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Original Research Article

Serum calcium and phosphorous balance in diabetic nephropathy and its correlation with glycated hemoglobin

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ABSTRACT

Background: Timely control of hemoglobin A1c (HbA1c) level is very important in patients with diabetic kidney disease. Diabetic nephropathy brings changes in mineral metabolism. The changes in calcium and phosphorous level is a reason for increased morbidity or decreased quality of life in these patients. Conflicting reports are available on serum calcium level and decline in kidney function. This study is to analyse the changes in calcium and phosphorous level in different stages of diabetic nephropathy and its correlation with glycated haemoglobin.
Methods: A cross sectional study with 60 diabetic nephropathy patients admitted in MES Medical College for a period of 1.5 years. Patients with cardiac, liver, thyroid dysfunction, under dialysis were excluded from the study. Fasting blood sugar, HbA1c, calcium, phosphorous, creatinine were assessed by VITROS 5600 integrated system. The study population is divided into groups by two different means, according to HbA1c and estimated glomerular filtration rate (eGFR) value. Statistical analysis was performed by statistical package for the social sciences (SPSS) software. Level of significance calculated at 95%.
Results: eGFR value showed a highly significant correlation with age ($p=0.016$), creatinine ($p\leq0.00001$), calcium ($p\leq0.00001$), phosphorous ($p\leq0.00001$) and HbA1c ($p=0.00001$). There was no significant difference in creatinine and eGFR between male and female subjects. Only eGFR ($p=0.0396$) showed a significant difference between poor and good glycaemic control groups.
Conclusions: This study shows highly significant correlation between the decreased eGFR hypocalcaemia, hyperphosphatemia, increased serum creatinine level and HbA1c. Strict glycemic control is crucial in maintenance of mineral homeostasis and prevention of blood calcium, phosphorous abnormalities.

Keywords: Glycated hemoglobins, Glomerular filtration rate, Diabetic nephropathy, Calcium

INTRODUCTION

Diabetic nephropathy (DN) is the major cause of chronic kidney disease and end-stage renal disease in people with type 2 diabetes mellitus (T2DM).[1] According to data from the Indian Council of Medical Research (ICMR), the prevalence of diabetes in the adult population of India has increased to 7.1 percent.[2] Importantly, as the incidence of T2DM has increased, so has the frequency of DN.[2,3]

Prevalence of disturbances in mineral metabolism is more in advanced stages of chronic kidney disease (CKD). Minimizing these derangements in mineral metabolism may be critical to delay progression of CKD.[4] The whole body balance of calcium and phosphate is maintained by fine adjustments of urinary excretion to equal the net intake. Kidney regulate the homeostasis of calcium and phosphorous. Regulation occurs through different mechanism including glomerular filtration.[5] The kidney disease: improving global outcomes (KDIGO) guidelines

recently identified aberrant bone mineral metabolism as CKD mineral and bone disease (CKD MBD), which contributes considerably to an increase in morbidity and mortality rates among patients with CKD.[6,7] In Indian CKD patients, mineral metabolism abnormalities are more common, more severe, and emerge earlier in the course of CKD than in western populations.[8] Monitoring for CKD-MBD should begin at early CKD stage. DN was the commonest cause for development of CKD.[9]

Hemoglobin A1c (HbA1c) is a blood test that is used to track long-term glycemic control in persons with diabetes mellitus. HbA1c is linked to the risk of diabetic complications.[10] Diabetes mellitus has a significant impact on calcium levels, and there is a strong negative link between glycemia management, as measured by a high HbA1c percentage, and a decrease in serum calcium levels, which is unaffected by gender or diabetes duration.[11] Recent studies showed conflicting reports on the link between serum calcium level and decline in the kidney function.[12]

This study is to find calcium and phosphorous balance in different stages of DN and its correlation with glycated hemoglobin.

METHODS

A cross-sectional study was done at MES Medical College, Kerala over a period of November 2019 to June 2021.

Study design

Study design was a cross sectional study.

Study place

The study was conducted at the MES Medical College, Kerala.

Study duration

This study was conducted from November 2019 to June 2021.

Inclusion and exclusion criteria

This study conducted in DN patients with age 40-60 admitted in MES Medical College, Kerala. Patients with history of cardiac disorders, liver diseases, thyroid dysfunction, and those under dialysis were excluded from the study.

