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Correlation of Glycated Albumin and Blood Glucose in Diabetic Patients with Chronic Kidney Disease

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ABSTRACT: **Background**: Diabetic nephropathy is the most common a etiology of end stage kidney disease (ESKD). Strict glycemic control reduces the development and progression of diabetes-related complications, and there is evidence that improved metabolic control improves outcomes in diabetic subjects with chronic kidney disease (CKD). **Materials and Methods**: The present study had been conducted on 150 diagnosed & clinically established patients of Diabetes mellitus with nephropathy, who attended OPD and wards of Medicine and Department of Urology, J.L.N. Medical College and Associated group of Hospitals, Ajmer. These patients were compared with 150 Diabetic without nephropathy subjects. Anthropometric measurements and biochemical estimations were performed. Ethical clearance was obtained before start of the study. **Results**: A strong correlation was observed between glycated albumin(GA) and blood glucose in diabetic subjects with nephropathy and in patients without nephropathy. **Conclusion:** Prospective studies testing pre-specified diabetes control targets based on glycated albumin and continuous glucose measurement remain to be performed in order to determine whether morbidity and mortality would be reduced with intensive glycemic control using these measurements as reference target.

Key words: Diabetes Mellitus, Chronic kidney disease, GA, Blood Glucose.

I. INTRODUCTION:

Chronic kidney disease (CKD) is a worldwide public health problem that affects millions of people of all racial and ethnic groups. Diabetes mellitus is a leading cause of CKD, and it is also an important comorbidity in established CKD[1]. The rapidly increasing prevalence of diabetes worldwide virtually ensures that the proportion of CKD attributable to diabetes will continue to rise.[2,3] Albumin is one of the most abundant plasma proteins[4]. The glycation of albumin to form glycated albumin (GA), the product of condensation of albumin and glucose, reflects glycemic state over a short period of preceding 2–3 weeks and is not influenced by RBC survival time[5]. Recently, several clinical trials provided evidence that GA provides more accurate index of the glycemic control in advanced CKD patients. Furthermore, the GA predicted the risk of death and hospitalization in hemodialysis patients[6]. GA measures specifically the glycation product of albumin; it has been developed as an index for glycemic control[7], but it is not affected by serum albumin levels because its ratio to total serum albumin is calculated[8]. To date, serum GA has been suggested as a more reliable and sensitive glycemic index to replace HbA1c in diabetic patients with CKD[5,9-11] because it is not influenced by anemia and associated treatments. In addition, GA may also reflect the status of blood glucose more rapidly than HbA1c, and it is beneficial to patients with wide variations in blood glucose or those at higher risk for hypoglycemia[12].

II. MATERIALS AND METHODS:

The present study has been conducted on 150 diagnosed & clinically established patients of Diabetes mellitus (type-I & type-II) with nephropathy,who attended OPD and wards of Medicine and Departement of Urology, J.L.N. Medical College and Associated group of Hospitals, Ajmer. These patients were compared with 150 Diabetic (type-I & type-II) without nephropathy subjects. They were divided according to the classification of chronic kidney disease (eGFR-MDRD) into CKD stage 1, 2 and 3 (eGFR>90, 89-60 and 59-30 ml/min/1.73 m2, respectively) .The study was carried out in the department of Biochemistry at J.L.N. Medical College, Ajmer. The study was approved by the Ethics committee of our college. All the anthropometric measurements including height, weight, body mass index (BMI) and blood pressure (BP) were performed. Blood sample collection was

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done by aseptic technique and subjected to the biochemical estimations. The fasting blood glucose (FBG), post prandial blood glucose (PPBG) (by Enzymatic GOD-POD End point method), serum creatinine (Jaffe's colorimetric kinetic method) ,serum Glycated albumin (Enzyme Linked Immunosorbent Assay.) and eGFR (estimated glomular filteration rate) by standarised modification of diet in renal disease (MDRD) equation (Leavey AS et al 1999)[13] were estimated in the groups. Patients on treatment for any thyroid dysfunction and taking medication due to thyroid disorder, uncontrolled hypertension, renal tumor, renal replacement therapy, non-diabetic CKD, polycystic kidney disease, renal malformation or agenesis, cancer, patient on glucocorticoids therapy, HIV positive case and pregnant women were excluded. Statistical significance is tested by assuming mean ranks in the test. P values < 0.05 were considered significant.

