Original Research Article

Effect of dietary factors and nutritional status on alterations in serum calcium and phosphorus levels in CKD Patients on treatment in a teaching hospital in Punjab

Abstract

Background:Calcium and Phosphorus, are fundamentally important in a wide array of biological functions.The control of phosphorus and calcium metabolism is one of the objectives in an adequate 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 & phosphorus homeostasis in CKD patients. Therefore, we conduct this study to describe effect of dietary factors and nutritional status on alterations in serum calcium and phosphorus levels in CKD Patients on treatment in our center.

Study design:Patients were selected based upon the inclusion and exclusion criteria.Approach to a Patient began by taking informed consent.

- The detailed Medical history as well as baseline demographic data, was recorded.
- Detailed dietary history of the patients was taken by recall of past three days method.
- Detailed history regarding the intake of phosphate binders both calcium based and Non-calcium based and Vitamin–D analogues was taken.

Also biochemical analysis of serum albumin corrected_calcium, phosphorus, serum albumin, and haemoglobin of all cases were done using fully automated equipments. All statistical analyses were performed using SPSS statistical software, version 17. 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:The present study was a hospital-based cross-sectional study. The study population of 330 patients comprised of adults of both sexes (215 males and 115 females). 66.4 % patients belonged to rural area in our study. Majority (58.2 %) of the study patients were taking vegetarian diet with a mean Value of BMI (Mean ± SD = 23.75 ± 4.70 kg/m^2). Our results indicated that most of the CKD patients were outside the recommended range of KDIGO guidelines for biochemical parameters.Hypocalcemia was detected in 50.6%, Hyperphosphatemia in 62.1% of CKD 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). It was observed that the percentage of vegetarians who were hyperphosphatemic was more than nonvegetarians and also found that the well nourished patients were more likely to be hyperphosphatemic as compare to poorly nourished patients, but statistically the values were found to be nonsignificant(Statistically p-value was not less than 0.05.

Conclusion:Only a small proportion of patients adhered to the targets advised in the KDIGO guidelines for control of bone metabolism and disease in CKD patients that mean majority of the patients were out of the target ranges.We demonstrated that in Punjab region, consumption of milk or milk products and alcoholic beverages is high and contributes to hyperphosphatemia so a dietary evaluation of phosphorus should be done

by an expert renal dietician and strict restriction of phosphorus rich dietary products must be done specially in patients on dialysis. Along with it the use of phosphate binding agents, is a must. The aim of the treatment must be control of phosphate retention, maintaining serum calcium concentration within the normal range (standard), with avoidance of hypercalcaemic episodes.

KEY WORDS: CALCIUM, CKD, KDIGO, PHOSPHORUS.

LEVEL OF EVIDENCE: IV

INTRODUCTION: **C**hronic kidney disease (CKD) is a worldwide public health problem that affects 5% to 10% of the world population[1], with increasing prevalence and adverse outcomes, including progressive loss of kidney functions, cardiovascular disease, and premature death [2, 3 & 4].

Chronic kidney disorders have a progressive course in most cases spanning months to years, and finally result in end-stage renal disease (ESRD) [5] & [3]. End-stage renal disease (ESRD) is reached as soon as the renal function drops below 10 to 15 percent of the normal function [6].

It is well known that calcium and phosphorus are minerals that are of great importance for the composition of bones and the regulation of several processes in the body[7]. The kidney plays a leading role in maintaining 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), various abnormalities of mineral and bone metabolism develop (like hyperphosphataemia, hypocalcaemia, and hyperparathyroidism are all commonly observed in patients with CKD) which can result in significant consequences[8].Disturbances in mineral metabolism in CKD which result in multisystem disorder have now been given a different 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].

The Kidney Disease Improving Global Outcomes (KDIGO 2009)[9] guidelines for bone metabolism and disease in CKD (USA) recommend that, in stage 5 CKD, 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 phosphorus and calcium metabolism is one of the objectives in an adequate 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 & phosphorus homeostasis in CKD patients.

