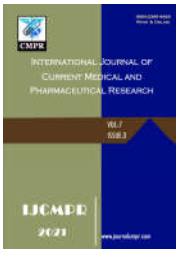
INTERNATIONAL JOURNAL OF CURRENT MEDICAL AND PHARMACEUTICAL RESEARCH
ISSN: 2395-6429, Impact Factor: 4.656
Available Online at www.journalcmpr.com
Volume 7; Issue 03(A); March 2021; Page No.5622-5626
DOI: http://dx.doi.org/10.24327/23956429.ijcmpr202103976



Research Article

DUAL ROLE OF SERUM CALCIUM, PHOSPHOROUS AND MAGNESIUM, AS A PREDICTOR OF RISK FACTORS AND EARLY DETECTION OF POOR OUTCOME IN LATE STAGES OF CHRONIC KIDNEY DISEASE. A CASE CONTROL STUDY

Deepthi M., Mangala Sirsikar and Shailaja A

Department of Biochemistry, Vydehi Institute of Medical Sciences and RC #82, Nallurahalli, Whitefield, Bangalore - 560 066

ARTICLE INFO

Article History:
Received 4th December, 2020
Received in revised form 25th January, 2021
Accepted 18th February, 2021
Published online 28th March, 2021

Key words:
Chronic Kidney Disease (CKD),Calcium, Phosphorus and Magnesium Balance, Hypocalcaemia, Hyperphosphatemia, Hypomagnesaemia

ABSTRACT

Background: Calcium, phosphate Magnesium is minerals that are important for health, they help to build strong bones and teeth, and also play a role in cell and nerve function. Patients with chronic kidney disease (CKD) have marked disruption in bone and mineral metabolism resulting in a complex disorder that has been termed CKD-mineral bone disorder (CKD-MBD). Chronic Kidney Disease (CKD) nowadays becomes an emerging condition with increasing morbidity and mortality. However, our understanding of calcium phosphorus and magnesium balance throughout the stages of chronic kidney disease is limited. It is associated with complex disturbances in calcium, phosphorous and magnesium levels especially in stage 4 and 5 of CKD. Both negative and positive balance have important implications in patients with chronic kidney disease, where negative balance may increase risk of osteoporosis and fracture and positive balance may increase risk of vascular calcification and cardiovascular events. Thus study is undertaken to find out role of these marker in serum as an early diagnostic and prognostic marker of CKD but also assess the severity of stage 4 and 5 of CKD in correlation with eGFR.
Aim and Objective: The main aim of this study is to compare the levels of serum, calcium, phosphorous, and magnesium levels in stages 4 and 5 of chronic kidney disease patients and compared with healthy individuals. To also to find out their association with eGFR, which is important predictor disease progression of CKD.
Materials and Method: Duration based case control study which includes50 CKD patients in stage 4 and 5, attending Nephrology out- patient department as cases and 50 healthy individuals between the age group 21 to 78 were included as control in study. Study was conducted at vydehi institute of medical sciences and RC. Serum levels of Calcium, Phosphorous, and Magnesium were measured; eGFR was calculated by CKD –MDRD Formula. All measured variables were correlated with e GFR and compared between cases and controls.
Statistical Analysis*:* Statistical analysis is done by SPSS Software.
Results: The results are presented as a mean ± SD and 'p' value of less than 0.05 is considered as significant. eGFR (ml/min) cases mean and SD 14.12±,10.72 102.97±27.4 6 in control, Serum Creatinine (mg/dl) 7.04±5.34 in cases 0.84±0.20 in control, Serum Calcium (Ca) (mg/dl) 8.11±1.09in cases and in control 9.31±0.42,Serum Phosphrous (P) (mg/dl) 4.86±1.83 in CKD 3.27±0.54 .Ca x P Ionic Product 38.99±13.77 in cases 30.46±5.03.Serum Magnesium (Mg) (mg/dl) 2.00±0.51 in CKD 1.91±0.30
Conclusion: Result of our study showed Hypocalcemia, Hyperphosphatemia and Hypomagnesemia. Hypocalcemia and Hyperphosphatemia due to failing kidney results in secondary hyper parathyroidism in advanced Chronic Kidney Disease. Hyperphosphatemia is a well-known risk factor for mortality in ESRD patients, which aggravates with low Mg. A low Mg in CKD is also associated with several complications such as hypertension, and vascular calcification. Hypomagnesemia is associated with an increased risk for both cardiovascular disease (CVD) and non-CVD mortality. Thus these parameters are used as early diagnostic and prognostic markers in CKD. Also predictors of poor out come and indicator of treatment with dialysis.

