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THE INTERSECTION OF CKD AND CARDIAC HEALTH: UNRAVELING THE LINK BETWEEN HYPERPHOSPHATEMIA AND ELEVATED SERUM CK-MB

Biochemistry

Dr Pritayan Bhattacharjee* Post Graduate Resident , Dept Of Biochemistry, Jln Medical College , Ajmer *Corresponding Author
Dr Sarla Mahawar Senior Professor, Dept Of Biochemistry, Jln Medical College, Ajmer
Dr Deepa Thadani Senior Professor & Hod, Dept Of Biochemistry, Jln Medical College, Ajmer
Dr Archit Soni Biochemist, Dept Of Biochemistry, Jln Medical College, Ajmer

ABSTRACT

Background: Chronic Kidney Disease (CKD) is a progressive condition affecting over 10% of the global population. It is frequently associated with an increased risk of cardiovascular complications, partly due to disturbances in mineral metabolism. This study investigates the correlation between hyperphosphatemia and elevated serum CK-MB levels in CKD patients, aiming to understand how these factors impact cardiac health. **Methodology:** This case-control study involved 100 healthy controls and 100 CKD patients of either sex, aged 40-90 years, attending the Urology Department of Jawaharlal Nehru Medical College. The study was approved by the institutional ethical committee. Serum phosphorus and CK-MB levels were measured, and their correlation was analyzed. **Results:** The study revealed a significant positive correlation between serum phosphorus levels and elevated CK-MB in CKD patients ($r = 0.21$, $p < 0.001$). Higher phosphorus levels were associated with increased CK-MB, indicating that hyperphosphatemia may contribute to cardiac myocyte injury in CKD patients. **Conclusion:** The study highlights a significant association between hyperphosphatemia and elevated serum CK-MB in CKD patients, emphasizing the potential role of phosphorus imbalance in worsening cardiac injury. These findings suggest that managing phosphorus levels could be crucial for mitigating cardiovascular risks in CKD. Further research is needed to explore the underlying mechanisms and potential therapeutic interventions.

KEYWORDS

Chronic Kidney Disease, Hyperphosphatemia, Serum CK-MB, Cardiac Health.

INTRODUCTION :

CKD is characterized by a gradual decline in kidney function over months or years, leading to a progressive and irreversible reduction in glomerular filtration rate (GFR). Regardless of the underlying cause, all kidney diseases ultimately advance to terminal renal failure [1]. Chronic kidney disease (CKD) presents a significant global health challenge, affecting up to 15% of adults worldwide and patients often face multiple comorbidities, heightening mortality risk and raising healthcare expenditures [2–4]. It is closely linked to an increased risk of cardiovascular disease (CVD). Cardiovascular complications, responsible for half of all advanced CKD-related deaths, encompass various conditions such as coronary artery disease (CAD), heart failure, arrhythmias, and sudden cardiac death. This risk amplifies as CKD progresses, evidenced by declining kidney function, particularly in terms of glomerular filtration rate [2,5].

In chronic kidney disease (CKD), phosphorus balance is disrupted, leading to a positive phosphate balance, particularly in the later stages (stages 4 and 5) of the disease [6,7]. This imbalance, known as hyperphosphatemia, is associated with several adverse cardiovascular effects, including hypertension, vascular and cardiac valvular calcification, atherosclerosis, left ventricular hypertrophy, and myocardial fibrosis [2,8]. Cardiac markers, like creatinine kinase-MB (CK-MB), are commonly employed in clinical settings as sensitive indicators of myocardial necrosis [9,10]. Interestingly, research has revealed elevated levels of cardiac markers in patients with different levels of kidney dysfunction [11–13].

The study aims to assess and analyze the levels of CKMB among chronic kidney disease patients who are not under dialysis with levels of serum phosphorus to establish baseline values

MATERIAL & METHODOLOGY

The present study comprised a case-control study design involving 100 individuals diagnosed with chronic kidney disease. Diagnosis was established through clinical history, physical examination, and evaluation of serum urea and serum creatinine levels. Cases were selected from the Urology and Medical wards of Jawahar Lal Nehru Medical College and Associated Group of Hospitals, Ajmer. Concurrently, age and gender-matched controls (n=100) were selected from the Medicine Outpatient Department of the same institution. A comparative analysis of patient data was conducted against the 100 healthy controls. Subjects diagnosed with chronic kidney disease who had not undergone haemodialysis and provided consent were included in the study.

