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RESEARCH ARTICLE

EFFECT OF DIETARY FACTORS AND NUTRITIONAL STATUS ON SERUM CALCIUM AND PHOSPHORUS LEVELS IN CKD PATIENTS ON TREATMENT IN A TERTIARY CARE SETTING IN NORTH INDIA

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ABSTRACT
The control of phosphorus and calcium metabolism is one of the objectives in treatment protocol for CKD patients. The levels of these minerals in serum are affected by dietary patterns and nutritional status of the patients. India being a large country, diet patterns vary from one state to another. Thus, we suspect a close association between dietary intake and alterations in homeostasis of calcium and phosphorus in CKD patients. Therefore, we conduct this study to describe the effect of dietary factors and nutritional status on serum calcium and phosphorus levels in CKD patients on treatment in a tertiary care setting in North India. In the present study 330 CKD patients coming to dialysis unit, were recorded with detailed Medical history as well as baseline demographic data. Also, biochemical analysis of serum albumin corrected, calcium, phosphorus, and serum albumin of all cases were done using fully automated equipment. All statistical analyses were performed using SPSS statistical software, version 17. Majority (58.2 %) of the study patients were vegetarians with a mean value of BMI (Mean±SD=23.75±4.70 kg/m^2). A negative but significant correlation was found between corrected calcium and phosphorus with 0.05 level of confidence interval (r=-0.149, p= 0.007). It was found that the well-nourished patients were more likely to be hyperphosphatemic as compared to poorly nourished patients, but statistically the values were found to be non significant (Statistically p-value was not less than 0.05).
Keywords: Calcium, CKD patients, diet, nutrition, phosphorus.

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INTRODUCTION

Chronic kidney disease (CKD) is a global health problem that affects 5% to 10% of the World population[1], with increasing prevalence and poor outcomes, with progressive loss of renal functions, cardiovascular disease, and early death[2-4].
Chronic kidney disorders have a progressive pattern in most cases taking months to years, and finally result in end-stage renal disease (ESRD)[3,5]. When renal function drops below 10 to 15 percent of the normal function ESRD is reached[6]. For the composition of bones and the regulation of several processes in the body, calcium and phosphorus have great importance[7]. The kidney plays important role in achieving calcium and phosphorus homeostasis in collaboration with other organs i.e. the parathyroid gland, intestines, and bones. Thus, along with the progression of chronic kidney disease (CKD), numerous abnormalities (like hypocalcemia, hyperphosphatemia and hyperparathyroidism) develop, which can result in noteworthy consequences[8]. Instabilities in mineral metabolism in CKD which result in multisystem disorder have now been given a distinct identity as CKD-MBD (Chronic Kidney Disease-Mineral and Bone disorder) by KDIGO[9,10]. KDIGO (Kidney Disease: Improving Global Outcomes) is an international initiative with a key mission of developing evidence-based clinical practice guidelines for the prevention, diagnosis, evaluation, and treatment of chronic kidney disease and has added "Mineral and Bone Disorder to CKD to be now called as CKD–MBD"[10,11]. These Guidelines for bone metabolism and disease in CKD (USA)

recommend that, the target levels for calcium (Ca) (corrected for serum albumin), phosphorus (P) and calcium×phosphorus (Ca×P) product levels should be maintained at 8.5-10.5 mg/dl, 2.5-4.5 mg/dl and <55 mg^2/dl^2, respectively.

The control of calcium and phosphorus metabolism is one of the objectives in an acceptable treatment protocol for CKD patients. The levels of these minerals in serum are also affected by dietary patterns and nutritional status of the patients. India being a large country, diet patterns vary from one state to another. Thus, we suspect a close association between dietary intake and alterations in calcium and phosphorus homeostasis in CKD patients and hence we conducted the present study.

MATERIALS AND METHODS

Study Design:

This study was a cross-sectional observational study.

