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Association of Calcium Phosphorus Product and Coronary Artery Calcification in End Stage Renal Disease Patients on Dialysis.

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ABSTRACT

Background: Patients with End Stage Renal Disease (ESRD) on dialysis have 2- to 5-fold more coronary artery calcification than age-matched individuals. One hypothesis for the disproportionate calcification burden in these patients is high serum phosphate levels; patients with chronic kidney disease (CKD) have elevated serum phosphate and calcium phosphorus product as a consequence of both reduced phosphate filtration and secondary hyperparathyroidism. **Methods:** This study was done on 50 CKD – ESRD patients on maintenance dialysis sand 20 normal subjects. Blood sample were obtained for serum Calcium, Phosphate, Parathyroid hormone of all CKD-ESRD patients prior to dialysis and of normal controls. All subjects were subjected to Multi Row Spiral Computed Tomography for detection of coronary artery calcification scoring (CACS). **Results:** The mean value of corrected Calcium Phosphorus product was 50.9 ± 15.6 mg2/dl2 in ESRD patients. The minimum value was 26.04mg2/dl2 and maximum value of the product 85.7 mg2/dl2 in ESRD patients. The mean CACS in 50 patients with ESRD was 91.4 ± 32.7agatston units. For CACS score 0-10,11-100,101-400 agatston unit the Calcium Phosphorus product was 26.04 ± 0, 45.18 ± 12.75, 63.31 ± 10.18 mg2/dl2. With increase in CACS, the Calcium Phosphorus (CaXPO4) products increased and this association was statistically significant. The CACS values in normal subjects were 7.75 ± 6.5 Agatston units. **Conclusion:** Our study results suggest a positive association between Calcium Phosphorus product and CAC in ESRD patients. Controlling Calcium Phosphorus product will reduce the coronary artery calcification burden.

Keywords: Coronary Artery Calcification, End Stage Renal Disease, Dialysis.

INTRODUCTION

The American Heart Association stated that the individuals with Chronic Kidney Disease (CKD) should be included in the highest-risk group for cardiovascular diseases and therefore they should receive aggressive preventive measures to reduce the prevalence and severity of cardiovascular diseases.[1,2]

Patients with End Stage Renal Disease (ESRD) who are on dialysis have 2- to 5-fold more chances of developing coronary artery calcification than age-matched individuals with angiographically proven coronary artery disease.[3]

In addition to increased traditional risk factors, CKD patients also have a number of nontraditional cardiovascular risk factors that may play a prominent role in the pathogenesis of arterial calcification, including duration of dialysis and disorders of mineral metabolism.[3]

Recently, interest has been focused on the roles of hyperphosphatemia, elevated levels of the calcium x phosphorus product ,hyperparathyroidism and obesity in the development of cardiovascular disease in ESRD. One hypothesis is that high serum phosphate levels contribute to vascular calcification. Patients with CKD have elevated serum phosphate as a consequence of both reduced phosphate filtration and secondary hyperparathyroidism. Phosphorus and calcium abnormalities appear to contribute to soft-tissue calcification, accelerated cardiovascular calcification and overall mortality in ESRD.[4-8] Indeed, elevated serum phosphorus levels are associated with an increased risk of death in such patients,[4,5] particularly from coronary artery disease . Similarly, studies have shown the association between increased calcium–phosphorus (CaxP) product and cardiac calcification or risk of death.[4-8] Although it was initially believed that high phosphate concentrations trigger vascular calcification simply by exceeding the calcium-phosphate solubility product, causing precipitation

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but studies have also shown that high phosphate levels induce Vascular Smooth Muscle Cells (VSMCs) to differentiate into an osteoblastic phenotype. Parathyroid hormone (PTH) plays a crucial role in calcium homeostasis, and PTH and PTH-related peptide (PTHrP) may function as mediators of pathological calcification.

