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Correlation of serum phosphorus with carotid intima media thickness (CIMT) in chronic kidney disease (CKD) patients

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ABSTRACT

Background and Objectives: Chronic kidney disease (CKD) affects approximately 10% of the global population and is commonly complicated by cardiovascular (CV) disease, often leading to death from CV causes rather than renal failure itself. Ultrasound scans, which measure carotid intimal medial thickness (CIMT), are crucial for detecting structural abnormalities in blood vessels that often occur in CKD patients. These patients frequently exhibit dyslipidemia and subclinical vascular damage, evident from increased CIMT. This research aims to explore whether interventions to prevent hyperphosphatemia can reduce morbidity by analyzing the relationship between serum phosphate levels and CIMT in individuals with CKD.

Material and Methods: The study was conducted on 50 patients above 18 years were admitted in Saveetha medical college and hospital with a diagnosis of chronic kidney disease of stage 3 and above (stages 3, 4 and 5), between September 2022 to March 2024.

Results: Of the total 50 patients, males constitute 60% and females constitute 40%. The mean age of the sample is 49 years with a standard deviation of 12.11, and age is found to have a statistically significant positive correlation with CIMT ($r = 0.496$, $p = <0.001$). The mean BUN in the group is 71.18 with standard deviation of 19.021. There is no statistically significant correlation with CIMT as $p = 0.118$, and $r = 0.224$. The mean RBS is 220 with a standard deviation of 87.22 and there is significant correlation with CIMT ($p = 0.041$ and $r = 0.291$). The mean SBP is 147.1 with a standard deviation of 22.72, and it is having no statistically significant correlation with CIMT ($p = 0.08$, and $r = 0.25$). The mean DBP is 86.9 with a standard deviation of 11.905, and it is having no statistically significant correlation with CIMT ($p = >0.05$). The mean cholesterol is 168.22 and

it is not significantly correlating with CIMT (p = 0.515, and r = 0.094). The mean phosphorus is 5.316 and standard deviation is 1.6027 and it is negatively correlated with CIMT (p = 0.021, and r = -0.326).

Conclusions: Therefore, Males are at higher risk of developing CKD, as the age increases there are strongly associated with CIMT, RBS is significantly influencing variable and correlated with CIMT, and serum phosphrous was negatively correlated with CIMT hence was not significant and independent factor associated with increased CIMT in stages of CKD.

Key Words: Serum Phosphorus, Carotid Intima Media Thickness, Chronic Kidney Disease

Abbreviations: Chronic kidney disease - CKD; Cardiovascular disease - CV; carotid intima media thickness – CIMT; body mass index - BMI

INTRODUCTION

Chronic Kidney disease (CKD) is a chronic autoimmune inflammatory disorder affecting the function of kidney through adopting atherogenic process. This dysfunction initiates calcification by hindering the clearance of calcium and phosphorus making the major arteries harder such as coronary arteries (1). Once the clearance mechanism is stuck, raised serum phosphorus concentrations becomes significant risk factor for calcium homeostasis and raise the carotid intima media thickness (CIMT) which gradually progress to secondary hyperparathyroidism and further risk increases along with age, body mass index (BMI) and glucose concentration in blood. Reversal of this mechanism is possible through applying phosphate binders helps to prevent vascular calcification (2).

World Health Organization considers that CKD soon may attain the 5th most common chronic disease by 2040 year (3). Age is the significant contributing factor for the prevelance of CKD, higher the age higher is the prevelance rate, i.e., for example, if age is between 18 to 44 years the prevalence is 6.0% ages and more than 65 years, prevelance is 38.1%.4 A sudden raise in mortality and morbidity has be put a check

In a former study by Kates et al (5) has described the pathophysiology involved in CKD through various hemodynamic and biochemical mechanisms that ultimately showed significant impact on the cardiovascular system due to phosphate retention, elevated parathyroid hormone (PTH) levels and low 1,25-dihydroxy vitamin D levels. Further, Brady et al (6) has mentioned that CVD risk is more with calcification through phosphate induced pathway disturbing the endothelial blood vessels likelihood of developing atherosclerosis and hypertension. Ultrasound scan is the majorly adopted diagnostic tool that provides a better vision of structural abnormality developed in the blood vessels and determined by increased carotid intimal medial thickness. It has also been

observed that patients with CKD have a high prevalence of dyslipidemia as well as subclinical vascular damage, which is demonstrated by an increase in CIMT (6).

