Original Article

Serum Intact Parathyroid Hormone Level is Inversely Correlated with Glycated Haemoglobin in Diabetic Chronic Kidney Disease Stages 3-5 Predialysis Patients

Haque WMM[a*], Rahim MA[b*], Mitra P[c], Samad T[b], Habib SH[d], Iqbal S[e]

Abstract

Introduction: *Diabetes mellitus (DM) is one of the leading causes of chronic kidney disease (CKD). Management of chronic kidney disease-mineral and bone disorder (CKD-MBD) is an integral component of CKD management; serum intact parathyroid hormone (iPTH) level is the key target. This study was designed to evaluate the relationship between glycated haemoglobin (HbAlc) and iPTH in diabetic CKD stages 3-5 patients not yet on dialysis.*

Methods: *This cross-sectional study was conducted in BIRDEM General Hospital, Dhaka, Bangladesh from January 2013 to December 2014. Diabetic patients suffering from CKD stages 3-5, who were not on dialysis, were consecutively and purposively included in this study. Along with base-line characteristics, clinical and laboratory data including HbAlc and iPTH levels were recorded for all patients. Data were analyzed by using SPSS version 20.0 and Pearson's correlation test was applied to evaluate the relationship between HbAlc and iPTH.*

Results: *Total patients were 306, including 166 (54.2%) males. Mean age was 56.5±11.3 years. Mean duration of DM and CKD were 12.8±7.6 and 2.9±1.7 years respectively. Among the study population, 49 (16.0%) were in CKD stage 3, 90 (29.4%) in CKD stage 4 and rest 167 (54.6%) in CKD stage 5. Mean HbAlc (%), serum creatinine (mg/dl), urea (mg/dl), calcium (mg/dl), phosphate (mg/dl), alkaline phosphatase (U/L) and iPTH (pg/ml) were 7.77±2.14, 6.8±3.0, 141.1±75.7, 8.1±1.2, 5.2±1.9,164.1±135.3 and 229.7±151.2 respectively. Mean HbAlc (%) and iPTH (pg/ml) in CKD stages 3, 4 and 5 were 8.36±1.59 and 171.7±127.9, 7.99±1.92 and 179.5±131.4, and 7.77±2.14 and 273.8±119.2 respectively. On correlation analysis, HbAlc had a significant negative correlation with iPTH (r=-0.002).*

Conclusion: *The results of current study showed that most diabetic CKD stages 3-5 predialysis patients had poor glycaemic control and HbAlc had negative correlation with iPTH. As iPTH level is influenced by presence and control of DM, the targets of iPTH in CKD stages 3-5 in general, as recommended in existing guidelines, may not be appropriate in diabetic CKD patients and this issue merits further investigation.*

Key words: *Chronic kidney disease, correlation, diabetes mellitus, glycated haemoglobin, intact parathyroid hormone.*

(BIRDEM Med J 2017; 7(2): 110-113)

Author information

a. Dr. Wasim Md. Mohosin Ul Haque, Associate Professor, Nephrology, BIRDEM General Hospital, Dhaka, Bangladesh.

b. Dr. Muhammad Abdur Rahim, Assistant Professor, Nephrology, BIRDEM General Hospital, Dhaka, Bangladesh.

c. Dr. Palash Mitra, Assistant Regiatrar, Nephrology, BIRDEM General Hospital, Dhaka, Bangladesh.

d. Dr. Tabassum Samad, Assistant Professor, Nephrology, BIRDEM General Hospital, Dhaka, Bangladesh.

e. Samira Humaira Habib, Principal Research Officer, Health Economics Unit, BADAS, Dhaka, Bangladesh.

f. Prof. Sarwar Iqbal, Professor, Nephrology, BIRDEM General Hospital, Dhaka, Bangladesh.