Therefore, we conduct this study to describe effect of dietary factors and nutritional status on alterations in serum calcium and phosphorus levels in CKD Patients on treatment in our center.

MATERIALS AND METHODS:

SOURCE OF DATA:

*Study Design:*This study was a hospital- based cross-sectional observational study.

*Research Setting:*The study was conducted under the Department of Physiology based on data collected on CKD patients coming to dialysis unit of department of Medicine, Gian Sagar Medical Hospital, Ramnagar, Patiala.

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

Sampling method – Non Random sampling method

Sample (enrolled patients during a period of four years) –Three hundred thirty (330) CKD patients on maintenance hemodialysis.

Ethical approval and informed consent: - This study was approved by ethical committee of Gian Sagar medical College and Hospital. An informed consent was taken from all the subjects before the initiation the study. All the subjects were duly informed about the purpose of asking questions as per Performa attached with consent form, details of blood sample collection, risk factors and precautions.

Sampling Criteria:*Inclusion criteria:* All the CKD Patients (>18 years) on maintenance hemodialysis coming to Dialysis Unit of Department of Medicine of Gian Sagar Medical College & Hospital, Ramnagar (Patiala) during study period (December,2012-December,2016) were enrolled in the study. Each patient was considered only once for the study. Both males and females were included in this study.

METHOD OF COLLECTION OF DATA: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 as per Performa attached.Blood sample was collected for laboratory investigations (like Serum calcium, Serum phosphorous, Serum albumin, and Hemoglobin). Blood sample were collected with aseptic precautions after obtaining informed consent from the patients.

Five milliliter of blood was taken from the antecubital vein of the patients under full aseptic conditions. Upon clotting, serum was separated out for the estimation of biochemical parameters. All the above parameters were done on fully automated equipment,s standardized in Gian Sagar Hospital..

- Dietary history of the patients was taken.
- Nutritional status of the patients was assessed by measuring BMI (Body Mass Index)[12].
- Detailed history regarding the intake of phosphate binders both calcium based and Non-calcium based 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 Collected in proformas and fed into custom built database. Observations and results were compiled at the end of the study.

The control of CKD-MBD was assessed in the backdrop of the KDIGO guidelines.

All the Demographic and laboratory parameters were compared in all groups by using appropriate statistical method.

Statistical Analysis:The data were analyzed 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 our study 66.4 % patients were predominantly belonging 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& 2).

