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Study Of Urinary Calcium/Creatinine Ratio (CCR) In Postmenopausal Women As A Biochemical Marker Of Hypercalciuria.

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ABSTRACT

Osteoporosis is a common disease which affects 1 in every 3 of postmenopausal women. It is characterized by low bone mass and micro architectural deterioration of bone tissue that lead to an increase in bone fragility and consequent risk of fracture. Radiological examination to assess bone mineral density with Dual energy X-ray absorptiometry (DEXA) scan is a gold standard diagnostic method of osteoporosis. However, it needs high technology and high cost and is not yet easily available in all health centres. Biochemical marker using Urinary Calcium/Creatinine ratio (CCR) in postmenopausal women as a measure of urinary calcium excretion could be developed for predicting hypercalciuria. To compare and correlate the Urinary Calcium Creatinine ratio (CCR) in premenopausal and postmenopausal women as a measure of hypercalciuria. The study population comprised of 50 postmenopausal women in 46-75 years of age with history of osteoporosis were taken as cases and 50 healthy premenopausal women in 20-35 years of age were selected as controls. Results are expressed as mean$\pm$SD .Student's t test was employed for the statistical analysis of data.P value less than 0.001 was taken as the significant value. The mean Urinary Calcium Creatinine ratio were found to be significantly higher in postmenopausal women compared to premenopausal women. Study showed a single estimation of Calcium to Creatinine ratio, in a spot urine sample, high in postmenopausal women is a good predictor of hypercalciuria and osteoporosis.

Keywords: Osteoporosis, Bone mineral density, Calcium/Creatinine ratio (CCR).

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INTRODUCTION

Osteoporosis is a common disease which affects 1 in every 3 of postmenopausal women. It is characterized by low bone mass and micro architectural deterioration of bone tissue that led to an increase in bone fragility and consequent risk of fracture [1]. While in most patients with reduced bone mass there are no obvious factors that can be associated with the appearance of the disease, it is well known that many conditions can induce a secondary form of osteoporosis [2].

Several examinations including radiological, biopsy and biochemical examinations have been developed based on reduction of bone mineral density in the osteoporosis. Radiological examination to assess bone mineral density with Dual energy X-ray absorptiometry (DEXA) scan is a gold standard diagnostic method of osteoporosis. However, it needs high technology and high cost and is not yet easily available in all health centres. Biochemical marker using Urinary Calcium/Creatinine ratio (CCR) in postmenopausal women as a measure of urinary calcium excretion could be developed for predicting hypercalciuria. Hypercalciuria was defined as Urinary Calcium/Creatinine ratio ($U_{Ca/Cr}$) > 0.20 [3].

The effect of idiopathic hypercalciuria on bone (defined as increased calcium excretion in the absence of secondary causes) has been widely evaluated in patients with calcium nephrolithiasis. Many authors have reported that the increase in urinary calcium excretion is associated with decreased bone mass and increased bone turnover in patients with osteoporosis [4-6].

It is generally agreed that hypercalciuria may be involved in the pathogenesis of low bone mass in patients referring for osteoporosis. However, the frequency and the pathogenic relevance of this metabolic defect in osteoporotic patients have not been clearly described as yet [7].

In a very recent paper focusing on the use of laboratory testing in revealing hidden alterations that can induce secondary osteoporosis, found that hypercalciuria was the most common defect, being present in approximately 10% of their otherwise healthy osteoporotic postmenopausal women [8].

The purposes of this study, therefore, to study the Urinary Calcium/Creatinine ratio (CCR) in postmenopausal women as a measure of hypercalciuria.

Aims And Objectives

- To estimate Spot urinary calcium, urinary creatinine and Urinary Calcium Creatinine ratio in subjects
- To compare and correlate the Urinary Calcium Creatinine ratio (CCR) in premenopausal and postmenopausal women as a measure of hypercalciuria.

MATERIALS AND METHODS

The study population comprised of 50 postmenopausal women in 46-75 years of age with history of osteoporosis were taken as cases and 50 healthy premenopausal women in 20-35 years of age were selected as controls.

After obtaining a written informed consent, the case details and clinical examination was performed and recorded.

Spot urine were collected from each subject. Urine samples were analysed for calcium and creatinine levels by fully automated analyzer. Urinary calcium was estimated by Arsenazo III Dye method and Urinary creatinine was estimated by Jaffe's kinetic method.

The Urinary Ca/Cr ratio is given as,

Urinary Calcium (mg/dl) / Urinary Creatinine (mg/dl)

Results are expressed as mean $\pm$SD. Student's t test was employed for the statistical analysis of data. P value less than 0.001 was taken as the significant value.

STATISTICS AND RESULTS

The control group comprised of 50 healthy premenopausal women and 50 cases of postmenopausal women with history of osteoporosis were enrolled.