Copyright © 2021 ***Deepthi M et al****. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.*

INTRODUCTION

Chronic kidney disease (CKD) constitutes a public health problem that is estimated to affect more than 10% of the global population, and the prevalence of which has increased in recent years. In India the projected number of deaths due to chronic diseases will rise from 3.78 million in 1990 (40.4% of all deaths) to an expected 7.63 million in 2020 (66.7% of all deaths[1,2]

Patients with chronic kidney disease (CKD) have marked disruption in bone and mineral metabolism resulting in a complex disorder that has been termed CKD-mineral bone disorder (CKD-MBD). Perturbations begin in the earliest stages of the CKD and worsen with progressive kidney disease. characterized by abnormal calcium, phosphorous, PTH, and Vitamin D metabolism, which, in addition to affecting the skeletal system, is related to the appearance of cardiovascular and soft tissue calcifications that in turn are associated with cardiovascular pathologies in patients with CKD.[3-6]

Large epidemiologic studies have shown a strong relationship between elevated levels of calcium (Ca), phosphorus (P), Ca-P

Corresponding author:* **Deepthi M
Department of Biochemistry, Vydehi Institute of Medical Sciences and RC Bangalore-66

product (Ca x P), and parathyroid hormone (PTH) with cardiovascular morbidity and mortality [7-8] The biochemical abnormalities are common in CKD and are the primary indicators by which the diagnosis and management of CKD-MBD is made.

Chronic Kidney Disease (CKD) is defined as the presence of kidney damage or GFR < 60 ml/min/1.73 m for at least 3 months, with pathological abnormalities or damage, including abnormalities in blood or urine tests or imaging studies[9.]

In advanced CKD (stage 4 and 5) circulating levels of parathyroid hormone (PTH) are progressively increased as kidney function declines, as a result of phosphate retention , hypocalcemia, decreased production of 1,25-dihydroxycholecalciferol[10]

Hyperphosphatemia, hypocalcaemia and decrease 1, 25-dihydroxycholecalciferol not only reflects disturbed mineral metabolism but also contributes major complications of chronic kidney disease (CKD) thus playing dual role. Further all these factors associated not only with an increased risk of cardiovascular mortality but also with a faster progression of CKD [11] act as double edge sword. It is also found that patients with high phosphate had a higher risk of ESKD when they had a low serum Mg level. Notably, an in vitro study has shown that Mg strongly inhibits phosphate-induced apoptosis of vascular smooth muscle cells, a key process of vascular calcification [12] Mg deficiency is associated with an increased risk of cardiovascular events and vascular calcification, both in individuals with and without CKD.

MATERIALS AND METHODS

This was a case controlled duration based study conducted for two years at vydehi institute of medical sciences and research centre Bangalore. 50 patients of Advanced Chronic Kidney Disease (stage 4 and 5) between the age group of 25 to 78 years and age/sex matched 50 healthy individuals as controls were enrolled in study. Informed consent was obtained from patients and 5 ml of blood samples were collected within 24 hours of admission in hospital. Serum levels of Magnesium) measured by Calmagite method, Serum Calcium (8.5-10.2mg/dl by ISE electrode method, Serum Phosphorous (2.5-4.5mg/dl) levels by Ammonium Molybdate method. Magnesium (1.8-2.9 mg/dl) by calmagite chromogen method, serum creatinine (0.60-1.24 mg/dl (M), 0.40-1.00mg/dl (F)) by modified jaffes method CKD was defined and classified as per kidney disease outcomes quality initiative (KDOQI) criteria. [13] The estimated glomerular filtration rates were calculated from serum creatinine level using the Modification of Diet in Renal Disease (MDRD) equations [14]. Accordingly eGFR was categorized as ≥90, 60 to 89, 45 to 59, 30 to 44, and 15 to 29 ml/min/1.73m2.GFR <60 ml/min/1.73 m2 for >3 months to indicate CKD and 15 to 29 ml/min/1.73m2. is considered as stage v with kidney faliure. The diagnosis of underlying basic kidney disease was made on clinical evidence. The definitions for hypocalcemia (cCa1<8.5mg/dl), hyperphosphatemia (phosphorus >4.5 mg/dl).[15]

Inclusion criteria

1. Patients in stages 4 & 5 of CKD -eGFR were 15 to 29 mL/min/ 1.73 m2&< 15 mL/min/ 1.73 m2 of both sexes, age group 25 to 78 years.
2. No treatment with Ca supplements, phosphate binders, or vitamin D derivates.