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

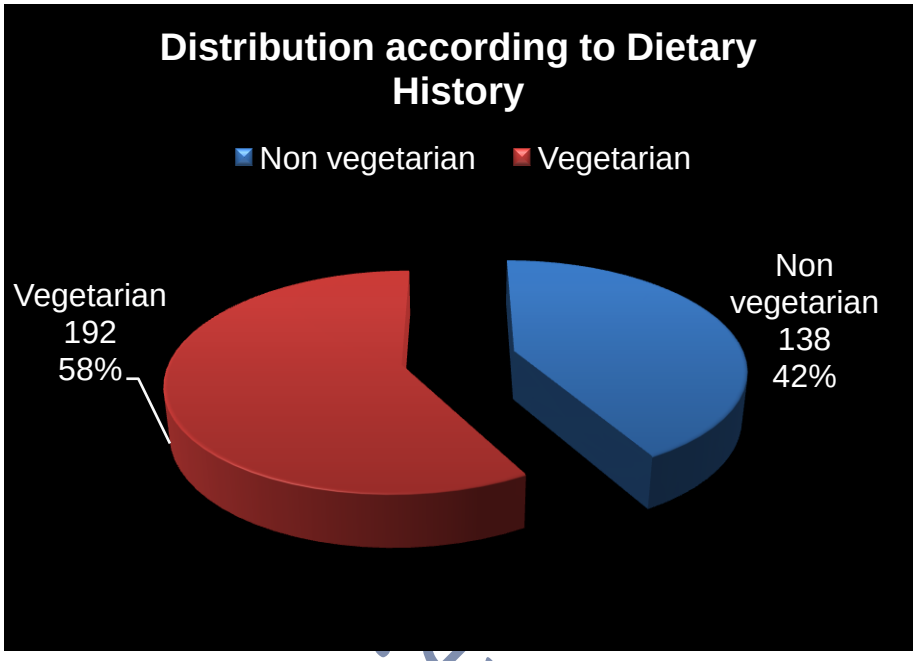


Figure 2 . Distribution according to nutritional Status in CKD patients.

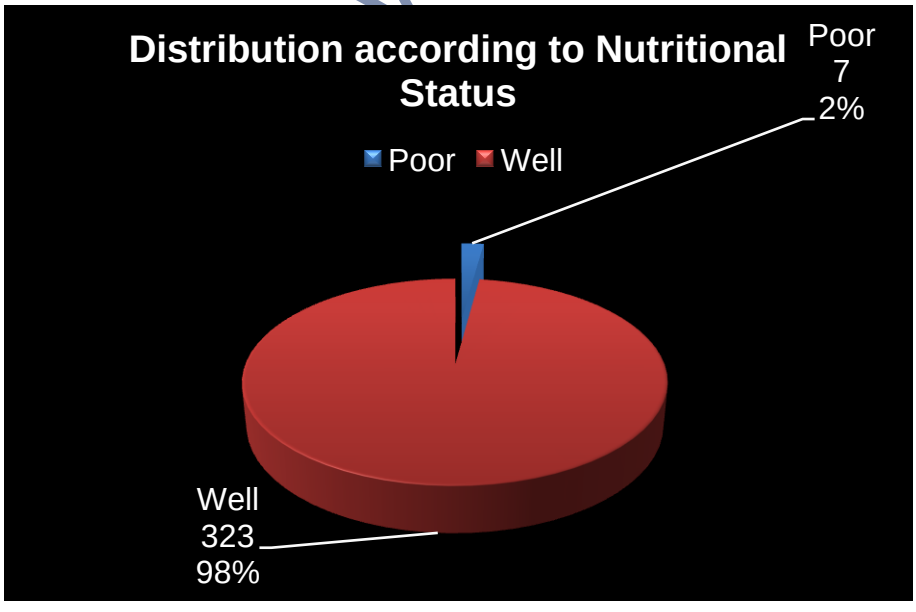


Table 1. Distribution of cases by levels of Laboratory Parameters in CKD patients

Laboratory characteristics of	Groups	Number of	%age

Patients		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**

In the present study it was observed that 44% patients had Hypocalcemia as compare to Hypercalcemia (17.5%)(Table 1and Figure 3.)

