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Original Research Article

A Prospective Cross-Sectional Study to Evaluate the Balance of Serum Calcium and Phosphorus in Diabetic Nephropathy and Its Correlation with Glycated Hemoglobin (HbA1c)

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Abstract

Aim: To evaluate the balance of serum calcium and phosphorus in diabetic nephropathy and its correlation with glycated hemoglobin (HbA1c).

Materials and methodology: Across-sectional study conducted in 40 patients with diabetic nephropathy admitted in DMCH, Laheriasarai, Darbhanga, Bihar, India during the period for 1 year. The subjects were sub-grouped into 2 groups on the basis of HbA1c levels i.e. Poor glycemic control (HbA1c $\geq$ 7%) and good glycemic control (HbA1c $\leq$ 7%). Fasting blood sugar, serum creatinine, calcium and phosphorus levels were measured and analyzed at daily level.

Results: Out of 40 patients, 21 (52.5%) were males and 19 (47.5%) were females. 42.5 % of the patients distributed in stage 3, 25 % in stage 4 and 32.5% in stage 5 of diabetic nephropathy. With decline in eGFR values, increased phosphorus, increased creatinine and decreased calcium levels were seen. A significant increase in phosphorus levels were observed with decline in eGFR values. A highly significant increase in creatinine levels were also seen at stage 5 of diabetic nephropathy.

Conclusion: This study showed a highly significant negative correlation with creatinine, phosphorous, HbA1c and a highly significant positive correlation with serum calcium level. Correlation between eGFR and other parameters in all the stages of diabetic nephropathy showed a highly significant decrease in serum calcium.

Keywords: HbA1c, eGFR, calcium.

Introduction

Diabetic nephropathy, also known as diabetic kidney disease, is the chronic loss of kidney function occurring in those with diabetes mellitus. It is the most common cause of end-stage renal disease and is a serious complication that affects approximately one quarter of adults with diabetes in the United States[1, 2].

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[3].

Pathophysiologic abnormalities in diabetic nephropathy begin with long-standing poorly controlled blood glucose levels. This is followed by multiple changes in the filtration units of the kidneys, the nephrons. Kidneys also regulate the homeostasis of calcium and phosphorous. The whole-body balance of calcium and phosphate is maintained by fine adjustments of urinary excretion.

Diabetic nephropathy is one of the leading causes of chronic kidney disease (CKD) and end-stage renal disease (ESRD) globally.Bone mineral metabolism abnormalities, which the KDIGO guidelines[4] recently defined as CKD-mineral and bone disorder (CKD-MBD), have been clearly implicated not only in the development of secondary hyperparathyroidism (SHPT) and renal osteodystrophy but have also been associated with the progression of CKD and its complications, including cardiovascular complications[5] and they ultimately contribute significantly to an increase in morbidity and mortality rates among patients with CKD. Monitoring for CKD-MBD should begin at early CKD stage[6, 7].

Diabetes may influence the bone in multiple pathways, some with contradictory effects. These mechanisms include changes in insulin and insulin-like growth factors levels, hyper calciuria associated with glycosuria, obesity, higher concentrations of advanced glycation end-products in collagen etc. Along these lines, many cohort studies undeniably indicated that diabetes itself is associated with increased risk of osteoporosis[8]. 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[9]. Hemoglobin A1c (HbA1c) is used routinely to monitor long-term glycemic control in people with diabetes mellitus, as HbA1c is related directly to risks for diabetic complications.

Materials and Methodology

This is a type of cross-sectional study conducted in 40 patients with diabetic nephropathy admitted in DMCH, Laheriasarai, Darbhanga, Bihar, India during the period for 1 year.

Inclusion/ Exclusion criteria

Patients with age of 40-60 years diagnosed with diabetic nephropathy and admitted to DMCH, Laheriasarai, Darbhanga (Bihar) were included in this study. Patients with history of cardiac disorders, liver diseases, thyroid dysfunction, and those under dialysis were excluded from the study.

Methodology

The subjects were sub-grouped into 2 groups on the basis of HbA1c levels i.e. Poor glycemic control (HbA1c $\geq$ 7%) and good glycemic control (HbA1c $\leq$ 7%). The stages of diabetic kidney disease were defined according to the estimated Glomerular Filtration Rate (eGFR) based on the guidelines of national kidney foundation[13]. Each group included approximately equal number of males and females. Fasting blood sugar, serum creatinine, calcium and phosphorus levels were measured and analyzed at daily level.

Results

A total of 40 DN patients of age from 40-60 were included in this study. Out of this, 21 (52.5%) were males and 19 (47.5%) were females. The eGFR showed a highly significant correlation with the parameters except fasting blood sugar level. With decrease in eGFR, hypocalcaemia and hyperphosphatemia were observed.

The subjects grouped into 3 groups according to the eGFR value and distributed in stage 3-5 of diabetic nephropathy. 42.5 % of the patients

distributed in stage 3, 25 % in stage 4 and 32.5% in stage 5 of DN.