Research Setting:

The study was conducted at the Gian Sagar Medical Hospital, Ramnagar, Patiala, under the Department of Physiology and dialysis unit, department of Medicine.

Study Population and Study Period: 330 Chronic Kidney Disease Patients>18 years of age and belonging to both sexes were on maintenance hemodialysis in dialysis unit of Gian Sagar Medical College and Hospital, Ramnagar (Patiala) over a period from December, 2012 to December, 2016. Each patient was considered only once for the study.

Ethical approval and informed consent:

After approval by ethical committee of Gian Sagar medical College and Hospital, this study was initiated. An informed consent was taken from all the subjects before inclusion in the study.

Data Collection and statistical analysis:

The study was started after proper approval from Institutional Research Ethics Committee. Patients were selected based upon the inclusion and exclusion criteria. Approach to a Patient began by taking informed consent. The baseline demographic data like age (yrs.), gender (M/F), weight (Kg), height (cm), BMI (Body Mass Index), religion, educational status (literate/illiterate), environmental status (urban/rural), were recorded. Blood sample was collected for laboratory investigations (like Serum calcium, Serum phosphorous, Serum albumin, and Hemoglobin).

Five milliliters of blood were taken from the antecubital vein of the patients under full aseptic conditions. Serum was separated out for the estimation of biochemical parameters upon clotting. Fully automated equipments standardized in Gian Sagar Hospital were used to perform these tests. Dietary history of the patients was taken in detail. Nutritional status of the patients was assessed by measuring BMI (Body Mass Index)[12]. Detailed history regarding the intake of both calcium-based and Non-calcium-based phosphate binders and Vitamin D analogues was taken. Normal values of serum calcium (corrected for albumin) and phosphate were defined as 8.5-10.5 mg/dl and 2.5-4.5 mg/dl respectively. The detailed data related to CKD-MBD was recorded. Observations and results were compiled at the end of the study. The control of CKD-MBD was assessed as recommended by KDIGO guidelines. Appropriate statistical methods were employed to compare all the Demographic and laboratory parameters using statistical package for social sciences SPSS (Statistical Package for Social Science) package version 17.0. Descriptive statistics such as range, mean and standard deviation were used to describe continuous variables while numbers and percentages were used to present discreet variables. Chi square test was used to test association between Demographical and laboratory parameters and Pearson's coefficient of correlation were used to assess the inter-relationship between various examined laboratory markers. The result was statistically significant when the P-value was less than 0.05.

Observations:

In present study 66.4 % patients predominantly belonged to the rural area as compared to 33.6% urban area. Majority (58.2%) of the study patients were taking vegetarian diet in the present study (Figure 1 and Figure 2). Majority (62%) of patients had hyperphosphatemia as compared to hypophosphatemia (1%, only) (Figure 4).

Statistical analysis:

Chi-square tests were used to see association between Phosphorus levels (hypo, normal and hyperphospha-temia) and other demographic variables like Dietary Factors and Nutritional status of the study patients. Pearson's Chi square test (Yates's correction for continuity) was used to examine the significance of association (contingency).

RESULTS

It was observed that the percentage of vegetarians who were hyperphosphatemic was more than non vegetarians and also found that the well nourished patients were more likely to be hyperphosphatemic as compared to poorly nourished patients, but statistically the values were found to be non significant (Table 2)

The above Figure 5 clearly shows hyperphosphatemia as a constant finding in all baseline demographic parameters of the CKD patients. In addition to this both poorly nourished patients and well nourished patients showed hyperphosphatemia. Similar findings were reported in both vegetarian and non vegetarian patients. A negative but significant correlation was found between corrected Ca and phosphorus with 0.05 level of confidence interval (r=-0.149, p= 0.007).

DISCUSSION

The minerals like calcium and phosphorus disrupted in CKD are critically important in the regulation of both initial bone formation during growth (bone modelling) and bone structure and function during adulthood (bone remodelling)[9]. As a result, bone abnormalities are found almost universally in patients with progressive loss of renal function in CKD[9]. Calcium and Phosphorus alterations in CKD patients can be attributed to many causes.