Exclusion criteria

1. current smoking habit (defined as patients smoking at least one cigarette per day during the previous 12 Months)
2. history of any clinical manifestations of cardiovascular disease (coronary artery disease, cerebral vascular disease, and/or peripheral vascular disease)
3. patients on glucocorticoid, bisphosphonate, nonsteroidal antiinflammatory drugs, phenytoin, or warfarin,
4. patients on immunotherapy or immunosuppressive treatment.
5. those having liver disease or history of bone fracture in preceding 6 months
6. Chronic Kidney Disease patients those who are on peritoneal dialysis or Hemodialysis. excluded

RESULTS

A *P* value of greater than 0.05 is considered insignificant; a *P* value of 0.05 or less is considered significant; and a P value of less than 0.01 is considered highly significant. In Chronic Kidney Disease patients and controls, Mean and Standard Deviations were calculated for all quantitative variables. Table 1 shows the Mean & SD Creatinine, calcium, phosphorus, magnesium of control and cases with the statistical significance (p=0.001)

Gender	Cases		Controls	
	No	%	No	%
Female	19	38.0	16	32.0
Male	31	62.0	34	68.0
Total	50	100.0	50	100.0

Samples are gender matched with P=0.529 in our study found that CKD more common in male (62%) compared to female (38%)

Table 2 CKD Stage in two groups studied

CKD Stage	No. of patients	%
III	4	8.0
IV	14	28.0
V	32	64.0
Total	50	100.0

In our study found that CKD patients in stage IV found to be 28%, stage V 64%

Table 3 Comparison of study variables in two groups studied

	Cases	Controls	P value
eGFR (ml/min)	14.12±10.72	102.97±27.4	<0.001**
Serum Urea (mg/dl)	119.88±71.2	23.67±5.76	<0.001**
Serum Creatinine (mg/dl)	7.04±5.34	0.84±0.20	<0.001**
Serum Calcium (Ca) (mg/dl)	8.11±1.09	9.31±0.42	<0.001**
Serum Phosphrous (P) (mg/dl)	4.86±1.83	3.27±0.54	<0.001**
Ca x P Ionic Product	38.99±13.77	30.46±5.03	<0.001**
Serum Magnesium (Mg) (mg/dl)	1.60 ±0.51	1.91±0.30	0.267

Pearson Correlation Coefficient between eGFR and serum calcium showed: the value of R is -0.2352 we also found negative positive eGFR& serum phosphorus is -0.0801. Negative correlation.

parameters	R Valve	eGFR	P valve
Serum Calcium	0.3567	Positive Correlation	p < .01
Serum Phosphorus	-0.2352	Negative Correlation	p < .01
Serum Magnesium	0.167	Positive Correlation	p < .01

DISCUSSION

Chronic Kidney Disease (CKD) encompasses a spectrum of different pathophysiological process associated with abnormal

kidney function and progressive decline in Glomerular Filtration Rate. CKD is classified into 0 - 5 stages based on the GFR Stage 1& 2 are not usually associated with any symptoms arising from the decrease in GFR. If GFR declines further to level of stage 3, 4 & 5 complications are more common, almost all the systems are affected especially anaemia, malnutrition, Bone Mineral Disease

ESRD is associated with aberrations in the metabolism of minerals, such as calcium, phosphates, magnesium, therefore, this study was conducted to evaluate the relationship between eGFR and the aforementioned minerals in ESRD patients. The maximum number (45%) of patients was from the age group of 51-60 years. Mean age of patients was 52.28 ± 16.25 years, which suggests that incidence of CKD increases with advanced age. Out of 50 patients included in this study, there were 31 males and 19 females giving a male to female ratio of 1.6:1. The mean age of our study population was similar to Mani MK *et al*[15]. We observed that males outnumbered females in both the groups. Agarwal *et al*.[16] in community based study showed a male prevalence of 48% among patients with serum creatinine more than 1.8 mg/dL, while other hospital-based studies found males constituting 60-78% of CKD population. Diniz *et al.* in 2012 observed in their study of 125 patients that the mean age was 57.4 ± 16.2 years with male to female ratio of 1.2:1[17]. The result is very much comparable with our study.