*First two authors had equal contributions and should be considered as first author

Address of correspondence: Dr. Wasim Md. Mohosin Ul Haque, Associate Professor, Nephrology, BIRDEM General Hospital, Dhaka, Bangladesh. Email: arko.amit@gmail.com, wmmhaque@live.com

Received: November 25, 2016 **Accepted:** February 28, 2017

Introduction

The prevalence of diabetes mellitus (DM) is increasing through-out the world and mostly contributed by type 2 diabetes mellitus.[1] DM is the leading cause of chronic kidney disease (CKD) and end-stage renal disease (ESRD) both in developed and developing countries.[2-7] Diagnosis of CKD among patients with DM merits considerable changes in antidiabetic management, cardiovascular risk modification and addressing other metabolic issues including chronic kidney disease-mineral and bone disorders (CKD-MBD). Treatment of CKD-MBD is an integral component of CKD management. Serum intact parathyroid hormone (iPTH) is the key target for management of CKD-MBD.[8] Hyperglycaemia suppresses PTH secretion in life[9,10] and in experiments.[11] CKD patients with DM have low iPTH when compared with non-diabetic CKD

patients.[9,10] Diabetic CKD patients with poor DM control have lower iPTH, irrespective of treatment modality (with or without dialysis).[9,10,12-13] Low iPTH is reported to cause adynamic bone disease.[14] Data regarding HbA1c and its relation with iPTH in CKD stages 3-5 predialysis patients are limited. This study was designed to evaluate serum Ca, PO4, alkaline phosphatase, iPTH, HbA1c level among diabetic CKD stages 3-5 predialysis patients and to evaluate the relationship between iPTH and HbA1c among them.

Methods

This cross-sectional study was conducted in Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) General Hospital, Dhaka, Bangladesh from January 2013 to December 2014. Diabetic patients suffering from CKD stages 3-5, irrespective of their treatment modality relating to CKD-MBD, who were not on dialysis, were consecutively and purposively included in this study. Patients with diagnosed parathyroid disorders, history of parathyroid surgery, primary bone disease or metastatic bone disease and diagnosed genetic or hereditary conditions were excluded from the study. Along with base-line characteristics, laboratory data including HbA1c and iPTH levels were recorded for all patients. HbA1c was done by BIO-RAD variant (modified HPLC method) and iPTH was detected by Chemiluminescent Micropartical Immunometric Assay (CMIA). CKD was diagnosed and staging done as per Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guidelines 2012.[8] eGFR was estimated by using chronic kidney disease-epidemiology (CKD-EPI) creatinine based formula.[15] Data were analyzed by using SPSS version 20.0 and Pearson's correlation test was applied to evaluate the relationship between HbA1c and iPTH.

Results

Total patients were 306 with slight male predominance (male 166, 54.2%). Mean age of the study participants, mean duration of DM and mean duration of CKD were 56.5±11.3, 12.8±7.6 and 2.9±1.7 years respectively. Among the study population, 49 (16.0%) were in CKD stage 3, 90 (29.4%) in CKD stage 4 and rest 167 (54.6%) in CKD stage 5. Two-thirds (202, 66%) of the study participants were receiving calcium and vitamin D, 52 (17%) were receiving only calcium and equal number (52, 17%) were not on any treatment regarding CKD-MBD. Base-line biochemical parameters are presented in Table I.

Table I. Base-line biochemical characteristics of the study population (N=306)

Biochemical parameter	Value
Urea	141.1±75.7 mg/dl
Creatinine	6.8±3.0 mg/dl
Ca	8.1±1.2 mg/dl
PO4	5.2±1.9 mg/dl
Alkaline phosphatase	164.1±135.3 U/L
iPTH	229.7±151.2 pg/ml
HbA1c	7.77±2.14 %

Selected biochemical parameters relating to CKD-MBD of different stages of CKD are presented in Table II. Glycaemic targets (HbA1c <7%) were rarely achieved among the study subjects (Table III) and majority of the study participants did not achieve iPTH targets[16] irrespective of treatment modality (Table IV and Table V). On correlation analysis, HbAlc had a significant negative correlation with iPTH(r=-0.002) (Figure 1).