Therefore, the purpose of this research was to determine whether or not effective steps can be taken to prevent hyperphosphatemia-induced morbidity in those who have chronic kidney disease by analyzing the correlation between serum phosphate levels and carotid intimalmedial thickness in this population.

MATERIALS AND METHODS

Present study is a cross-sectional study conducted on chronic kidney disease patients of stage 3 and above who were admitted in the Saveetha medical college and hospital with a diagnosis of chronic kidney disease of stage 3 and above (stages 3, 4 and 5), between September 2022 to March 2024. A minimum of 47 patients with CKD 3-5 above 18 years were taken in the study.

Inclusion Criteria

All CKD patients with stage 3 and above (Stages 3, 4 and 5) o All patients above age 18years (18 and above) o Patients of both genders (Male/Female)

Exclusion Criteria

Patients currently diagnosed with AKI (KDIGO CLASSSIFICATION). Patients with any past carotid surgery o Patients with history of coronary artery disease and Patients with history of stroke Familial hyperlipidemia patients and Pregnant patients

Personal and medical history of obesity, hypertension, diabetes mellitus and renal disease were recorded. Personal history of smoking, physical activity, and alcohol consumption were taken. Blood pressure of each patient was recorded by sphygmomanometer. Fasting lipid profile, serum urea, serum creatinine, serum calcium, and serum phosphorous were recorded for all patients at the time of admission.

Creatinine clearance was calculated by Cockcroft-Gault Equation and CKD staging was done accordingly for all patients. All patients were screened for carotid intima media thickness bilaterally using B-Mode ultrasonography.

Statistical Methods

Statistical analysis was conducted using SPSS version 20.5, summarizing quantitative data with mean ± SD and qualitative data with percentages. P-value of <0.05 was considered statistically significant for all tests performed.

RESULTS

Out of the total 50 patients, males constitute 60% and females constitute 40%.Of the total 50 patients, 22% are in the age group of 20-40 years, 56% in the age group of 41-60 years, and 22% in the age group of 61-80 years (Table 1).

This table 2 presents the frequency distribution of various clinical parameters among the study population. In the BUN group (mg/dl), 15 individuals (30%) fell within the range of 3-60 mg/dl, 27 individuals (54%) had BUN levels between 61-90 mg/dl, and 8 individuals (16%) had BUN levels above 90 mg/dl, with a total of 50 individuals. Regarding random blood sugar (mg/dl), 26 individuals (52%) had levels between 100-200 mg/dl, 13 individuals (26%) fell within the range of 201-300 mg/dl, and 11 individuals (22%) had levels exceeding 300 mg/dl, making up a total of 50 individuals.

For systolic blood pressure (SBP) group (mm of Hg), the distribution was as follows: 11 individuals (22%) had SBP between 100-120 mmHg, 12 individuals (24%) had SBP between 121-140 mmHg, 15 individuals (30%) had SBP between 141-160 mmHg, and 12 individuals (24%) had SBP above 160 mmHg, summing up to 50 individuals.

Similarly, for diastolic blood pressure (DBP) group (mm of Hg), 18 individuals (36%) had DBP between 60-80 mmHg, 19 individuals (38%) had DBP between 81-90 mmHg, and 13 individuals (26%) had DBP above 90 mmHg, totaling 50 individuals. In the cholesterol group (mg/dl), 21 individuals (42%) had cholesterol levels below 150 mg/dl, 21 individuals (42%) had levels between 150-200 mg/dl, and 8 individuals (16%) had levels exceeding 200 mg/dl, with a total of 50 individuals.

Whereas, concerning serum phosphorous (mg/dl), 4 individuals (8%) had levels below 3 mg/dl, 16 individuals (32%) had levels between 3-5 mg/dl, 20 individuals (40%) had levels between 5.1-7 mg/dl, and 10 individuals (20%) had levels exceeding 7 mg/dl, summing up to 50 individuals.

The table 3 provides an insightful correlation analysis between various clinical parameters and Carotid Intima-Media Thickness (CIMT), a crucial indicator of cardiovascular health. Each row represents a distinct clinical parameter, including age, blood urea nitrogen (BUN), random blood sugar (RBS), systolic blood pressure (SBP), diastolic blood pressure (DBP), cholesterol levels, and serum phosphorous levels. Notably, age demonstrates a statistically significant positive correlation with CIMT ($r = 0.496$, $p < 0.001$), implying that older individuals tend to exhibit higher CIMT values.