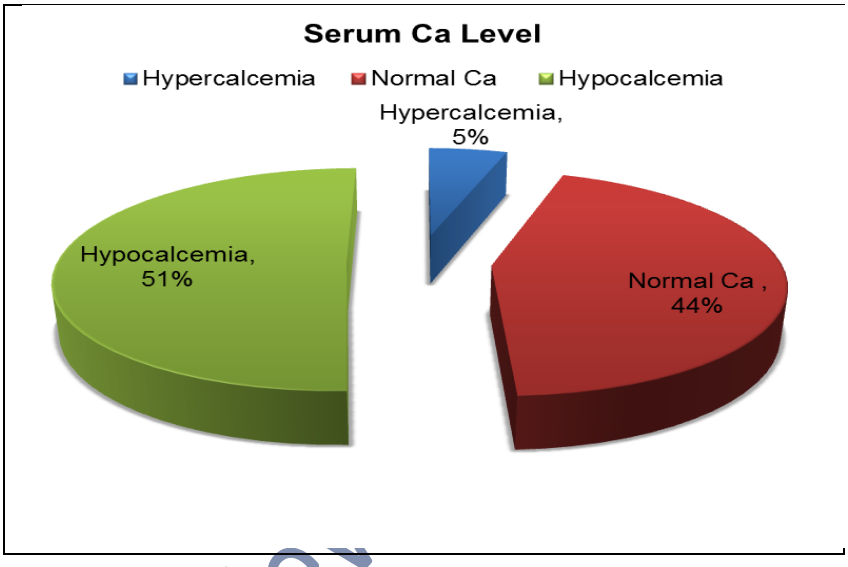


Figure 3. Alterations of Calcium level in CKD patients.

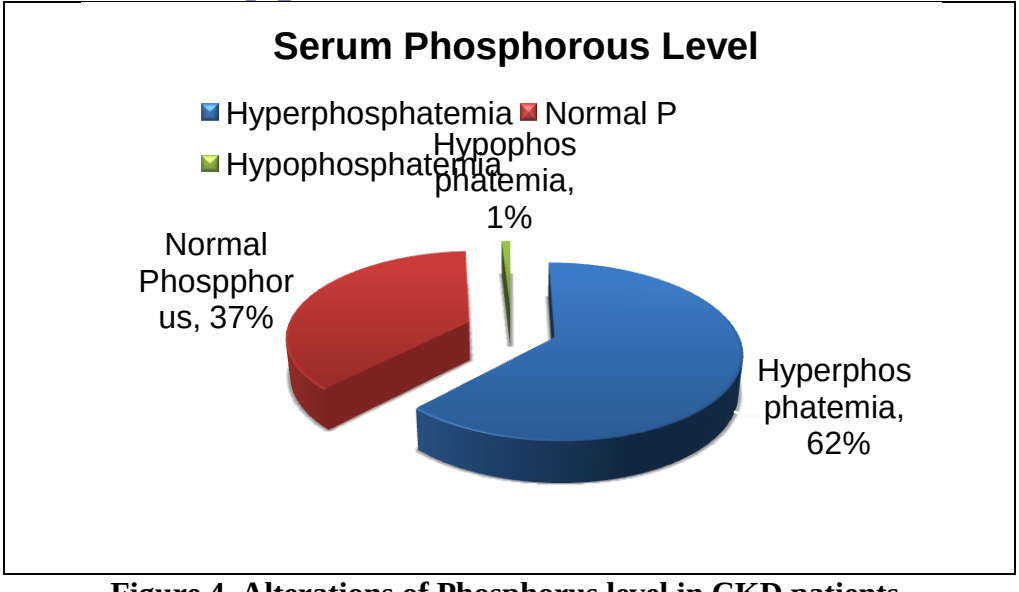


Figure 4. Alterations of Phosphorus level in CKD patients.

In the present study it was observed that majority (62%) of patients had Hyperphosphatemia as compared to Hypophosphatemia (1%, only).

Case Processing Summary:- Chi-square test was used to see association between three different categories of the Phosphorus levels (hypo, Normal and Hyperphosphatemia) and

other demographic variables like Dietary Factors and Nutritional status of the study patients along with Correlation analysis among laboratory findings.