Sample size

Sample size is calculated using the equation for calculation of sample size from coefficient of correlation. A total of 60 DN patients were included as per the inclusion and exclusion criteria.

Methodology

60 DN patients were sub grouped in two different ways according to HbA1c and estimated glomerular filtration rate (eGFR) values. The stages of diabetic kidney disease were defined according to the eGFR based on the guidelines of national kidney foundation.[13] The different stages of DN determined by eGFR value, calculated using modification of diet in renal disease (MDRD) equation.[14] Subjects were also grouped in to two, those with poor glycaemic control and good glycaemic control (HbA1c ≥7% and HbA1c <7%). Serum creatinine, fasting blood sugar, HbA1c, calcium and phosphorous were measured by the fully automated analyser, VITROS 5600 integrated system.

Ethical approval

Ethical approval for the study was obtained from research ethics board, scientific committee, MES Medical College (IEC/MES/07/2019). Informed consent was taken and confidentiality maintained.

Statistical analysis

Descriptive statistics like percentages, means was used for data summarization and presentation. The data were expressed as mean SD. Pearson correlation coefficient and unpaired t test were employed for inferential statistical analysis and a $p<0.05$ was considered as statistically significant. The significance of study parameters between different stages of DN has been measured by analysis of variance (ANOVA).

RESULTS

A total of 60 DN patients of age from 40-60 were enrolled in this study. Out of this 31 (52%) were males and 29 (48%) females (Figure 1). The study parameters are expressed as mean±standard deviation (SD). The eGFR showed a highly significant correlation with the parameters except fasting blood sugar level (Table 1). Hypocalcaemia and hyperphosphatemia were observed with decrease in eGFR.

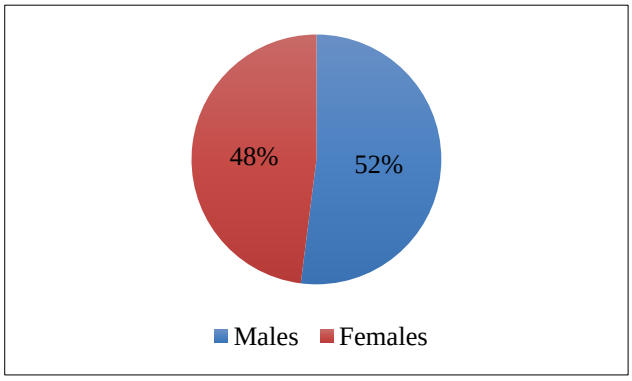

Figure 1: Gender distribution among the 60 participants.

Table 1: Correlation of study parameters with eGFR.

Parameters	Mean±SD	Correlation with eGFR	
		r	P value
Age	57.4±7	0.308	0.01666
FBS	164.7±50.4	-0.1632	0.21336
Cr	4.07±3.51	-0.7408	<0.00001*
HbA1c	8.95±28.9	-0.5315	0.00001*
Ca	8.4±0.54	0.7033	<0.00001*
P	5.07±1.04	-0.6771	<0.00001*

*Indicates highly significant; significance is measured at the level of p<0.05

HbA1C variability is associated with progression of diabetic nephropathy. But other parameters showed no significant difference between the poor and good glycemic control groups (Table 2).

The subjects grouped in to 3 according to the eGFR value and distributed in stage 3-5 of diabetic nephropathy. 38 % of the patients distributed in stage 3, 22 % in stage 4 and 40% in stage 5 (Figure 2).

Analysis of variance (ANOVA) analysis showed a significant difference in creatinine, calcium and phosphorous between these 3 groups (Table 3). Decreased calcium, increased phosphorous and increased creatinine level were observed with a decline in eGFR value. Correlation between eGFR and other parameters is determined in each group (Table 4). A highly significant decrease in serum calcium with decrease in eGFR observed in stage 3. Creatinine showed a highly significant increase with decline in eGFR in stage 3, 4 and 5 of DN.