Present study population of 330 patients comprised adults, mainly illiterate (54.5%), and coming from rural-strata (66.4%) with a mean age of 52.67±15.05 (range 25 to 98 years), of whom mostly patients were

taking vegetarian diet (58.2%).The mean age of our study population was similar to other studies like a mean age of 49.3 years with range 17-80[13] and a mean age of 46.6±13.4 years[14]. However, higher mean age was reported in other Western and Indian studies[15-17]. In the present study it was observed that alterations in biochemical profile were common in CKD patients. 55.8% of patients for corrected serum calcium and 63.0% of patients for phosphorus were out of the target range.

The percentage of patients, who were in the recommended range, was less than that obtained in other studies[18,19]. The inability of the CKD Patients to achieve the above said target range may be on account of implementing different modalities for regulation of calcium and phosphorus levels in Indian dialysis population as given below: -

1. Patients were using calcium based phosphate binders only (like calcium acetate or calcium carbonate) in our centre as compared to non-calcium based phosphate binders (like sevelamer hydrochloride, or lanthanum carbonate, which is widely used in USA and Europe for the treatment of hyperphosphatemia in patients with CKD[20-21].
2. In our centre (Punjab region) we found patients were taking diet mostly of milk, cheese, and butter with high content of phosphorous due to easily availability because most of the rural households have cattle of their own and believed that milk and milk products are of high nutritional value in all aspects. They would also sometimes replace meals with milk so balanced nutrition is not achieved in such cases.
3. In addition to this, the consumption of alcoholic beverages also high in Punjab and these factors also contributes to hyperphosphatemia seen in patients from this region.
4. Moreover, phosphate binders as prescribed by nephrologist to cure this problem were not properly adhered to by dialysis patients. Evidence of present study showed that 75.8 % CKD patients were not using the phosphate binders. Only 24.2% CKD Patients were using these binders (calcium-based phosphate binders).

Serum calcium, phosphorus concentrations should therefore be measured in all CKD patients on a regular basis. Measurements should be made more frequently when a patient receives concomitant therapy for anomalies in plasma calcium and phosphorus[22]. To obtain low phosphorus levels an adequate management program is necessary, which can only be accomplished by thorough dietary counselling and administration of a balanced mix of medications. The diets rich in phosphorus such as milk, cheese, dried beans, peas, nuts, and peanut butter and Drinks like cocoa, dark sodas, and beer should be consumed in quantities which are strictly recommended by an expert renal dietician. Its required medications called phosphate binders (such as calcium carbonate (Tums), calcium acetate (PhosLo), sevelamer hydrochloride (Renagel), or lanthanum carbonate (Fosrenol) may also be added with meals and snacks to bind phosphorus in the bowel. These medications decrease the absorption of phosphorus into the blood.

Overall, reducing dietary intake of phosphorus in dialysis patients is one of the most important steps in controlling PTH levels. Overactive parathyroid glands are controllable with a change in diet, dialysis treatment, or medication in most of the cases. A dietary plan to control phosphorus levels in the blood should be developed by a qualified renal dietician. Strict compliance to the diet must be done by the patients and physicians should motivate the patients to do the same.

CONCLUSION

Our findings support a strict control of mineral metabolism in CKD patients. The importance of educating and stimulating dialysis patients in order to achieve optimal observance to the treatment program and dietary suggestions should be highlighted to both patients and doctors. A strict dietary plan along with inclusion of phosphate binders in diet to control phosphorus levels in the blood should be provided by the renal dietician. Regular dietary follow-ups and counselling is necessary to ensure the success of diet and treatment programmes. The aim of the treatment must be control of phosphate retention, maintaining serum calcium concentration within the normal range (standard), with prevention of hypercalcaemic incidents.