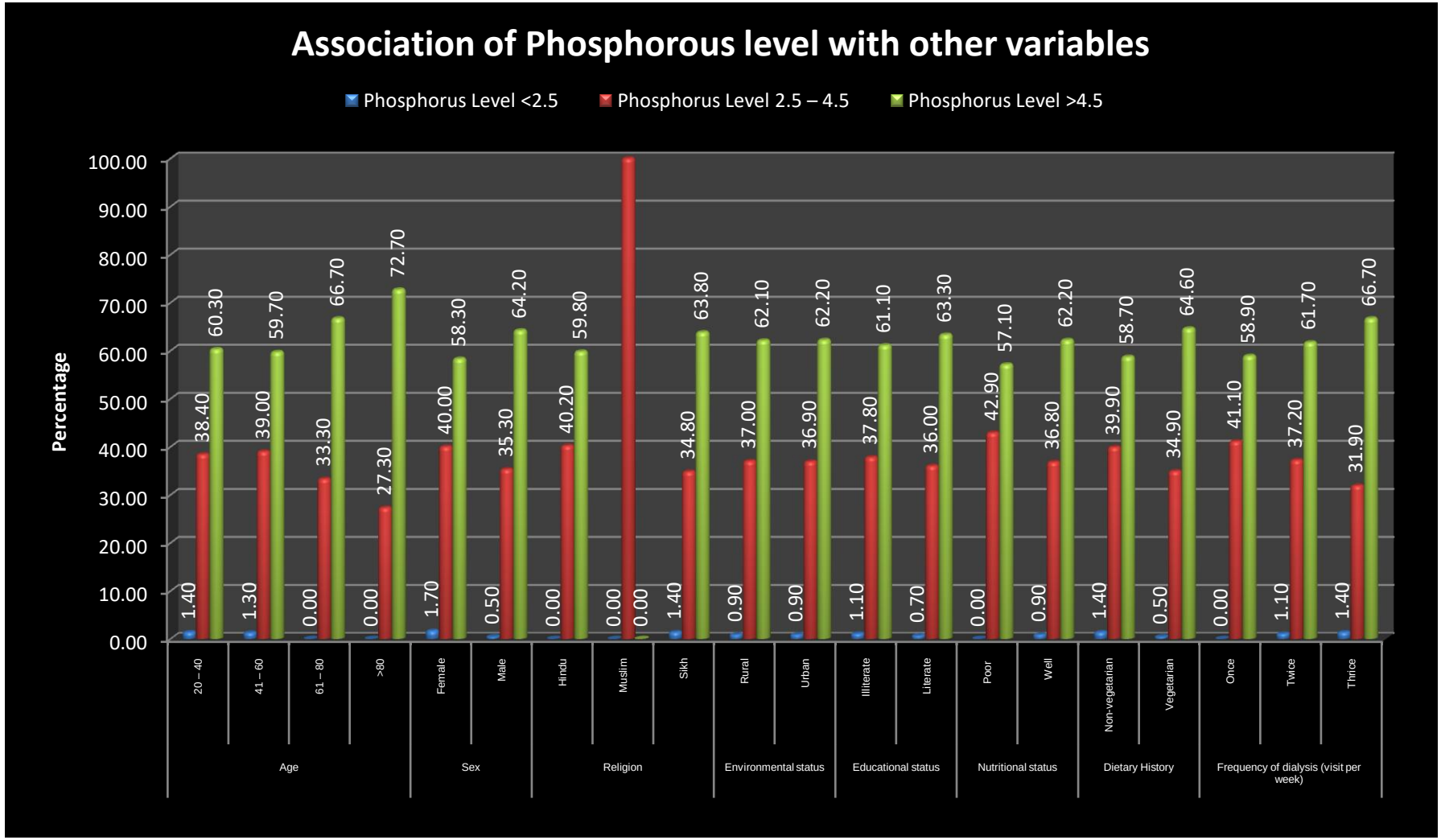
Pearson's Chi square test (Yates's correction for continuity) was used to examine the significance of association (contingency).

STATISTICAL RESULTS: Case Processing Summary : Tables and Graphs

It was observed that the percentage of vegetarians who were hyperphosphatemic was more than nonvegetarians and also found that the well nourished patients were more likely to be hyperphosphatemic as compare to poorly nourished patients, but statistically the values were found to be nonsignificant(Statistically p-value was not less than 0.05, table no 2)

