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A Study on eGFR and Its Relation to HbA1c and Urinary Albumin-Creatinine Ratio in Type 2 Diabetes Mellitus Patients

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Abstract

Diabetic nephropathy is a persistent micro vascular complication arising from poorly controlled diabetes mellitus (DM), often culminating in end-stage renal disease (ESRD). Two early indicators of renal impairment are micro albuminuria (MA) and glomerular filtration rate (GFR). Renal function can be more reliably assessed using the urinary albumin-creatinine ratio (ACR) in a spot urine sample. Additionally, GFR can be estimated using formulae based on a single blood sample for serum creatinine (S.Cr), such as the Cockcroft-Gault (C-G) formula, which correlates well with CCR. The objective of this study was to investigate the correlation between HbA1c and urinary ACR and estimated GFR (eGFR) in individuals with Type 2 DM. A cross-sectional study evaluated fifty 78 known Type 2 DM patients aged 40-60 years. Participants were categorized based on HbA1c levels (<8% and >8%), duration of DM (>5 years and <5 years), and blood pressure status (normotensive or hypertensive). Fasting blood sugar (FBS), S.Cr, and urinary albumin and creatinine levels were measured. eGFR and urinary ACR were subsequently calculated. Results were anlysed with a p-value of <0.05 considered significant using SPSS version 18.0. A significant difference in S.Cr and HbA1c was observed between groups with HbA1c levels <8% and >8%. Diastolic blood pressure (DBP) was notably elevated in hypertensive Type 2 DM patients. The duration of DM did not significantly correlate with renal functional parameters. S.Cr and urinary ACR showed a significant positive correlation with HbA1c levels >8%, and a significant correlation with ACR, but not S.Cr, was noted in subjects with HbA1c levels <8%. Elevated HbA1c is associated with increased urinary ACR. Monitoring urinary ACR is recommended for risk assessment in Type 2 DM patients with elevated HbA1c levels.

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Key Words

eGFR, HbA1c, albumin: creatinine ratio, type 2 DM, nephropathy

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INTRODUCTION

Diabetes Mellitus (DM) is a clinical syndrome characterized by hyperglycemia resulting from an absolute or relative deficiency of insulin. There are two clinically significant types of DM: Type 1 Diabetes Mellitus (T1DM) and Type 2 Diabetes Mellitus (T2DM). Type 2 DM accounts for approximately 90% of the diabetic population in any given country. In the year 2000, the global prevalence of DM across all age groups was 2.8%[1,2]. A recent study indicates that the prevalence of DM is 7.2% with an impaired glucose regulation (IGR) rate of 6.5% among the rural population[3].

Traditional blood glucose estimations do not reliably indicate diabetic control due to significant fluctuations. Hemoglobin A1c (HbA1c) offers an average measure of glycemia over the previous 6-8 weeks, with normal values ranging between 5-7% of adult hemoglobin[4]. Clinically, serum creatinine (S. Cr) or urea, or both, are often the initial tests conducted based on local practices. Although serum creatinine is specific, its levels may not surpass the upper reference limit until the glomerular filtration rate (GFR) is reduced by 60% from normal. Creatinine clearance rate (CCR) is generally a more sensitive indicator of early glomerular dysfunction than serum creatinine concentration[5]. Micro albuminuria (MA) serves as an early marker of reversible nephropathy, identifying the initial stages of progressive glomerular disease. Early detection of diabetic nephropathy relies on tests for urinary albumin excretion, which can be measured using either the 24-hour albumin excretion rate (AER) or the spot urine albumin-to-creatinine ratio (ACR)[6]. The spot urine ACR provides comparable results to the 24-hour AER[7].

The National Kidney Foundation (NKF) and the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) in the USA recommend the following for assessing renal impairment: 1) Serum creatinine alone should not be used, 2) GFR should be estimated using standard prediction equations (eGFR), with the Modification of Diet in Renal Disease (MDRD) formula preferred over the Cockcroft-Gault (CG) formula alone; 3) The ACR (mg/g or µg/mg) on spot urine provides useful information, with values = 30 indicating normal levels, 30-300 indicating micro albuminuria (MA), and >300 indicating macro albuminuria[9]. Both albuminuria and eGFR have independent additive values, thus both are recommended for identifying early risks of renal impairment at a reversible stage[9].