AUTHORS' CONTRIBUTION

The manuscript was carried out, written, and approved in collaboration with all authors.

CONFLICT OF INTEREST

No specific grant from any agency in the public, commercial, or non-profit sectors was received for this study.

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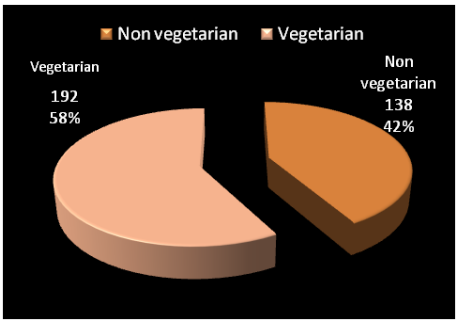

Figure 1: Distribution according to Dietary History in CKD patients.

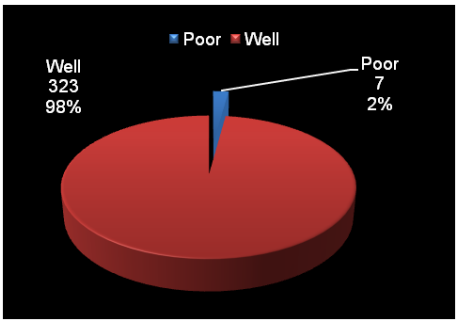

Figure 2: Distribution according to nutritional Status in CKD patients.

Table 1. Distribution of cases by levels of Laboratory Parameters in CKD patients

Laboratory characteristics of Patients	Groups	Number of CKD patients (n = 330)	%
Albumin-corrected serum Ca(mg%)	Less than 8.5	167	50.6
	8.5-10.5	146	44.2
	More than 10.5	17	5.2
Serum phosphorus level (mg%)	Less than 2.5	3	.9
	2.5-4.5	122	37.0
	More than 4.5	205	62.1

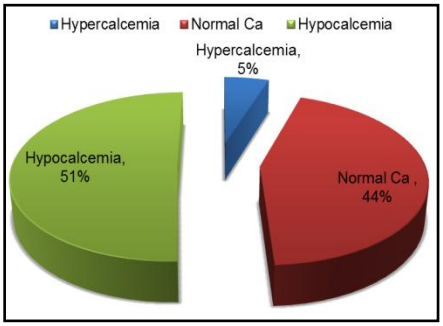

Figure 3: Alterations of Calcium level in CKD patients.

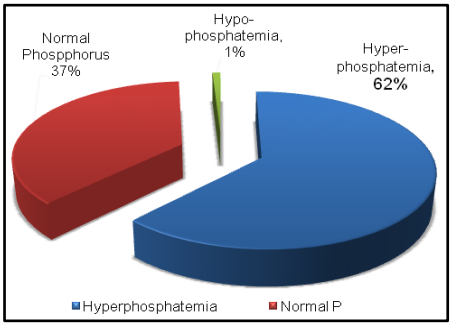

Figure 4: Alterations of Phosphorus level in CKD patients.

Table 2: Association of phosphorus levels with demographic history of the study patients