Table II. Some serum biochemical parameters according to CKD stages (N=306)

CKD stage	N (%)	Mean Ca (mg/dl)	Mean PO4 (mg/dl)	Mean alk. phos (U/L)	Mean albumin (gm/dl)
3	49 (16.0)	9.11±0.78	4.02±1.54	114.36±44.11	36.75±10.77
4	90 (29.4)	8.65±0.87	4.09±1.22	140.83±93.10	35.63±7.0
5	167 (54.6)	8.06±1.15	5.21±1.95	164.05±135.34	31.43±6.49

Table III. Glycaemic status according to CKD stages (N=306)

CKD stage	N (%)	HbA1c (%)			
		Mean	<7	7 or more	Missing value
3	49 (16.0)	8.36±1.59	7 (14.3)	36 (73.3)	6 (12.2)
4	90 (29.4)	7.99±1.92	24 (26.7)	44 (48.9)	22 (24.4)
5	167 (54.6)	7.77±2.14	48 (28.7)	88 (52.7)	31 (18.6)

Table IV. Serum iPTH level according to CKD stages (N=306)

CKD stage	N (%)	iPTH pg/ml			
		Mean	Below target	Within target	Above target
3	49 (16.0)	171.70±127.90	5 (10.2)	10 (20.41)	34 (69.4)
4	90 (29.4)	179.46±131.40	20 (22.2)	15 (16.7)	55 (61.1)
5	167 (54.6)	273.80±119.20	67 (40.1)	46 (27.3)	54 (32.3)

Table V. Distribution of study subjects according to different treatment modality and iPTH targets (N=306)

Patients	iPTH below target	iPTH within target	iPTH above target
Total (306)	92 (30.1)	71 (23.2)	143 (46.1)
With supplementation (254)	79 (31.1)	51 (20.1)	124 (48.8)
Without supplementation (52)	13 (25.0)	20 (38.5)	19 (36.5)

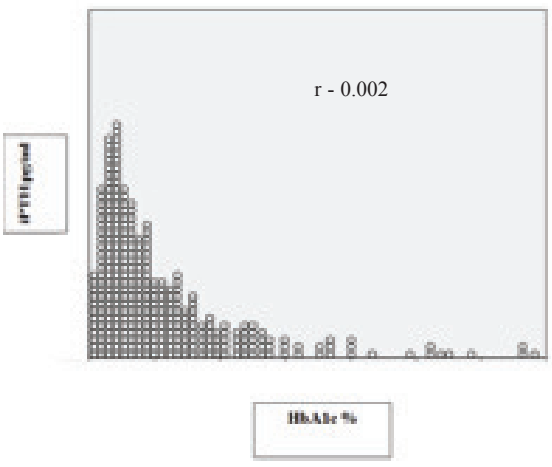

Figure 1. *Relationship between HbA1c and PTH Level*

Discussion

The complex pathophysiology of CKD-MBD is less well understood and much less studied in developing countries like ours. CKD-MBD has two distinct components; high PTH related to high bone turn over and low PTH resulting in adynamic bone disease.[14] Diabetic patients[17] and those with poor glycaemic control[9,12,13] are reported to have low iPTH and at high risk of vascular calcification[18], accelerated peripheral vascular disease[19] and adverse cardiovascular events.

From the results of current study, it is evident that only a few patients could achieve iPTH targets, irrespective of treatment modality. None of them were checked for PTH before starting treatment and none were monitored.

HbA1c were rarely achieved in this study, in spite of its limitations in assessing glycaemic control in patients with CKD. American Diabetic Association has relaxed HbA1c targets of patients with CKD with comorbidities[20]; still, most patients remained beyond control.

We could find an inverse relation with HbA1c and iPTH in this study. In different studies in Egypt[12], Japan[13], Taiwan[18], Brazil[21] almost similar findings were reported, irrespective of their treatment modality; whether on maintenance haemodialysis or not. Some authors still believe bone biopsy as the gold standard for diagnosis CKD-MBD.[22]

Current study had some potential limitations. It was a single center study, included small number of patients and we could not go for bone biopsy. HbA1c may not be the only indicator of glycaemic control in patients with CKD.

In conclusion, the results of current study showed that most diabetic CKD stages 3-5 predialysis patients had poor glycaemic control and most patients did not achieve their iPTH targets. Assessment of CKD patients regarding CKD-MBD remained grossly substandard. HbAlc had negative correlation with iPTH. As iPTH level is influenced by presence and control of DM, the targets of iPTH in CKD stages 3-5 in general, as recommended in existing guidelines, may not be appropriate in diabetic CKD patients and this issue merits further investigation.

Declaration: This paper was presented in the 33rd World Congress of Internal Medicine, Bali, Indonesia, 2016.