The exact degree of hyperglycemia necessary to directly damage the vasculature or to enable the harmful effects of other factors remains uncertain. The relationship between hyperglycemia and MA is non-linear. An HbA1c level of 8.1% (average blood glucose of 200 mg/dL) is a threshold above which the risk of MA increases logarithmically. DM with MA is associated with increased insulin resistance and poorer glycemic control[9,10]. Monitoring glycemic control and screening for MA, along with timely therapeutic intervention, have become standard practices in diabetes care worldwide. This study was designed to investigate the relationship between HbA1c, a marker for glycemic control, and two early indicators of renal functional impairment: the albumin-to-creatinine ratio (ACR), which reflects micro albuminuria (MA), and estimated glomerular filtration rate (eGFR), which reflects creatinine clearance rate (CCR) in individuals with Type 2 Diabetes Mellitus (T2DM).

MATERIAL AND METHODS

This cross-sectional study was conducted in 78 known Type 2 DM patients aged 40-60 years who were consecutively recruited from the OPD. Exclusion criteria included Type 1 DM, congestive cardiac failure, urinary tract infection, known nephropathy, and pregnancy. Height, weight, and BMI were measured, and blood pressure (BP) was assessed using a sphygmomanometer via the auscultatory method. Patients were categorized based on various parameters: HbA1c <8% (n = 16), HbA1c >8% (n = 34), duration of DM (DOD) <5 years (n = 17), DOD >5 years (n = 33), hypertensive (n = 25) and normotensive (n = 25). Diagnosis of DM was made using WHO (2000) criteria: FBG = 7.0 mmol/L and two-hour post glucose load = 11.1 mmol/L. Serum creatinine was measured to calculate eGFR using the Cockcroft-Gault (C-G) formula. Hypertension was defined as BP = 140/90 mmHg.

From each study subject, 5 ml of fasting venous blood was drawn using a disposable syringe under aseptic conditions. One ml of blood was transferred to an EDTA containing tube for HbA1c analysis, while the remaining 4 ml was placed in a cleaned and dried test tube without anticoagulant for FBG and S.Cr analysis. A spot morning urine sample was collected to estimate urinary albumin and creatinine.

Results were expressed as mean±SD. Data analysis was performed using SPSS version 18.0, with independent t-tests and Pearson's correlation tests employed to assess significance. A $p<0.05$ was considered statistically significant.

RESULTS AND DISCUSSIONS

Baseline characteristics are presented in Table 1, and comparisons between two groups based on HbA1c levels are shown in Table 2. There was a significant difference in HbA1c and serum creatinine (S.Cr) between the groups. An independent t-test was conducted, with $p<0.05$ as the significance level. Renal functional parameters (S.Cr, ACR, and eGFR), HbA1c,

Table 1: Baseline parameters among total study participants (n=78)

Variables	Values (Mean ± SD)
Age (Range 40-57 years)	47.52 ± 4.73
Male (n=36)	52.46 ± 4.64
Female (n=42)	46.91 ± 5.33
BMI (Kg/m²)	23.41 ± 4.15
DOD (Duration of Diabetes, in years)	6.68 ± 1.74
FBS (mmol/L)	11.56 ± 4.41
HbA1c (%)	8.95 ± 2.89
ACR (mg/gm)	231.07 ± 180.15
eGFR (ml/min)	72.46 ± 21.99
S. Creatinine (mg/dL)	1.11 ± 0.32

Table 2: Comparison of baseline parameters as per HbA1c levels

Parameters	HbA1c <8% (n=25, Gr I)	HbA1c >8% (n=53, Gr II)	p-value
DOD (years)	6.29 ± 1.9	6.43 ± 1.51	0.87
FBS (mmol/L)	8.95 ± 3.28	11.61 ± 4.76	0.07
HbA1c (%)	6.26 ± 1.48	10.57 ± 1.93	<0.01
ACR (mg/gm)	239.24± 186.59	243.78± 197.93	0.91
eGFR (C-G formula)	71.79 ± 22.84	68.33 ± 20.59	0.52
S. Creatinine (mg/dl)	0.98 ± 0.16	1.07 ± 0.32	<0.05

Table 3: Correlation of HbA1c with various parameters

Correlation Parameters	'r' value	'p-value
Total Study Subjects		
FBS	0.151	0.284
ACR	0.506	<0.01
eGFR	0.192	0.151
S. Creatinine	0.349	<0.01
HbA1c<8%		
FBS	0.198	0.413
ACR	0.621	<0.01
eGFR	0.037	0.922
S. Creatinine	0.128	0.648
HbA1c>8%		
FBS	0.036	0.857
ACR	0.893	<0.01
eGFR	0.227	0.166
S. Creatinine	0.364	<0.05

and blood pressure (BP) parameters were compared between normotensive (n = 39) and hypertensive (n = 39) groups. No significant differences in HbA1c, ACR, eGFR, S.Cr, and systolic BP (SBP) were observed between normotensive and hypertensive patients. However, diastolic BP (DBP) was significantly higher in hypertensive patients (p<0.05).