Patient characteristics (Demographic history)		Phosphorus level			$\chi 2$ value	P-value
		Low (<2.5mg%)	Normal (2.5 – 4.5mg %)	High (>4.5mg%)		
Age	20 – 40	1 (1.4%)	28 (38.4%)	44 (60.3%)	2.752	0.839^{NS}
	41 – 60	2 (1.3%)	62(39.0%)	95 (59.7%)		
	61 – 80	0 (0.0%)	29 (33.3%)	58 (66.7%)		
	>80	0 (0.0%)	3 (27.3%)	8 (72.7%)		
Sex	Female	2(1.7%)	46 (40.0%)	67 (58.3%)	2.200	0.333^{NS}
	Male	1 (0.5%)	76 (35.3%)	138 (64.2%)		
Religion	Hindu	0 (0.0%)	49 (40.2%)	73 (59.8%)	4.276	0.370^{NS}
	Muslim	0 (0.0%)	1(100.0%)	0 (.0%)		
	Sikh	3 (1.4%)	72 (34.8%)	132 (63.8%)		
Environmental status	Rural	2 (0.9%)	81 (37.0%)	136 (62.1%)	.000	1.000^{NS}
	Urban	1 (0.9%)	41 (36.9%)	69 (62.2%)		
Educational status	Illiterate	2 (1.1%)	68 (37.8%)	110 (61.1%)	.313	0.855^{NS}
	Literate	1 (0.7%)	54 (36.0%)	95 (63.3%)		
Nutritional Status	Poor	0(.0%)	3(42.9%)	4(57.1%)	.161	0.923^{NS}
	Well	3(0.9%)	119(36.8%)	201(62.2%)		
Dietary History	Non-vegetarian	2 (1.4%)	55 (39.9%)	81 (58.7%)	1.743	0.418^{NS}
	Vegetarian	1 (.5%)	67 (34.9%)	124 (64.6%)		

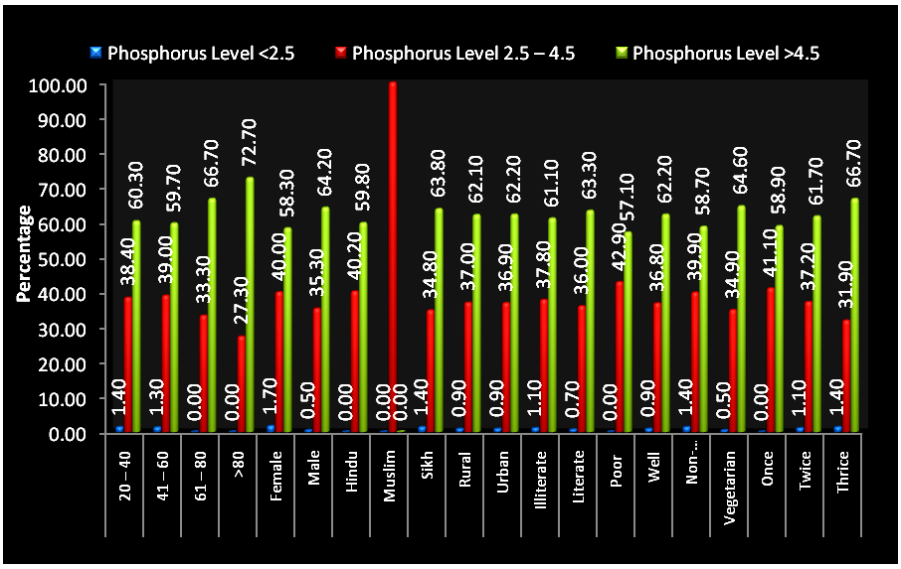

Figure 5: Association of Phosphorous level with other variables

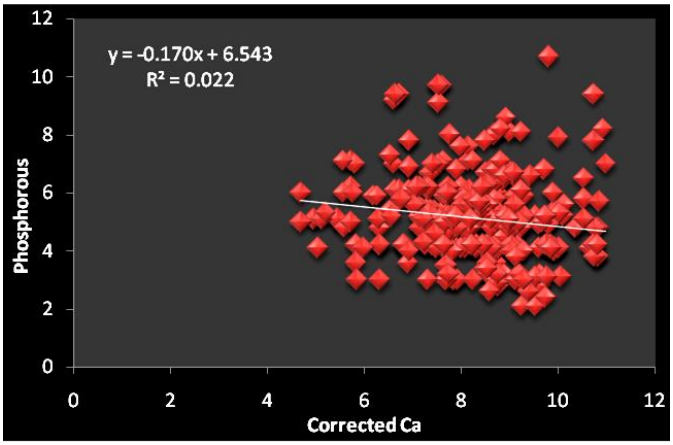

Figure 6: Relationship between corrected Calcium with Phosphorus among cases