Exclusion criteria:

Patients with a history of dialysis, Acute kidney injury, acute infection, acute myocardial infarction, active liver disease or liver dysfunction, haematological , malignant overt diseases and any other cardiovascular disease, Cases associated with other inflammatory diseases such as cancer or autoimmunity, Kidney transplant patients, Pregnant and lactating women, patients taking drugs that increases Serum Phosphorus, and those who didn't provide consent all were excluded from the study.

Procedure

Blood samples were collected after an overnight fast (12-14hrs) under aseptic conditions from all the study participants. All samples were centrifuged and analysed for serum urea, serum creatinine, serum phosphorus and CK-MB. Serum urea was measured by Berthelot enzymatic calorimetric method , Serum Creatinine by Jaffe's calorimetric kinetic method ,Serum inorganic phosphorus was estimated by phosphomolybdate method, Serum CK-MB was estimated by IFCC immunoinhibition method using Beckman Coulter Biochemistry Analyzer (DXC700).

Data analysis

Collected data were entered into Microsoft Excel spreadsheet and then analysed by IBM SPSS (version 26). Data had been summarized as mean and standard deviation for numerical variables and count and percentages for categorical variables. A p-value<0.05 was considered significant.

RESULTS

Among the 100 cases, the majority were in the age group of 61 to 80 years, with a mean age of 69.0 (±10.7) years and the majority were females. Most of the participants were in the stage V of chronic kidney disease **(Table 1)**.

Table 1: Baseline characteristics of the cases (N=100)

Age group (in years)	**Percentage**
41-60	26.0%
61-80	56.0%
>80	18.0%
Gender	**Percentage**
Male	39.0%
Female	61.0%
Stage of CKD	**Percentage**
Stage IV	33.0%

Stage V	67.0%

Among the cases, the mean serum urea level was calculated to be 197.3±70.1mg/dl, the mean creatinine level was 5.9±3.7 mg/dl, serum phosphorus level was calculated to be 6.1±2.9 mg% and the mean serum CK-MB was 36.3±29.9 U/L. The difference between the levels of serum urea, creatine, phosphorous and CK-MB among the cases and controls were statistically significant (Table 2).

Table 2: Biochemical Parameters among cases and controls

Biochemical Parameters	Cases (CKD patients)	Controls (Healthy individuals)	p-value
Urea (mg/dl)	**197.3±70.1**	**23.36±6.7**	**<0.001***
Creatinine (mg/dl)	**5.9±3.7**	**0.86±0.52**	**<0.001***
Serum Phosphorus (mg%)	**6.1±2.9**	**3.9±0.5**	**<0.001***
Serum CK-MB (U/L)	**36.3±29.9**	**17.6±6.8**	**<0.001***

*Statistically significant

The serum phosphorus levels typically ranged between 4.5-6.5 mg% for most of the patients (32% of cases) with chronic kidney disease (CKD), as indicated in Figure 1.

Additionally, the CK-MB levels were predominantly below 25 U/L in the majority of CKD patients(33% of cases), as shown in Figure 2.

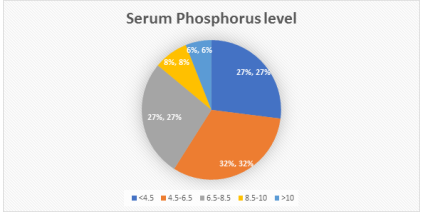

Figure 1: Serum phosphorus level among CKD patients

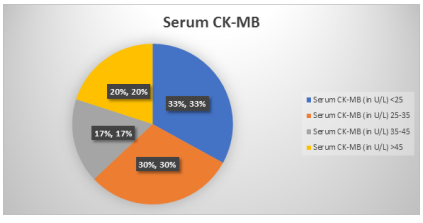

Figure 2: Serum CKMB level among CKD patients

There was a positive correlation between serum phosphorus levels and serum creatinine levels (Figure 3), serum CK-MB levels and serum creatinine levels (Figure 4) and serum CK-MB and serum phosphorus levels (Figure 5). The correlations between serum phosphorus levels and serum creatinine levels (p=.000) and serum CK-MB and serum phosphorus levels (p=.034) were significant.