We also found that Mean serum levels of phosphate were above the normal range, whereas those of calcium, magnesium were below the normal range in both groups of patients, there was statistically significant difference of these values between the two groups.

The mean value of serum calcium and serum phosphorous was 8.11±1.09 and 4.86±1.83 mg/dL, respectively. Agarwal showed that the mean corrected serum calcium in stage 4 and 5 CKD was 8.8 and 8.1 mg/dL, and the values for serum phosphate, was 4.6 and 6.0 mg/dL, Our study corroborated with the study of Agarwal[18]. The proposed mechanism is that, Due to decreased GFR and altered endocrine function of kidneys, the parathyroid-vitamin D-renal axis gets deranged which results in phosphate retention, hypocalcemia, decreased active vitamin D, and secondary hyperparathyroidism in majority of patients.[19] Furthermore, it was observed that serum phosphorus value has linear negative correlation with serum calcium ($P \leq 0.001; r = -0.805$), whereas linear positive correlation with serum eGFR ($P = 0.003, r = 0.378$). O'Seaghdha *et al*.[20] demonstrated that the relative risk of developing ESRD was much higher in CKD patients with serum phosphorus concentrations >4 mg/dL in NHANES participants. Our result is consistant and comparable with their study.

One of the most expected mechanism is that Hyperphosphatemia is defined as an abnormally high serum phosphate concentration > 4.8 mg/dl.. In CKD, the decline in the glomerular filtration rate (GFR) is compensated for by an early elevation of the FGF-23 concentration to induce decreased proximal tubule phosphate re-absorption and attempt to maintain normal phosphate concentrations. FGF-23 also reduces the concentration of 1α, $25(OH)_2D_3$, lowering the effects of NaPi co-transporters in the intestine and consequently reducing phosphate absorption. These compensatory mechanisms attempt to normalise serum phosphate and calcium concentrations in CKD patients. However, as GFR continues to decline and falls below 25 ml/min, the renal phosphate excretion reaches its maximum and excess dietary phosphate accumulates leading to persistent hyperphosphatemia[3]. (KDIGO) guidelines for the management of hyperphosphatemia in also suggest that in chronic kidney disease patients not receiving dialysis, serum phosphate level require maintenance in the normal range (i.e., under 4.5 mg/dL [1.45 mmol/L]). Hence hyperphosphatemia may be a useful marker to determine timing of hemodialysis initiation in patients with advanced CKD.[13]

In this study, Mg levels in patients were significantly lower than the control group. Serum magnesium mean and SD of stage V in our study 1.6±0.51 compared to 2.16±0.51in control. Low Magnesium levels well correlated with eGFR which is statistically significant. van Laecke *et al*., 21 in there study found that that hypomagnesaemia (<1.8 mg/dL)was a significant predictor of a faster decreaseing lomerularfiltration rate(GFR <60 ml/min/1.73 m2) and higher risk of mortality in 1650 patients with chronic kidney disease. Our result is comparable with their study.

The kidney is crucial in the maintenance of normal serum Mg concentrations. The ability of excretion deteriorates when renal function declines[22]. In advanced CKD stage 4–5, compensatory mechanisms become inadequate and the fraction of filtered Mg excreted increases as a result of the impaired tubular reabsorption. This becomes even more marked when the glomerular filtration rate falls below 10 mL/min. So, the compensatory rise in fractional Mg excretion is insufficient to prevent an increase in serum Mg concentration. Sakaguchi *et al*. demonstrated a significant interaction between serum Mg and P levels on CKD progression[23]

Mg possesses an anti-atherosclerotic effect, which is mediated partly via its anti-inflammatory and antioxidant properties; conversely, by inhibiting endothelial proliferation, upregulating plasminogen activator inhibitor-1 and vascular cell adhesion molecule-1, Mg deficiency promotes endothelial dysfunction.[24]

MBDs are well described in patients with CKD. However, only few studies addressed these disorders in Indian patients. LaClair, *et al*.[25] in there study found hypocalcemia (Ca<8.5 mg/dL) in 8% and 28%, and hyperphosphatemia (PO4>4.5 mg/dL) in 20% and 50% of patients of CKD stages 4 and 5, respectively. Thus, the western data showed a lower prevalence of hypocalcemia and hyperphosphatemia (except hyperphosphatemia in stage 5) in comparison to the data of Agarwal, *et al*. from India. Moreover, we found much higher prevalence of hypocalcemia and hyperphosphatemia even in comparison to the findings by Agarwal. Not many studies done in mineral derangement in CKD in India. Thus our study has contributed its uniqueness in understanding hereditary information about CKD so that many more researchers can actively take up innovative advance projects.