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%)	29 (33.3%)	58 (66.7%)		
	>80	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 (.5%)	76 (35.3%)	138 (64.2%)		
Religion	**Hindu**	0 (.0%)	49 (40.2%)	73 (59.8%)	4.276	0.370^{NS}
	Muslim	0 (.0%)	1(100.0%)	0 (.0%)		
	Sikh	3 (1.4%)	72 (34.8%)	132 (63.8%)		
Environmental status	**Rural**	2 (.9%)	81 (37.0%)	136 (62.1%)	.000	1.000^{NS}
	Urban	1 (.9%)	41 (36.9%)	69 (62.2%)		
Educational status	**Illiterate**	2 (1.1%)	68 (37.8%)	110 (61.1%)	.313	.855^{NS}
	Literate	1 (.7%)	54 (36.0%)	95 (63.3%)		
Nutritional Status	**Poor**	0(.0%)	3(42.9%)	4(57.1%)	.161	.923^{NS}
	Well	3(.9%)	119(36.8 %)	201(62.2 %)		
Dietary History	**Non-vegetarian**	2 (1.4%)	55 (39.9%)	81 (58.7%)	1.743	.418^{NS}
	Vegetarian	1 (.5%)	67 (34.9%)	124 (64.6%)		


Association of Phosphorous level with other variables
Phosphorus Level <2.5
Phosphorus Level 2.5 – 4.5
Phosphorus Level >4.5
Percentage
100.00
90.00
80.00
70.00
60.00
50.00
40.00
30.00
20.00
10.00
0.00
1.40
38.40
60.30
1.30
39.00
59.70
0.00
33.30
66.70
0.00
27.30
72.70
1.70
40.00
58.30
0.50
35.30
64.20
0.00
40.20
59.80
0.00
100.00
0.00
1.40
34.80
63.80
0.90
37.00
62.10
0.90
36.90
62.20
1.10
37.80
61.10
0.70
36.00
63.30
0.00
42.90
57.10
0.90
36.80
62.20
1.40
39.90
58.70
0.50
34.90
64.60
0.00
41.10
58.90
1.10
37.20
61.70
1.40
31.90
66.70
20 – 40
41 – 60
61 – 80
>80
Age
Female
Male
Sex
Hindu
Muslim
Sikh
Religion
Rural
Urban
Environmental status
Illiterate
Literate
Educational status
Poor
Well
Nutritional status
Non-vegetarian
Vegetarian
Dietary History
Once
Twice
Thrice
Frequency of dialysis (visit per week)

The above figure 5. clearly shows hyperphosphatemia as a constant findings in all baseline demographic parametrs 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.