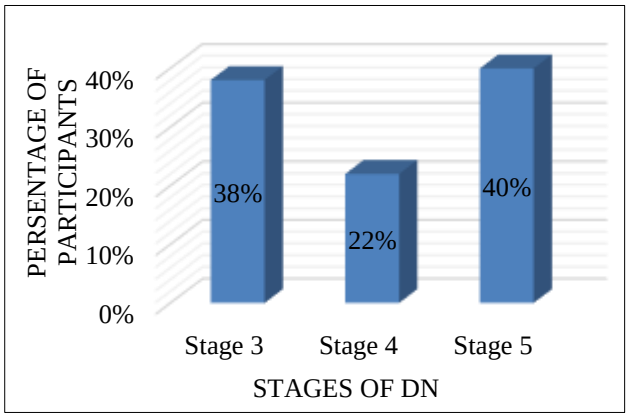

Figure 2: Distribution of DN patients at different stages.

Table 2: Comparison of Ca and P in good and poor glycemic control group.

Parameters	HbA1c <7	HbA1c ≥7	T value	P value
	Mean±SD	Mean±SD		
Calcium	8.53±0.59	8.37±0.53	0.8365	0.2031
Phosphorous	4.62±0.81	5.17±1.07	-1.5242	0.0664
Creatinine	2.61±1.9	4.41±3.7	-1.4891	0.0709
eGFR	34.7±7.12	22.96±17.3	1.96396	0.0272*

*Indicates highly significant; significance is measured at the level of p<0.05

Table 3: Correlation of eGFR with other parameters in different stages of DN.

Parameters	Stage 3			Stage 4			Stage 5		
	Mean SD	R value	P value	Mean SD	R value	P value	Mean SD	R value	P value
Age	59.5±6.7	-0.048	0.828	59.1±6.8	0.389	0.189	54.4±6.4	0.212	0.319
FBS	152.8±39.2	0.008	0.97	173.9±55.7	-0.095	0.757	171.2±56.9	0.061	0.779
Creatinine	1.46±0 .32	-0.706	0.00016*	2.73±0.59	-0.760	0.002*	7.29±3.45	-0.706	0.0001*
HbA1c	8.04±2	-0.369	0.0831	7.87±1.01	-0.165	0.601	10.41±1.81	-0.332	0.113
Calcium	8.81±0.24	0.784	<0.00001*	8.32±0.47	0.111	0.718	8.04±0.5	0.439	0.032
Phosphorous	4.28±0.58	-0.427	0.0421	5.18±0.6	-0.017	0.956	5.8±1.06	-0.304	0.149

*Indicates highly significant; significance is measured at the level of p<0.05

DISCUSSION

In the present study, we investigated the correlation of eGFR with fasting blood sugar, serum creatinine, calcium, phosphorous and HbA1c. The result showed a highly significant negative correlation with creatinine, phosphorous, HbA1c and a highly significant positive correlation with serum calcium level. Similar to this, Freethi et al reported a significant increase in serum phosphorous level in cases when compared with control.[15] Floege et al also reported hyperphosphatemia as the

disease progresses and concluded it as a risk factor for increased mortality rate in CKD.[16] Haglin et al, Park et al and Pawar et al showed the negative correlation between serum phosphate levels and fasting blood sugar levels.[17-19] Hus et al revealed a significant decrease in calcium among these patients and agrees with the study reported in Iraq.[20,21] Lupica et al reported unexpected hypercalcemia in diabetic kidney disease without any microangiopathic alterations.[22]

In our study we observed a significant difference in serum calcium, phosphorous and creatinine in different stages of diabetic nephropathy. Correlation between eGFR and other parameters in 3 stages of DN showed a highly significant decrease in serum calcium in stage 3 of diabetic nephropathy. Janmaat et al demonstrated that lower baseline serum calcium, but within the normal reference range, is associated with a subsequent more rapid eGFR decline in individuals with CKD stages 3b-5.[23] Lim et al reported low serum calcium to be associated with a faster kidney function decline in a pooled cohort of CKD stage 3–4 patients.[24] Schwarz et al found no association between calcium and CKD progression in CKD stage 1–5 patients.[12]

Limitations

Present study was single centred with small sample size.

CONCLUSION

This study showed a highly significant correlation between the decreased eGFR hypocalcaemia, hyperphosphatemia, increased serum creatinine level and HbA1c. Analysing the correlation in different stages of diabetic nephropathy, lowered calcium level highly correlated with declined kidney function strict glycemic control is crucial in maintenance of mineral homeostasis and prevention of blood calcium, phosphorous abnormalities.

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