The present study has some limitations: serum PTH not measured in our study as Hypocalcaemia, Hyperphosphatemia, and Hypomagnesaemia suggestive of secondary hyperthyroidism very well correlated with e-GFR.

CONCLUSIONS

In patients with chronic kidney disease, lower serum magnesium concentrations are associated with a higher risk of death and a faster decline in kidney function. Despite the

availability of global and regional guidelines to detedt adverse clinical outcomes associated with chronic kidney disease–mineral and bone disorder (CKD-MBD), most CKD patients are still affected by the consequences of abnormalities of CKD-MBD. A triad of low calcium, elevated phosphate levels and low magnesium levels was associated with increased mortality. Alterations in the control mechanisms for calcium and phosphorus homeostasis occur early in the course of CKD and progress as kidney function decreases; if left untreated, then alterations can result in significant consequences.

Disclosure

The authors report no conflicts of interest in this work.

Reference

1. World Health Organization: Preventing Chronic Disease: A Vital Investment. Geneva, WHO, 2005.
2. Grassmann A, Gioberge S, Moeller S, *et al*: ESRD patients in 2004: global overview of patient numbers, treatment modalities and associated trends. Nephrol Dial Transplant 2005;20:2587–2593.
3. Isakova T, Wahl P, Vargas GS, Gutierrez OM, Scialla J, Xie H, *et al*. Fibroblast growth factor 23 is elevated before parathyroid hormone and phosphate in chronic kidney disease. Kidney Int. 2011;79(12):1370–1378.
4. Kalantar-Zadeh K, Kuwae N, Regidor DL, Kovesdy CP, Kilpatrick RD, Shinaberger CS, *et al*. Survival predictability of time-varying indicators of bone disease in maintenance hemodialysis patients. Kidney Int 2006;70:771-80.
5. Young EW, Albert JM, Satayathum S, Goodkin DA, Pisoni RL, Akiba T, *et al*. Predictors and consequences of altered mineral metabolism: The dialysis outcomes and practice patterns study. Kidney Int 2005; 67:1179-87.
6. Wald R, Tentori F, Tighiouart H, Zager PG, Miskulin DC. Impact of the kidney disease outcomes quality initiative (KDOQI) clinical practice guidelines for bone metabolism and disease in a large dialysis network. *Am J Kidney Dis* 2007;49:257-66.]
7. Coresh J, Astor BC, Greene T, Eknoyan G, Levey AS. Prevalence of chronic kidney disease and decreased kidney function in the adult US population: Third National Health and Nutrition Examination Survey. *Am J Kidney Dis* 2003;41:1-12.
8. Mizobuchi M, Towler D, Slatopolsky E. Vascular calcification: The killer of patients with chronic kidney disease. *J Am Soc Nephrol* 2009;20:1453-64.
9. Burtis CA, Ashwood ER, Bruns DE. Tietz textbook of clinical chemistry and molecular diagnostics. 4th Edition; Elsevier Health Sciences;2012:1693.
10. Levin A, Bakris G, Molitch M, Smulders M, Tian J, Williams L, *et al*. Prevalence of abnormal serum vitamin D, PTH, calcium, and phosphorus in patients with chronic kidney disease: results of the study to evaluate early kidney disease. Kidney international. 2007;71(1):31-8