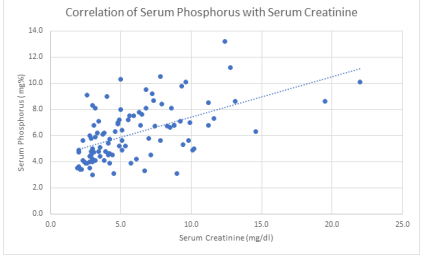

Figure 3: Correlation of Serum Phosphorus with Serum Creatinine among CKD patients (having Pearson correlation r value of 0.59)

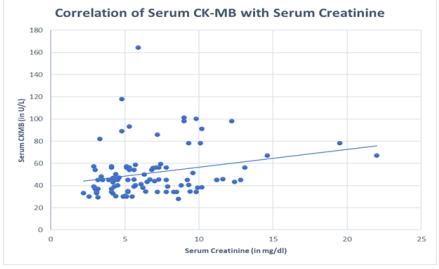

Figure 4: Correlation of Serum CK-MB with Serum Creatinine (having pearson correlation r value of 0.041)

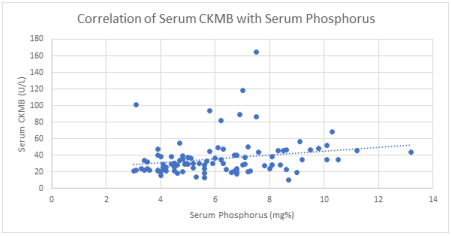

Figure 5: Correlation of Serum Phosphorus with Serum CKMB among CKD patients (having Pearson correlation r value of 0.21)

DISCUSSION

Chronic kidney disease (CKD) has emerged as a significant global health concern, with a pooled prevalence of 14% (95% CI 11–18%) among the general population of South East Asia [14]. This rise is attributed partly to the increasing incidence of diabetes and hypertension worldwide [15,16]. CKD is characterized by structural or functional renal anomalies coupled with a persistent decline in renal function, leading to complications such as chronic inflammatory syndrome, electrolyte imbalances, and uremic toxicity. Cardiovascular complications are the primary cause of mortality in CKD patients, with ischemic cardiac pathology being both a consequence and complication of the disease.

Phosphate, primarily excreted in urine, plays a crucial role in bodily functions, with only a small fraction circulating in the blood. However, its accumulation can have detrimental effects, notably in end-stage renal disease where widespread vascular and soft tissue calcifications occur due to chronic phosphate buildup [17]. In early CKD stages, serum phosphate levels are typically maintained within the normal range, thanks to compensatory mechanisms such as increased fibroblast growth factor-23 (FGF-23) and parathyroid hormone levels, until the estimated glomerular filtration rate (eGFR) declines to 30 mL/min/1.73 m². Subsequently, hyperphosphatemia ensues [18,19].

Our study revealed elevated serum phosphate levels in CKD patients not undergoing hemodialysis compared to healthy controls, highlighting the importance of monitoring phosphate levels in CKD management.

Our study revealed a statistically significant elevation in mean serum CK-MB levels (36.3±29.9 U/L) compared to healthy controls. This finding aligns with the observations of Ashfaq et al., who reported similarly elevated serum CK-MB levels (46.9±9.86 U/L) in patients with stage 4 & 5 CKD [20]. Evidence from various studies suggests that cardiac markers like CK-MB increase as CKD progresses. This phenomenon may be attributed to phosphate overload, which has been shown to directly induce apoptosis of human vascular endothelial cells, as demonstrated by Di Marco et al [21].

In a cross-sectional study conducted by Wang S et al., involving 151 patients with varying degrees of kidney function, the relationship between serum phosphate and cardiac markers (CMs), including CK-MB, was investigated. They observed a gradual increase in both phosphate and CMs as glomerular filtration rate declined in CKD patients ($p<0.01$). Furthermore, they noted significantly higher levels of serum CMs and poorer cardiac function in CKD patients with hyperphosphatemia ($p<0.05$). Their findings led to the conclusion that hyperphosphatemia may contribute to myocardial damage in CKD patients by promoting apoptosis of human cardiomyocytes, thus elevating cardiac markers [13].

CONCLUSION

Our study investigated the baseline serum phosphate and serum CK-MB levels in CKD patients who had not yet undergone hemodialysis, comparing them with those of healthy controls. We found a significant increase in both parameters compared to the healthy control group. However, it is important to note that our study has limitations, including a small sample size and a single-center design. Therefore, caution should be exercised when generalizing our results, and further studies are needed to validate our findings. Nonetheless, our study provides valuable insights into the relationship between serum phosphate and serum CK-MB levels in CKD patients, which may

inform future management strategies for this population.

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