III. RESULTS:

The present study had been concluded on 300 subjects with age group (18-70 years). These were further divided into 2 groups. Group I comprised of 150 subjects who were Diabetic without Nephropathy (Control), Group II comprised of 150 subjects who were Diabetic with Nephropathy patients.

Table1: Comparison of parameters of diabetic without nephropathy and diabetic with nephropathy subjects.

S.NO.	Parameters	Group I (Mean ± SD) (n=150)	Group II (Mean ± SD) (n=150)
1.	Blood Sugar (F) (mg/dl)	111.22 ± 12.88	111.86 ± 12.82
2.	Blood Sugar (PP) (mg/dl)	158.54± 24.63	170.0 ± 49.40
3.	Serum Creatinine (mg/dl)	0.75 ± 0.08	0.99 ± 0.23
4.	Serum GA (%)	21.33 ± 2.73	21.34 ± 3.17
5.	eGFR (ml/min/1.73m^2)	118.11 ± 14.23	84.76 ± 22.95

Table:2 Comparison of parameters of the subjects studied.

S. NO.	Parameters	Controls (non-CKD) (n=150)	CKD Patients (n=150)		
			CKD-1 (n=60)	CKD-2 (n=70)	CKD-3 (n=20)
1.	Blood Sugar (F) (mg/dl)	111.22 ± 12.88	106.98±12.84	112.77±11.39	123.33 ±9.45*
2.	Blood Sugar (PP) (mg/dl)	158.54± 24.63	148.83±16.77	172.69±50.36	224.12±67.31*
3.	Serum Creatinine (mg/dl)	0.75 ± 0.08	0.78± 0.09	1.07± 0.16	1.34 ± 0.14
4.	Serum GA (%)	21.33 ± 2.73	19.31 ± 2.35*	21.94 ± 2.56	25.33±2.55**
5.	eGFR (ml/min/1.73m^2)	118.11 ± 14.23	108.57±12.36	73.51± 9.20	52.72± 3.77*

*****Highly significant as compared to diabetic without nephropathy (non-CKD) (p value <0.0001).
******Highly significant as compared to non-CKD or CKD-1 or CKD-2 (p value <0.0001).

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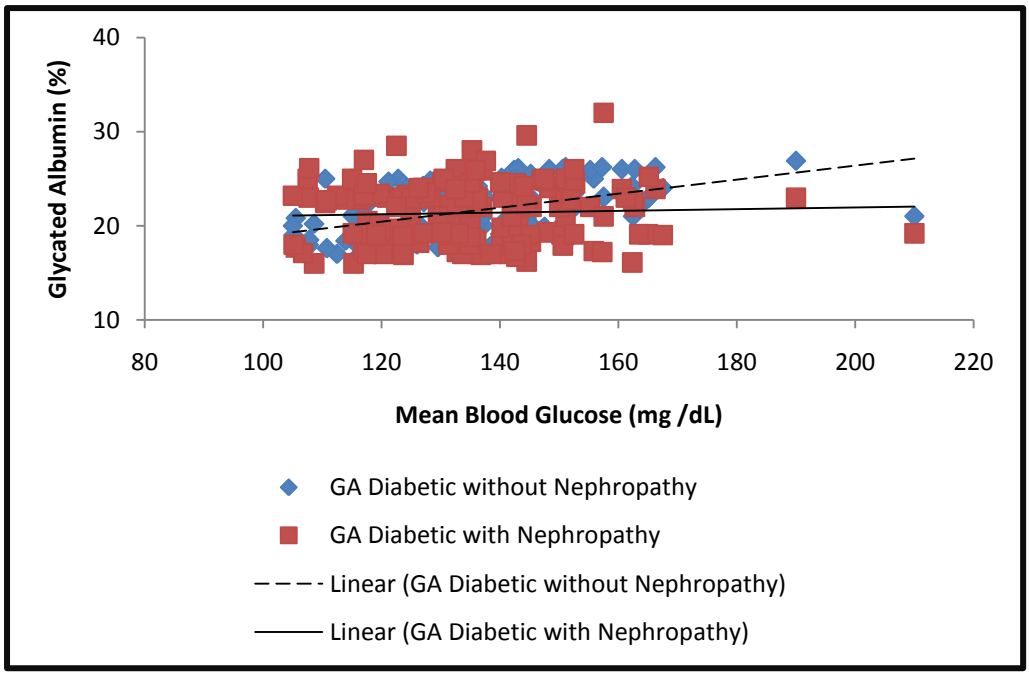
Graph 1: Correlation of serum glycated albumin (GA) with mean blood glucose.