No significant differences in HbA1c and renal functional parameters were found between groups based on the duration of diabetes (DOD <5 years: n=27, DOD >5 years: n=51). The association of HbA1c with fasting blood sugar (FBS), S.Cr, ACR, and eGFR was assessed among the total study subjects (n=50), Group I with HbA1c <8% (n=25), and Group II with HbA1c >8% (n=53) (Table 3),

Diabetic nephropathy is a chronic micro vascular complication in patients with uncontrolled Type 2 Diabetes Mellitus (T2DM). The progression of chronic kidney disease (CKD) in these patients ranges from hyper filtration to micro albuminuria, macro albuminuria, and ultimately renal failure[11]. In the early stages of renal impairment, traditional markers such as urea and creatinine may remain within normal ranges despite early glomerular changes, including thickening of the basement membrane and accumulation of matrix material in the mesangium, which eventually lead to nodular deposits and micro albuminuria (MA). At this stage, pharmacological interventions can potentially reverse the glomerular pathological changes[2]. Thus, monitoring for glycemic control along with early detection of reversible nephropathy through MA assessment is crucial for newly diagnosed or known T2DM patients.

Our study included 78 known T2DM patients aged between 40 and 57 years. The age distribution was comparable to the studies by Sheikh[12] and Mogensen[13]. Unlike the study by Venugopal and Lyer[14], where most subjects were overweight or obese, the majority of subjects in our study had a normal BMI. Overweight or obesity was not observed as a complication in our cohort.

We compared baseline characteristics between two study groups based on HbA1c levels. Group II, with HbA1c > 8%, had significantly higher HbA1c levels, indicative of poor diabetes control. No significant differences were found between the groups in terms of duration of diabetes (DOD), fasting blood sugar (FBS), ACR, and eGFR. However, serum creatinine (S. Cr) levels were significantly different, albeit within the normal reference range, possibly indicating gradual glomerular membrane changes in uncontrolled diabetes with a trend towards impaired renal function.

Ardekani, Modarresi, and Amirchaghmaghi[15] reported a 7.3% and 28.1% prevalence of MA in

patients with DOD = 10 years and >10 years, respectively. In our study, DOD did not significantly affect HbA1c, ACR, eGFR, or S. Cr levels, as all subjects had DOD < 10 years. Nonetheless, MA increased with DOD beyond five years, with a mean ACR of 254.78 mg/g in subjects with DOD > 5 years compared to 234.72 mg/g in those with DOD < 5 years, suggesting a longer duration might be needed for significant glomerular changes.

Half of the diabetic patients in our study had hypertension, with significantly raised diastolic blood pressure (DBP). Similar findings were reported by Venugopal and Lyer[14], where nearly 50% of diabetic subjects had hypertension and significantly higher MA compared to normotensives. Although no significant differences in urinary ACR and eGFR were found between normotensives and hypertensives in our study, ACR was elevated in hypertensives. Hypertension is prevalent among T2DM patients and can precede diabetes onset, potentially due to underlying insulin resistance. Hypertension can exacerbate MA and accelerate the progression of diabetic nephropathy.

The association of HbA1c with FBS, S. Cr, ACR, and eGFR was assessed using Pearson's correlation test. HbA1c showed significant correlation with S. Cr and ACR in the total study population, with this correlation remaining significant in Group II (HbA1c > 8%) and only with ACR in Group I (HbA1c < 8%). Similar significant associations were reported by Sheikh[12], who found a positive correlation between HbA1c and both MA and S. Cr, and by Venugopal and Lyer[14], who found a significant correlation between HbA1c and MA. S. Cr is widely used as an index of renal function. The observed correlation of raised HbA1c with S. Cr and ACR likely reflects the impact of poorly controlled diabetes on renal impairment. There was no significant correlation between HbA1c and eGFR, indicating that MA, as reflected by ACR, is a more sensitive marker for early diabetic nephropathy than eGFR. This study confirms that HbA1c is associated with ACR.

CONCLUSION

The key conclusion from this study emphasizes that elevated HbA1c levels in monitoring diabetes mellitus necessitate attention to renal function tests. For the early diagnosis of preventable renal impairment, micro albuminuria (MA) assessed via 24-hour urinary albumin is accurately reflected by the spot urine albumin-creatinine ratio (ACR).

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