Table 1: Gender of all the patients

Gender	Number (%)
Male	19 (52.50%)
Female	21 (47.50%)

Table 2: Stages of diabetic nephropathy according to eGFR values

Stages of DN	Number (%)
Stage 3	17 (42%)
Stage 4	10 (25%)
Stage 5	13 (33%)

Table 3: Comparison of calcium and phosphorus levels in good and poor glycemic control group

Parameters	Glycemic control group		P value
	HbA1c ≤ 7% Mean ± SD	HbA1c ≥ 7% Mean ± SD	
eGFR	35.2 ± 8.21	23.43 ± 19.7	0.027
Calcium	9.01 ± 0.69	8.77 ± 0.82	0.215
Phosphorus	5.23 ± 1.21	4.97 ± 1.54	0.071
Creatinine	3.04 ± 2.6	4.55 ± 4.1	0.068

HbA1c variability is associated with progression of diabetic nephropathy. But Calcium and phosphorus parameters showed no significant difference between both the control groups.
With decline in eGFR values, increased phosphorus, increased creatinine and decreased calcium levels were seen. A significant increase in phosphorus levels were observed with decline in eGFR values. A highly significant increase in creatinine levels were also seen at stage 5 of diabetic nephropathy.

Table 4: Correlation of eGFR with other parameters in different stages of diabetic nephropathy

Parameters	Stage3		Stage4		Stage 5	
	Mean± SD	P value	Mean ±SD	P value	Mean±SD	P value
Age	57.2 ± 8.4	0.745	56.6 ± 8.0	0.254	52.4 ± 8.0	0.298
FBS	158.4 ± 40.5	0.86	183.2 ± 59.3	0.691	180.6 ± 61.4	0.742
Creatinine	2.01± 0.83	0.00012	3.12 ± 1.02	0.0019	7.44 ± 4.11	0.0001
HbA1c	8.83 ± 3.21	0.0657	8.06 ± 1.86	0.722	11.08 ± 2.55	0.23
Calcium	8.97 ± 0.36	0.002	8.47 ± 0.66	0.675	8.23 ± 0.71	0.066
Phosphorus	4.54 ± 0.72	0.0665	5.64 ± 0.82	0.894	6.21 ± 1.42	0.154

Discussion

In this study, we investigated the correlation of eGFR and HbA1c with fasting blood sugar, serum creatinine, calcium, phosphorous. 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.[10] The term diabetes mellitus describes a metabolic disorder of multiple etiologies characterized by chronic

hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both. The long-term effects of diabetes mellitus include progressive development of the specific complications of retinopathy, nephropathy, and neuropathy [11]. The complications of diabetes mellitus are far less common and less severe in people who have well-controlled blood sugar levels [12].

Hemoglobin A1c (HbA1c) is used routinely to monitor long-term glycemic control in people with diabetes mellitus, as HbA1c is related directly to risks for diabetic complications [13]. It is an indicator of average blood glucose concentration over the period of 2-3 months [14]. The test HbA1c does not change with any recent changes in diet, exercise, or medicines [15]. Hough [16] stated that involvement of the skeletal system must be regarded as yet another complication of diabetes. Sultan et al [17] have shown that the reduction in serum calcium level in type2 diabetes mellitus is most probably due to hyperglycemia which increases calcium and phosphorus excretion in urine which is proportional to the degree of glucosuria, hypercalciuria by osmotic diuresis caused stimulation of bone resorption caused by secondary hyperparathyroidism. In response to urinary calcium loss, PTH secretion is mildly but significantly stimulated to maintain serum calcium concentrations. Excess urinary calcium seems to be derived from bone [18].

Little evidence is available regarding the relationship between HbA1c levels and clinical outcomes in patients with advanced CKD. Se Won Oh *et al*. enrolled a 5-year cohort of 799 patients with DM and an eGFR<60 ml/min/1.73m^2 and reported that patients with a baseline HbA1c of <6.5% had reduced a risk for ESRD by comparing those with a HbA1c of >6.5%. [19] Floege et al also reported hyperphosphatemia as the disease progresses and concluded it as a risk factor for increased mortality rate in CKD [20]. Haglin et al, Park et al and Pawar et al showed the negative correlation between serum phosphate levels and fasting blood sugar levels[21-23]. Hus et al revealed a significant decrease in calcium among these patients and agrees with the study reported in Iraq [24, 25]. Lupica et al reported unexpected hypercalcemia in diabetic kidney disease without any microangiopathic alterations[26].

Conclusion

This study showed a highly significant negative correlation with creatinine, phosphorous, HbA1c and a highly significant positive correlation with serum calcium level. Correlation between eGFR and other parameters in all the stages of diabetic nephropathy showed a highly significant decrease in serum calcium in stage 3 of diabetic nephropathy. Attention should be paid to BMD and other bone metabolism markers in diabetes patients.

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