Table 1: Comparison of spot urinary calcium, spot urinary creatinine & Urinary Calcium to Creatinine ratio between premenopausal women and Postmenopausal women.

Parameters	Premenopausal women	Postmenopausal women	P value
Spot Urine Calcium(mg/dl)	3.8+2.03	21.2+4.33	<0.01
Spot Urine Creatinine (mg/dl)	116.32+13.29	129.32+11.21	<0.01
Urine Calcium/Creatinine ratio	0.043+0.021	0.234+0.09	<0.001

The mean Urinary Calcium Creatinine ratio were found to be significantly higher in postmenopausal women compared to premenopausal women.

Table 2: Result of statistical analysis.

Test	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	P value
CCR	81.2	96.4	86.6	94.7	93.1	<0.001

It is evident from the table:2 that the ratio of Calcium/Creatinine (≤0.04) test has sensitivity of 81.2%, specificity of 96.4%, positive predictive value of 86.6%, negative predictive value of 94.7%., and diagnostic accuracy of 93.1%.

Table 1 shows values of spot urinary calcium, spot urinary creatinine and urinary Calcium creatinine ratio in case and control groups.

The mean spot urinary calcium excretion in control was 3.8 ± 2.03mg/dl which was found to be significantly low (p value <0.01) as compared to cases 22.2 ± 4.33 mg/dl. The mean spot urinary creatinine levels in cases were 129.32 ± 11.21 mg/dl and in control was 116.32 ± 13.29 mg/dl (p value <0.01).

The premenopausal women had Urinary Calcium Creatinine ratio of 0.043 ± 0.021 while postmenopausal women had 0.234 ± 0.09 values. The mean difference of 0.191 was observed between control and cases.

Statistical analysis showed that the Urinary Calcium/Creatinine ratio in postmenopausal women were significantly higher than premenopausal women. The P value was highly significant (p<0.001).

DISCUSSION

No clear-cut indications for the inclusion or exclusion of Urinary Calcium/Creatinine ratio measurement as a first line diagnostic tool in patients with osteoporosis are currently available. This probably occurs because there are no comprehensive data on the prevalence and the role of this defect in postmenopausal women with low bone density. This study demonstrates that an apparently primary form of hypercalciuria is present in postmenopausal women with osteoporosis [9-13].

In this study, the prevalence of hypercalciuria was much higher in postmenopausal women than control. In postmenopausal women, higher Urinary Calcium/Creatinine ratio have been observed with greater bone mineral density loss and elevated markers of bone turn over, establishing a positive linear relationship between markers of bone resorption and Urinary Calcium/Creatinine ratio. The finding of hypercalciuria is surprisingly common in patients with a 'primary' form of osteoporosis. The relationships between bone metabolism and idiopathic hypercalciuria have been extensively studied in patients with calcium Nephrolithiasis [3, 14, 15].

Postmenopausal women are associated with the decrease in oestrogen levels in the body that leads to decrease of urinary calcium resorption in the kidney. Ratio of Urinary Calcium/Creatinine is a biochemical marker that is used at an early stage to assess bone metabolism. The increase of Urinary

Calcium/Creatinine ratio may be the predictor of low bone mineral density in postmenopausal women and may indicate an increase in bone resorption by osteoclasts [16].

This study may only partially help in addressing the issue of a possible cause–effect relationship between hypercalciuria and osteoporosis in those women carrying this defect.

These observations suggest that hypercalciuria is a specific and important landmark of osteoporosis. The mean UCa/UCr ratio increases along with the decrease of bone mineral density. The mean UCa/UCr ratio was higher in osteoporosis group compared to normal group. Several considerations may strengthen the importance and the specificity of the relationship between osteoporosis and hypercalciuria [17-21].

An increased risk of fractures has been reported in patients with osteoporosis. Although the reason for this remains unclear, hypercalciuria, which is present in up to 60–70% of these patients, may be one of the factors involved [22-23].

CONCLUSION

We can conclude that a single estimation of Calcium to Creatinine ratio, in a spot urine sample, high in postmenopausal women is a good predictor of hypercalciuria and osteoporosis.

Hypercalciuria is a very frequent feature in postmenopausal women with reduced bone density. Increased Urinary Calcium excretion and bone loss appear to be linked, and these subjects seem to suffer from osteoporosis[24-26]. Therefore, it can be recommended as a screening test for all postmenopausal women as it justifies the cost.

Limitations

One limitation of the study was that the sample size was small. Another limitation was that the study group consisted already diagnosed osteoporotic patients.

To say that Urinary Calcium Creatinine ratio can be used to diagnose hypercalciuria and predictor of osteoporosis, a study comprising of bone mass density should be performed simultaneously.

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