11. Mehrotra R, Peralta CA, Chen SC *et al*. No independent association of serum phosphorus with risk for death or progression to end-stage renal disease in a large screen for chronic kidney disease. Kidney Int 2013; 84: 989–997.
12. Kircelli, F., Peter, M.E., Sevinc Ok, E. *et al*. Magnesium reduces calcification in bovine vascular smooth muscle cells in a dose-dependent manner. Nephrol Dial Transplant. 2012; 27: 514–521
13. National Kidney Foundation: K/DOQI Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, classification, and stratification. *Am J Kidney Dis* 2004; 39 [Suppl 1]: S1– S266.
14. Levey AS, Coresh J, Greene T, Stevens LA, Zhang YL, Hendriksen S, Kusek JW, Van Lente F: Using standardized serum creatinine values in the Modification of Diet in Renal Disease study equation for estimating glomerular filtration rate. Ann Intern Med 2006;145: 247–254, 2006
15. Mani MK. Chronic renal failure in India. Nephrol Dial Transplant 1993;8:684-9
16. Agarwal SK, Dash SC, Irshad M, Raju S, Singh R, Pandey RM. Prevalence of chronic renal failure in adults in Delhi, India. Nephrol Dial Transplant 2005; 20:1638-42).
17. Cristina M. Soares, José Silvério S. Diniz, Eleonora M. Lima *et.al* "Predictive factors of progression to chronic kidney disease stage 5 in a predialysis interdisciplinary programme' Nephrology Dialysis Transplantation, March 2009;24(3): 848–855.
18. Agarwal SK: Assessment of renal bone mineral disorder in naïve CKD patients: A single center prospective study. *Indian J Nephrol* 2007;17:96.
19. Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Work Group. KDIGO clinical practice guideline for the diagnosis, evaluation, prevention, and treatment of chronic kidney disease-mineral and bone disorder (CKD-MBD). Kidney Int Suppl 2009;76;113: S1-130.
20. O'Seaghdha CM, Hwang SJ, Muntner P, Melamed ML, Fox CS. Serum phosphorus predicts incident chronic kidney disease and end-stage renal disease. Nephrol Dial Transplant. 2011;26:2885–90.
21. S. Van Laecke, W. Van Biesen, R. Vanholder. Hypomagnesaemia, the kidney and the vessels Nephrol Dial Transplant.2012;27 (11) : 4003-4010.
22. Cunningham J, Rodríguez M, Messa P: Magnesium in chronic kidney disease stages 3 and 4 and in dialysis patients. *Clin Kidney J* 2012; 5(suppl 1):i39–i51
23. Sakaguchi Y, Iwatani H, Hamano T, Tomida K, Kawabata H, Kusunoki Y, *et al*. Magnesium modifies the association between serum phosphate and the risk of progression to end-stage kidney disease in patients with non-diabetic chronic kidney disease. Kidney Int. 2015;88:833–42.
24. Maier JA, Malpuech-Brugère C, Zimowska W, Rayssiguier Y, Mazur A: Low magnesium promotes endothelial cell dysfunction: implications for atherosclerosis, inflammation and thrombosis. Biochim Biophys Acta 2004; 1689:13–21.
25. LaClair RE, Hellman RN, Karp SL, Kraus M, Ofner S, Li Q, *et al*. Prevalence of calcidiol deficiency in CKD: A cross-sectional study across latitudes in the United States. *Am J Kidney Dis* 2005;45:1026-33.
26. World Health Organization: Preventing Chronic Disease: A Vital Investment. Geneva, WHO, 2005.
27. Grassmann A, Gioberge S, Moeller S, *et al*: ESRD patients in 2004: global overview of patient numbers, treatment modalities and associated trends. Nephrol Dial Transplant 2005;20:2587–2593.