The mean+S.D. value of fasting blood glucose , post prandial glucose and serum creatinine were 111.22+12.88 mg/dl, 158.54+24.63 mg/dl and 0.75 ± 0.08 mg/dl in diabetic without nephropathy subjects and 111.86+12.82 mg/dl, 170+49.40 mg/dl and 0.99 ± 0.23 respectively in diabetic with nephropathy subjects. These values were higher in diabetic with nephropathy subjects as compared to diabetic without nephropathy. No significant difference was observed in mean value of GA between both groups. The mean+S.D. value of eGFR was lower in diabetic with nephropathy subjects as compared to diabetic without nephropathy (Table 1). Table:2 illustrates the mean value of Bood Glucose (Fasting & PP) and Serum creatinine levels were highly significantly ($p<0.0001$) elevated in the CKD-3, even with lower eGFR levels. Serum glycated albumin in CKD stage 3 (25.33+2.55) was highly significant ($p<0.0001$) as compared to non CKD (21.33+2.73), CKD stage 1 (19.31+2.35) and CKD stage 2 (21.94+2.56). A strong positive correlation was found between GA and mean blood glucose in both groups (Graph:1) .

IV. DISCUSSION:

Many authors demonstrated previously that the HbA1c does not reflect the actual glycemic state in diabetic patients on HD. GA is a promising marker reflecting short-term glycemic control[14]. The GA was shown to provide a more accurate marker to assess glycemic control even in diabetic CKD patients, however, the HbA1c falsely underestimated the glycemic state. The HbA1c is currently the most widely used glycemic control marker, and the diabetic CKD patients were recommended the hemoglobin A1c (HbA1c) level of 7.0 % to prevent or delay progression of the microvascular complications. In previous reports, the HbA1c assay has serious limitations with falsely underestimating glycemic state in ESRD patients on hemodialysis[15]. However it was unclear whether the limitations of HbA1c extended to pre-dialysis diabetic CKD patients. Although the GA which not influenced by diseases of shortened RBC life span, and use of iron supplements and EPO therapy provides a reliable marker of glycemic control than the HbA1c in ESRD patients, there are not many studies on GA also provides a more appropriate assay to assess glycemic control in pre-dialysis diabetic CKD patients [16,17]. Our results provide a supportive evidence of relationships between the HbA1c or GA and serum glucose concentration in pre-dialysis diabetic CKD patients and demonstrate that the HbA1c also underestimates significantly glycemic status in pre-dialysis diabetic CKD patients, especially CKD stage 4-5, whereas the GA was shown to correlate closely with the mean serum glucose concentration. The HbA1c primarily reflects mean serum glucose levels over time and does not reflect glycemic excursions. On the other hand, the GA correlates

with maximum blood glucose levels in diabetic patients and reflects glycemic excursions as well as mean serum glucose[18].The GA is not affected by RBC survival, iron supplement or EPO therapy commonly used in ESRD patients. Also, the GA was not associated with serum albumin concentration since the GA value is determined as ratio of GA concentration to total serum albumin[19]. A study by Hirata et al reported that GA to HbA1c ratios can be a good predictor of glycemic control in the presence of diabetic nephropathy due to its close relationship between glucose levels after meals and pancreatic beta cell secretory function[20]. National kidney foundation has defined chronic kidney disease (CKD) as either kidney damage or glomerular filtration rate (GFR) below 60 ml/min/1.73m2 for three or more months with or without evidence of kidney damage, irrespective of the cause. Improved glycemic control slows the progression of CKD. The results of the present study are in accordance to the previous studies done by Takahashi S. et al. (2007)[21] , Peacock TP et al. (2008)[5] , Vijay Viswanthan et al. (2009)[22] and Agarwal R et al. (2011)[23].

V. CONCLUSION:

Prospective studies testing pre-specified diabetes control targets based on glycated albumin and continuous glucose measurement remain to be performed in order to determine whether morbidity and mortality would be reduced with intensive glycemic control using these measurements as reference target. The GA might be an useful indicator of glycemic control in diabetic CKD patients

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