminish the interference of primary osteoporosis on the results males and females were individually paired with controls. Overall, CKD females were associated with a higher prevalence of enostosis and CSHC and higher teeth loss. Findings such as calcification of the stylohyoid complex and the presence of radiopaque areas suggest aberrant calcium and phosphorus deposition resulting from altered mineral metabolism.

Kansu *et al.*,[6] showed no statistically difference between the actual pulp calcification in renal patients where this study attem-pted to correlate pulp calcification and carotid artery calcification under vision about altered calcium and phosphorus metabolism. As this

was a retrospective case-control study, clinical dental and periodontal parameters could not be assessed. Future investigations should correlate imaging and clinical findings to further explore the influence of altered bone metabolism in oral health status in CKDPS patients.

## CONCLUSIONS

A significant reduction in panoramic radiographic morphometric indices was observed among female CKDPS patients, suggesting decreased bone density and altered mineral metabolism. Panoramic radiography may serve as a valuable adjunctive tool for detecting early signs of osteoporosis in this population, supporting timely preventive and therapeutic measures. Moreover, it can assist dental professionals in managing patients with altered bone metabolism and minimizing related complications.

## CONFLICT OF INTERESTS

The authors have no conflicts of interest.

## ETHICS APPROVAL

This study is in accordance with the Declaration of Helsinki and was approved by the Institutional Ethics Committee on Human Research (protocol number 753.254/2014).

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## AUTHORS' CONTRIBUTIONS

**Thaís Feitosa de Oliveira:** Investigation; Data curation; Formal analysis.

**Mariana Quirino Silveira Soares:** Conceptualization; Methodology; Writing – original draft.

**Izabel Regina Rubira-Bullen:** Investigation; Data curation; Formal analysis.

**Viviane Sarmento:** Investigation; Data curation; Formal analysis.

**Walmyr Mello:** Investigation; Data curation; Formal analysis.

**Maria Fernanda Camargo:** Investigation; Data curation; Formal analysis.

**Heitor Marques Honório:** Investigation; Data curation; Formal analysis.

**Paulo Sérgio da Silva Santos:** Investigation; Data curation; Formal analysis.

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