So the present study was done:

1. To find out the association of calcium phosphorus product with coronary artery calcification in CKD ESRD patients on dialysis.
2. To find out the calcium phosphorus product values in ESRD patients on dialysis

MATERIALS AND METHODS

Study design

The present study was a cross sectional study. A total of 70 patients were enrolled for the study. Out of which 20 individuals were normal participants and 50 individuals were CKD – ESRD patients on maintenance dialysis. The study was conducted in Mission of Mercy hospital and research center, Kolkata from April 2017 to November 2017. The study was approved by institutional ethics committee.

Eligibility criteria

Inclusion criteria for the study group was all the patients with CKD- ESRD on dialysis attending the dialysis unit of Mission of Mercy Hospital for more than 3 months while exclusion criteria was patients with active infection, inflammation and patients unwilling to participate in study.

Informed consent was taken from all the participants included in the study.

Methodology

Details of the patients were recorded in a structured proforma using questionnaire method and a detailed history was taken and patient were examined thoroughly.

Prior to dialysis blood sample were obtained from all the subjects who were enrolled for the study. These blood samples were analysed for serum Calcium, Phosphate and Parathyroid hormone. Both the study groups were subjected to Multi Row Spiral Computed Tomography (MSCT) for detection of coronary artery calcification scoring (CACS). The biochemical abnormalities and the extent of coronary calcification were recorded.

Statistical analysis

Statistical data was analysed by non-parametric tests like Chi (x2) test using alpha error of 5% and parametric test Z test. A p value of < 0.05 was considered as significant. Simple Odd's ratio was calculated.

RESULTS

The results of the data of the patient values were analysed.

Corrected Calcium

The mean value of corrected calcium was 8.95 ± 1.23 mg/dl in ESRD patients. The minimum value of corrected calcium was 7.40 mg/dl and maximum value was 11.50 mg/dl in ESRD patients. The mean value of corrected calcium was 8.15 ± 1.03 mg/dl in normal subjects.

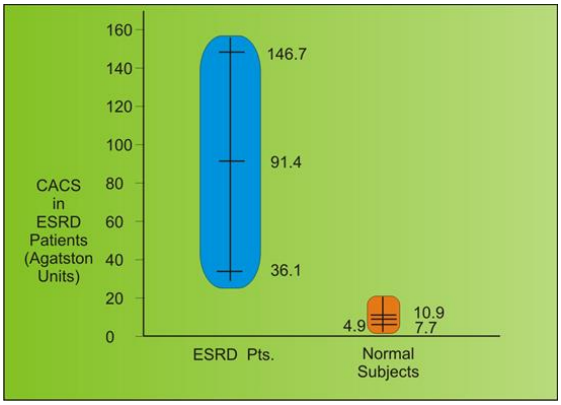

Figure 1: Prevalence of coronary artery calcification in ESRD patient on dialysis P < 0.05.

Table 1: Association of Coronary Artery Calcification scoring and Calcium Phosphorus product in ESRD patients.

CACS (Agatston Units)	CaXPO4 (mg2/dl2)
0-10	26.04 ± 0 (a)
11-100	45.18 ± 12.75 (b)
101-400	63.31 ± 10.18 (c)
> 400	

a vs b, z = 8.05, p < 0.05
b vs c, z = 6.02, p < 0.05
With increase in CACS, the CaXPO4 increases and this association is statistically significant
(p<0.05)

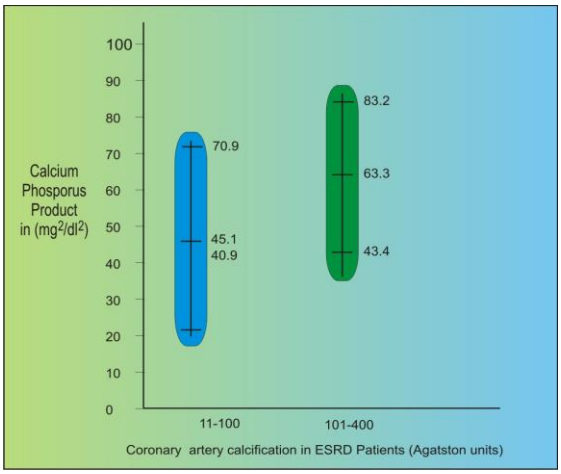

Figure 2: Association of Coronary Artery Calcification Scoring and Calcium Phosphorus product in ESRD patients