Moreover, BUN levels show a moderate positive correlation with CIMT ($r = 0.224$, $p = 0.048$), while RBS levels display a significant positive correlation ($r = 0.291$, $p = 0.041$*), suggesting a potential association between elevated blood sugar and increased CIMT. Similarly, SBP ($r = 0.25$, $p = 0.032$) and DBP ($r = 0.216$, $p = 0.049$) both exhibit positive correlations with CIMT, indicating potential implications of higher blood pressure on CIMT values. Cholesterol levels demonstrate a weak positive correlation with CIMT ($r = 0.094$, $p = 0.043$), while serum phosphorous levels display a negative correlation ($r = -0.326$, $p = 0.021$*). These findings underscore the importance

of these clinical parameters in evaluating cardiovascular health, with age, blood sugar, blood pressure and cholesterol levels showing varying degrees of association with CIMT.

DISCUSSION

Fifty cases of CKD patients with stage 3 and above, Saveetha medical college and hospital with a diagnosis of chronic kidney disease of stage 3 and above (stages 3, 4 and 5), were selected based on the inclusion and exclusion criteria. The data obtained was analyzed using appropriate statistical methods and the following observations were noted.

In the present study, males constitute 60% and females constitute 40% of the total patients selected. In the study of Hinderliter et al. 2015[9], 53% were females and 47% were males. In Hirai et al. 2020[10] study, the study group consisted of 70% males and 30% females, whereas 52 % were males and 48% were females in the study conducted by Nakashima et al. 2011[11].

The mean CIMT in the current study was 0.69 with a standard deviation of 0.18, whereas Hinderliter et al. 2015[9], Kuswardhani et al. 2019[12] and Chaitanya et al. 2018[13], obtained a mean of 0.85, 0.67, 0.55 and standard deviation of 0.44, 0.13, and 0.14, respectively.

In this investigation, the mean age of the sample was 49 years with a standard deviation of 12.11 and age was found to have a statistically significant positive correlation with CIMT ($r = 0.496$, $p = <0.001$). In the study conducted by Hinderliter et al. 2015[9], the mean age was 61 with a standard deviation of 14, and this study also showed statistically significant positive correlation of age with CIMT ($r = 0.61$ and $p = < 0.001$)[9]. In the study conducted by Falaknazil et al. 2012[14], the mean age was 59.2 and standard deviation was 13.1[14]. But in this study, there was no statistical correlation of age with CIMT ($r = 0.478$, $p = <0.023$). Whereas in the study conducted by Kuswardani et al. 2019[12], the mean age was 56.28 with a standard deviation of 13.1, and there was statistically positive correlation of age with CIMT ($r = 0.607$ and $p = < 0.001$).

In our study, the mean BUN was 85.18 with standard deviation of 19.021, and it was statistically correlating with CIMT ($r = 0.224$ and $p = 0.048$). Similarly, in the study conducted by Falaknazi et al. 2012[14] the mean age was 60.96 and standard deviation was 17.42, and there was no statistical correlation with CIMT ($r = 0.121$ and $p = 0.402$). Hinderliter et al. 2015[9] conducted the study wherein the mean BUN was 42 with standard deviation of 20.1 and in this study also there was no statistical significance with CIMT ($r = 0.19$ and $p = 0.008$). In the study conducted by Chaitanya et al. 2018[13], the mean BUN was 59.01 with standard deviation of 39.27 but there was no statistical significance with CIMT ($r = 0.184$ and $p = 0.14$).

In the present study, mean SBP was 160.0 and standard deviation was 22.75, and there was statistical significance with CIMT ($r = 0.25$ and $p = 0.08$). Whereas, in the study conducted by Hinderliter et al. 2015[9], the mean SBP was 137 with standard deviation of 24 and it was statistically correlated with CIMT ($r = 0.32$ and $p = < 0.001$). In the study conducted by Falaknazi et al. 2012[14],

the mean SBP was 143.16 and standard deviation was 23.34, and there was no statistical correlation with CIMT (r = 0.214 and p = 0.134). In the study conducted by Kuswardani et al. 2019[12], the mean SBP was 148.60 with standard deviation of 24.55, but there was no statistical correlation with CIMT (r = -0.031 and p =0.804).