28. Isakova T, Wahl P, Vargas GS, Gutierrez OM, Scialla J, Xie H, *et al*. Fibroblast growth factor 23 is elevated before parathyroid hormone and phosphate in chronic kidney disease. Kidney Int. 2011;79(12):1370–1378. doi: 10.1038/ki.2011.47. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
29. Kalantar-Zadeh K, Kuwae N, Regidor DL, Kovesdy CP, Kilpatrick RD, Shinaberger CS, *et al*. Survival predictability of time-varying indicators of bone disease in maintenance hemodialysis patients. Kidney Int 2006; 70:771-80.
30. Young EW, Albert JM, Satayathum S, Goodkin DA, Pisoni RL, Akiba T, *et al*. Predictors and consequences of altered mineral metabolism: The dialysis outcomes and practice patterns study. Kidney Int 2005; 67:1179-87.
31. Wald R, Tentori F, Tighiouart H, Zager PG, Miskulin DC. Impact of the kidney disease outcomes quality initiative (KDOQI) clinical practice guidelines for bone metabolism and disease in a large dialysis network. Am *J Kidney Dis* 2007;49:257-66.
32. Coresh J, Astor BC, Greene T, Eknoyan G, Levey AS. Prevalence of chronic kidney disease and decreased kidney function in the adult US population: Third National Health and Nutrition Examination Survey. Am *J Kidney Dis* 2003;41:1-12.
33. Mizobuchi M, Towler D, Slatopolsky E. Vascular calcification: The killer of patients with chronic kidney disease. J Am Soc Nephrol 2009;20:1453-64.
34. Burtis CA, Ashwood ER, Bruns DE. Tietz textbook of clinical chemistry and molecular diagnostics. 4th Edition; Elsevier Health Sciences;2012:1693.
35. Levin A, Bakris G, Molitch M, Smulders M, Tian J, Williams L, *et al*. Prevalence of abnormal serum vitamin D, PTH, calcium, and phosphorus in patients with chronic kidney disease: results of the study to evaluate early kidney disease. Kidney international. 2007;71(1):31-8
36. Mehrotra R, Peralta CA, Chen SC *et al*. No independent association of serum phosphorus with risk for death or progression to end-stage renal disease in a large screen for chronic kidney disease. Kidney Int 2013; 84: 989–997.
37. Kircelli, F., Peter, M.E., Sevinc Ok, E. *et al*. Magnesium reduces calcification in bovine vascular smooth muscle cells in a dose-dependent manner. Nephrol Dial Transplant. 2012; 27: 514–521
38. National Kidney Foundation: K/DOQI Clinical Practice Guidelines for Chronic Kidney Disease: Evaluation, classification, and stratification. *Am J Kidney Dis* 39 [Suppl 1]: S1– S266, 2004 [PubMed] [Google Scholar
39. Levey AS, Coresh J, Greene T, Stevens LA, Zhang YL, Hendriksen S, Kusek JW, Van Lente F: Using standardized serum creatinine values in the Modification of Diet in Renal Disease study equation for estimating glomerular filtration rate. Ann Intern Med 145: 247–254, 2006 [PubMed] [Google Scholar]
40. Almadén Y, Canalejo A, Ballesteros E, Añón G, Cañadillas S, Rodríguez M. Regulation of arachidonic acid production by intracellular calcium in parathyroid cells: Effect of extracellular phosphate. *J Am Soc Nephrol* 2002;13:693-8.
41. Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Work Group. KDIGO clinical practice guideline for the diagnosis, evaluation, prevention, and treatment of chronic kidney disease-mineral and bone disorder (CKD-MBD). Kidney Int Suppl 2009;76;113: S1-130.
42. O'Seaghdha CM, Hwang SJ, Muntner P, Melamed ML, Fox CS. Serum phosphorus predicts incident chronic kidney disease and end-stage renal disease. Nephrol Dial Transplant. 2011;26:2885–90.
43. Schwarz S, Trivedi BK, Kalantar-Zadeh K, Kovesdy CP. Association of disorders in mineral metabolism with progression of chronic kidney disease. *Clin J Am Soc Nephrol*. 2006;1:825–31.
44. S. Van Laecke, W. Van Biesen, R. Vanholder Hypomagnesaemia, the kidney and the vessels Nephrol Dial Transplant, 27 (11) (2012), pp. 4003-4010
45. Cunningham J, Rodríguez M, Messa P: Magnesium in chronic kidney disease stages 3 and 4 and in dialysis patients. *Clin Kidney J* 2012; 5(suppl 1):i39–i51
46. Sakaguchi Y, Iwatani H, Hamano T, Tomida K, Kawabata H, Kusunoki Y, *et al*. Magnesium modifies the association between serum phosphate and the risk of progression to end-stage kidney disease in patients with non-diabetic chronic kidney disease. Kidney Int. 2015;88:833–42.
47. Maier JA, Malpuech-Brugère C, Zimowska W, Rayssiguier Y, Mazur A: Low magnesium promotes endothelial cell dysfunction: implications for atherosclerosis, inflammation and thrombosis. Biochim Biophys Acta 2004; 1689:13–21.

How to cite this article:

Deepthi M *et al* (2021) 'Dual Role of Serum Calcium, Phosphorous And Magnesium, As A Predictor of Risk Factors And Early Detection of Poor Outcome In Late Stages of Chronic Kidney Disease. A case control study', *International Journal of Current Medical and Pharmaceutical Research,* 07(03), pp 5622-5626.

****