Calcium Phosphorus Product

The mean value of corrected Calcium Phosphorus product was 50.9 ± 15.6 mg2/dl2 in ESRD patients.. The minimum value was 26.04mg2/dl2 and maximum value of the product 85.7 mg2/dl2 in ESRD patients. The mean value of corrected Calcium Phosphorus product was 21.9 ± 0.6 mg2/dl2 in normal subjects.

Prevalence of Coronary Artery Calcification in ESRD patient on dialysis

The mean CACS in 50 patients with ESRD was 91.4 ± 32.7agatston units. The maximum CACS was 204.0 while the minimum case was 8 Agatston units. The mean CACS in normal subjects was 7.75 ± (6.5) agatston units.

The difference in the prevalence of CACS between the ESRD patients on dialysis and normal subjects was statistically significant (Z = 14.3, P < 0.05).

Table 2: Association of CaXPO4 with Coronary Artery Calcification in ESRD patients

Determinant	Simple Odd's Ratio Increased CACS in ESRD patients
CaXPO4	2.67

Higher Odd's Ratio indicates towards stronger association.

DISCUSSION

Disturbances in mineral metabolism and bone diseases are common complications of CKD and an important cause of morbidity, mortality and decreased quality of life. Studies have shown that disorders of bone and mineral metabolism are associated with increased risk of coronary artery calcification which contributes to increased cardiovascular mortality and morbidity.[9] Cardiovascular disease accounts for high mortality among ESRD patients.[10] Patients with ESRD have more chances of developing Coronary Artery Calcification (CAC) than age matched individuals with angiographically proven coronary artery disease. CKD patients have a number of nontraditional risk factors that may play a prominent role in the pathogenesis of CAC along with traditional risk factors.

Interest has been focused on the roles of hyperphosphatemia, elevated levels of the calcium x phosphorus product, hyperparathyroidism and obesity in the development of cardiovascular disease in ESRD. One hypothesis accounting for the disproportionate calcification burden in these patients is that high serum phosphate levels contribute to vascular calcification; patients with CKD have elevated serum phosphate as a consequence of both reduced phosphate filtration and secondary hyperparathyroidism.[11]

This study was a cross sectional study conducted on 50 patients with ESRD on dialysis. Our study was conducted to find out the association of calcium phosphorus products with coronary artery calcification in ESRD patients on dialysis.

In the present study, CAC scoring was studied in 50 ESRD patient on dialysis and 20 normal subjects. The difference in CACS between ESRD patients and normal subjects was statistically significant (z = 14.3, p < 0.05). This is in confirmatory with the studies done by Stumpor et al.[12] and Meijanian et al.[13] who showed that there is excess CAC in CKD patients compared to general population. Their study had an incidence of CAC of 53.8% and 96% respectively in the ESRD population whereas in our study the prevalence was 96%.

In this study, CACS correlated with Calcium phosphorus product. This finding is similar to the studies done by Jono et al,[14] and Moe et al,[15] who showed CACS to be correlated with Calcium phosphorus product.

CONCLUSION

Coronary artery calcification (CAC) is associated with increased cardiovascular morbidity and mortality and utmost care to be taken to modify most of the traditional and non-traditional risk factors responsible for CAC. CAC is amplified in CKD patients and it progresses rapidly.

Our study results suggest a positive association with blood calcium phosphorus product and CAC in ESRD patients. In ESRD patients, serum calcium phosphorus product is elevated compared to normal subjects. So from our study it is evident that controlling calcium phosphorus product will reduce the coronary artery calcification burden.

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