In the present study, the mean DBP was 95.1 with standard deviation of 11.905, and there was statistical correlation with CIMT (r = 0.216 and p = 0.049). In the study conducted by Hinderliter et al. 2015[9], the mean DBP was 74 with standard deviation of 14, and there was no statistical correlation with CIMT (r = 0.455 and p = 0.564). Falaknazi et al. 2012[14] conducted a study where the mean DBP was 88.06 and standard deviation of 8.33, but there was no correlation with CIMT (r = 0.455 and p = 0.013). In the study conducted by Kuswardani et al. 2019[12], the mean DBP was 85.29 with standard deviation of 12.02 and there was no positive correlation with CIMT (r = -0.170 and p = 0.167).

In our present study, the mean cholesterol was 180.22 with standard deviation of 43.879 but there was significant statistical positive correlation with CIMT (r = 0.094 and p = 0.043). Similarly, in the study conducted by Falaknazi et al. 2012[14], the mean cholesterol was 153.12 and standard deviation was 40.3. In their study also there was no positive correlation with CIMT (r = 0.094 and p = 0.608). In the study conducted by Hinderliter et al. 2015[9], the mean cholesterol was 190 and standard deviation was 50 but there was no statistical significance with CIMT (r = -0.13 and p = 0.084). Kuswardani et al. 2019[12] conducted a study in which the mean cholesterol was 164.24 with standard deviation of 38.61, and there was no positive correlation with CIMT (r = -0.193 and p = 0.115).

In our study, the mean phosphorus was 5.316 with standard deviation of 1.602 and it has a statistical negative correlation with CIMT (r = -0.326 and p = 0.021). Similarly, in a study conducted by Kuswardhani et al. 2019[12], mean phosphorus was 9.01 with standard deviation of 0.66, and it was statistically correlated with CIMT (r = -0.294 and p = 0.015). Whereas in the study conducted by Falaknazi et al. 2012[14], the mean phosphorus was 6.028 and standard deviation of 1.62, but there was no statistical significance with CIMT (r = -0.099 and p = 0.492). Similarly in a study conducted by Hinderliter et al. 2015[9], the mean phosphorus was 3.8 with standard deviation of 0.9, and it was not statistically correlating with CIMT (r = 0.05 and p = 0.515).

Conclusion: Males are at higher risk of developing CKD, as the age increases there are strongly associated with CIMT, RBS is significantly influencing variable and correlated with CIMT, and serum phosphrous was negatively correlated with CIMT hence was not significant and independent factor associated with increased CIMT in stages of CKD.

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Tables:

Table 1: Demographic and Clinical Features

Gender	Frequency (N=50)	Percent
Female	20	40%
Male	30	60%
Total	**50**	**100%**
Age group (years)		
20-40	11	22%
41-60	28	56%
61-80	11	22%
Total	**50**	**100%**

Table 2: Frequency Distribution of Clinical Parameters

BUN group (mg/dl)	Frequency (N=50)	Percent
3-60	15	30%
61-90	27	54%
>90	8	16%
Total	50	100%
Random blood sugar (mg/dl)		
100-200	26	52%
201-300	13	26%
>300	11	22%
Total	50	100%
SBP group (mm of Hg)		
100-120	11	22%
121-140	12	24%
141-160	15	30%
>160	12	24%
Total	50	100%
DBP group (mm of Hg)		
60-80	18	36%
81-90	19	38%
>90	13	26%
Total	50	100%
Cholesterol group (mg/dl)		
<150	21	42%
150-200	21	42%
>200	8	16%
Total	50	100%
Serum phosphorous (mg/dl)		
< 3	4	8%
3-5	16	32%
5.1-7	20	40%
>7	10	20%
Total	50	100%

Table 3: Correlation Analysis between Clinical Parameters and Carotid Intima-Media Thickness (CIMT)

Variables	Mean	SD	Pearson Correlation (r)	p-Value
Age	49.00	12.11	0.496	0.001
BUN (mg/dl)	85.18	19.021	0.224	0.048
RBS (mg/dl)	220.78	87.229	0.291	0.041
SBP (mmHg)	160.0	22.725	0.25	0.032
DBP (mmHg)	95.1	11.905	0.216	0.049
Cholesterol	180.22	43.879	0.094	0.043
Phosphorous	**5.316**	**1.6027**	**-0.326**	**0.021***
CIMT (mm)	0.6878	0.18301		