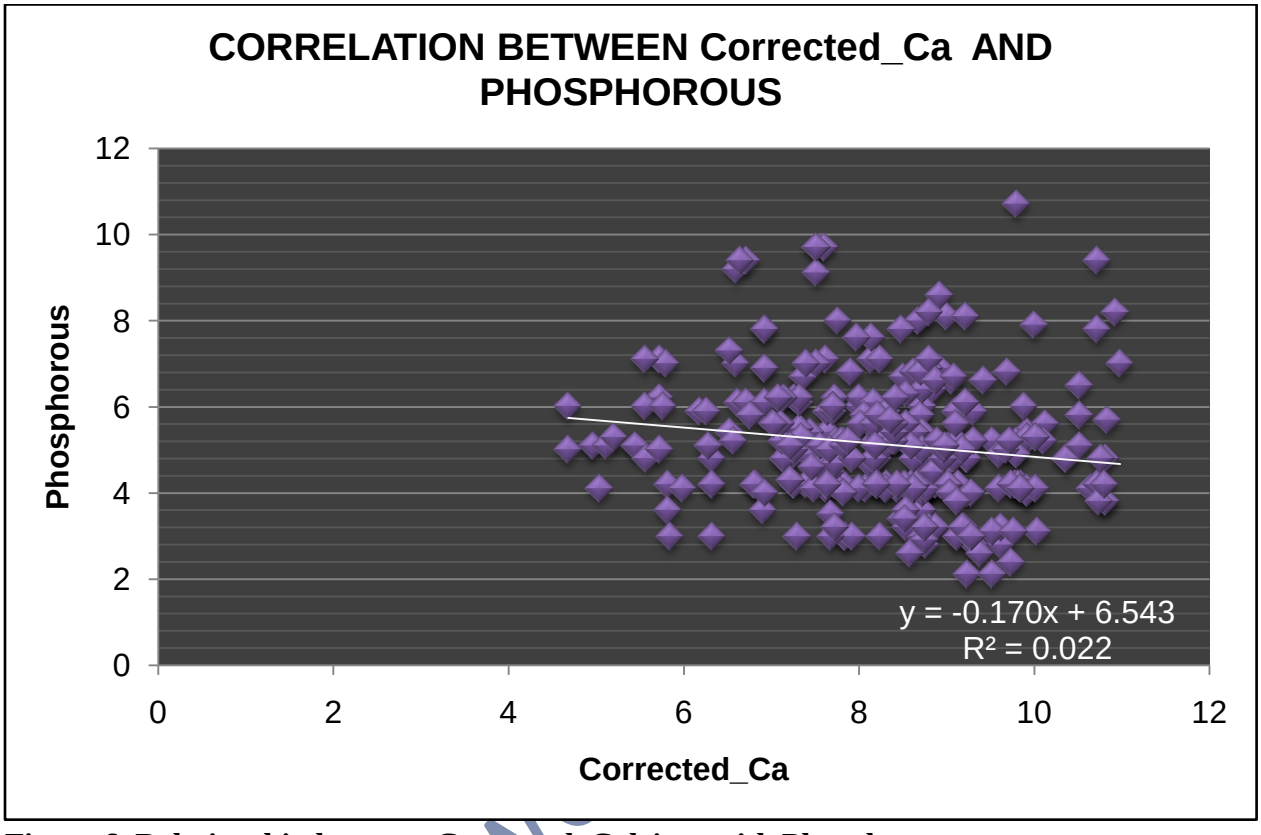


Figure 6. Relationship between Corrected_Calcium with Phosphorus among cases

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).

RESULTS & 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 .This particular study was conducted to find out effect of dietary factors and nutritional status on alterations in serum calcium and phosphorus levels in CKD Patients on treatment in Gian Sagar Medical College and hospital in Punjab.

The present study was a hospital-based cross-sectional observational study. The study population of 330 patients comprised adults, mainly illiterate (54.5%) predominantly belonging to the rural (66.4%)-strata and Sikh community (62.7%) 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 a Western and an Indian study[15-17].

In the present study it was observed that alterations in biochemical profile were common in CKD patients. Only a small proportion of patients adhered to the targets. Proportion of the CKD patients who were out of the target range was as follows:
55.8% for corrected serum calcium (target range 8.5-10.5 mg/dl).
63.0% for phosphorus (target range 2.5-4.5 mg/dl).

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 easly 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 this 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).

In CKD patients at every stage of the disease plasma or serum calcium, phosphorus concentrations should therefore be measured on a regular basis. Measurements should be made more frequently when a patient receives concomitant therapy for abnormalities in plasma calcium and phosphorus[22]. To obtain low phosphorus levels an optimal management regimen is necessary, which can only be achieved by intensive 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 medicataion 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 which preven damage to the bones and thus, prevents bone disease. Usually, overactive parathyroid glands are controllable with a change in diet, dialysis treatment, or medication.

A renal dietitian can help develop a dietary plan to control phosphorus levels in the blood. 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. We would like to emphasize the importance of educating and stimulating dialysis patients

in order to achieve optimal adherence to the treatment regimens and dietary recommendations.

A renal dietitian can help develop a dietary plan to control phosphorus levels in the blood. Along with it the use of phosphate binding agents, is a must. The aim of the treatment must be control of phosphate retention, maintaining serum calcium concentration within the normal range (standard), with avoidance of hypercalcaemic.

Conflict of interest *:*This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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