References

1. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diabetes Care 2004; 27:1047-53.
2. Bailey RA, Wang Y, Zhu V, Rupnow MFT. Chronic kidney disease in US adults with type 2 diabetes: an updated national estimate of prevalence based on Kidney Disease: Improving Global Outcomes (KDIGO) staging. BMC Res Notes 2014;7:415.
3. The UK Renal Registry. The Sixth Annual Report 2003.
4. ANZ Data Registry. The twenty-sixth report. Adelaide: Australia and New Zealand Dialysis and Transplant registry 2003.
5. Singh AK, Farag YMK, Mittal BV, Subramanian KK, Reddy SRK, Acharya VN et al. Epidemiology and risk factors of chronic kidney disease in India – results from the SEEK (Screening and Early Evaluation of Kidney Disease) study. BMC Nephrology 2013;14:114.
6. Ahmed ST, Rahim MA, Ali MZ, Iqbal MM. Prevalence of primary renal diseases among patients on maintenance haemodialysis: A hospital based study. KYAMC Journal 2012:2(2):182-86.
7. Fiseha T, Kassim M, Yemane T. Prevalence of chronic kidney disease and associated risk factors among diabetic patients in southern Ethiopia. American Journal of Health Reseasrch 2014;2(4):216-21.
8. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney inter 2013;3(Suppl):1–150.
9. Martinez I, Saracho R, Moina I, Montenegro J, Llach F. Is there a lesser hyperparathyroidism in diabetic patients with chronic renal failure? Nephrol Dial Transplant 1998;3(suppl 3):9-11.
10. Nagasaka S, Murakami T, Uchikawa T, Ishikawa San-E, Saitu T. Effect of glycaemic control on calcium and phosphorus handling and parathyroid hormone level in patients with non-insulin-dependent diabetes mellitus. Endocrine J 1995;42(3):377-83.
11. Sugimoto T, Ritter C, Morrissey J, Hayes C, Slatoplosky E. Effects of high concentrations of glucose on PTH secretion in parathyroid cells. Kidney Int 1990;37:1522-27.
12. Ali AR, Emam AA, Assal HS, Abbas AB. Intact parathyroid hormone in Egyptian type 2 diabetics with chronic haemodialysis: impact of glycaemic control. Kidney 2009. DOI 10.1007/s00596-009-0116-z (accessed Jan 1, 2015)
13. Murakami R, Murakami S, Tsuhima R, Ueda C, Mikami K, Ebina T et al. Glycaemic control and serum intact parathyroid levels in diabetic patients on haemodialysis therapy. Nephrol Dial Transplant 2008;23:315-20.
14. Coen G. Adynamic bone disease: an update and overview. J Nephrol 2005;18:117-22.
15. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF 3rd, Feldman HI et al. CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration). A New Equation to Estimate Glomerular Filtration Rate. Ann Intern Med 2009;150(9): 604-12.
16. National Kidney Foundation. K/DOQI clinical practice guidelines for bone metabolism and disease in chronic kidney disease. Am J Kidney Dis 2003;42(4 Suppl 3):S1-201
17. Inaba M, Okuno S, Nagasue K, Otoshi T, Kurioka Y, Maekawa K et al. Impaired secretion of parathyroid hormone is coherent to diabetic hemodialyzed patients. Am J Kidney Dis 2001; 38: S139–S142.
18. Guh JY, Chen HC, Chuang HY, Huang SC, Chien LC, Lai YH. Risk factors and risk for mortality of mild hypoparathyroidism in haemodialysis patients. Am J Kid Dis 2002;39:1245-54.
19. Gnudi L. Serum intact parathyroid hormone in diabetic patients on haemodialysis: what is the treatment goal? Nephrol Dial Transplant 2008;23:24-26.
20. American Diabetic Association. Standards of Medical Care in Diabetes – 2017. Diabetes Care 2017;40(S 1):S90.
21. Paula FJ, Lanna CM, Shuhama T, Foss MC. Effect of metabolic control onparathyroid hormone secretion in diabetic patients. Braz J Med Biol Res 2001;34:1139-45.
22. Gal-moscovici A, Popovtzer MM. New worldwide trends in presentation of renal osteodystrophy and its relationship to parathyroid hormone levels. Clin Nephrol 2005;63:284-89.