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Correlation of HbA1C with UACR and Serum Creatinine Level in Type 2 Diabetes Mellitus

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ABSTRACT

Introduction: Diabetes mellitus (DM) is a major emerging clinical health problem in this world. It is a clinical syndrome characterized by hyperglycaemia due to absolute or relative deficiency of insulin. Type 2 DM comprises about 90% of the diabetic population of any country. Diabetic nephropathy is a chronic microvascular complication of poorly controlled diabetes mellitus (DM), leading to end-stage renal disease (ESRD). Diabetic nephropathy is estimated to turn into the most frequent cause of ESRD in the developing world. About 20% to 30% of people with either type 1 or type 2 diabetes develop nephropathy, whose incidence increases with the duration of diabetes.

Objective: To check the association of HbA1c (a marker for glycemic control) & two early markers of renal functional impairments: ACR (reflection of MA) serum creatinine in Type 2DM.

Methods: This study was a case-control study, conducted in the Medicine Department at DMMC & SMHRC, Nagpur in collaboration with ABVRH, Sawangi (Meghe) from September 2020 to November 2020. In the present study, the total number of subjects included was 100 having an age group between 41-70. The subjects were grouped into two types Group 1: 50 (control) Healthy Individuals Group 2: 50 (study) Type 2 diabetes mellitus

Results: In the present study mean levels of HbA1c, microalbumin, serum creatinine and UACR were significantly increased in the study group as compared to the control group and also find a correlation of glycosylated Haemoglobin with UACR and serum creatinine levels in type 2 diabetes mellitus patient.

Conclusions: Raised HbA1c is associated with urinary ACR. Urinary ACR should be estimated in monitoring risk assessment of Type 2DM in patients with raised HbA1c.

Key Words: HbA1c, U. ACR (Albumin: Creatinine Ratio), serum creatinine, Type 2 DM

INTRODUCTION

Diabetes mellitus is described by chronic hyperglycemia due to carbohydrate, fat, and protein metabolism disturbances. Absolute or relative deficits in insulin secretion, insulin action, or both are associated with diabetes mellitus.¹

In India, the prevalence of diabetic nephropathy ranges from 32% to 57% and overt proteinuria is found in 5% to 28% of diabetic patients.² Diabetes mellitus contributes to a third of all patients in dialysis units in India. Diabetic nephropathy is a major public health problem because most diabetic patients in India have almost entirely unavailable dialysis and kidney transplantation therapy.^{3,4} According to the International Diabetes Federation (IDF) in 2013, 382 million people

worldwide had diabetes, in which type 2 made up about 90% of the cases. This is equivalent to 8.3% of the adult population with equal rates in both men and women. More than 80% of diabetic patient's deaths obtain in little and middle-income countries. The number of groups with diabetes is estimated to rise to 592 million by 2035.^{5,6}

The leading cause of chronic kidney disease (CKD) in the United States and other western societies is diabetic nephropathy. In the United States, diabetes is responsible for 30-40 % of all ESRD cases.⁶ India currently has an approximate overall incidence rate of CKD and end-stage renal disease (ESRD) of 800 per million population (pmp) and 150-200 pmp, respectively. It was noted that DM was detected in 31.2 % of patients as the cause of CKD. The measurement of

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urine microalbumin levels has become the gold standard for tracking the development of diabetic nephropathy and is also predictive of elevated levels of HbA1C.⁷

Type 2 DM comprises about 90% of the diabetic population of any country. A chronic microvascular complication of poorly regulated diabetes mellitus (DM) is diabetic nephropathy, leading to end-stage renal disease (ESRD).⁸ Diabetic nephropathy is estimated to turn into the most frequent cause of ESRD in the developing world. About 20% to 30% of people with either type 1 or type 2 diabetes develop nephropathy, whose incidence increases with the duration of diabetes.^{9,10,11} Micro albuminuria significantly increases the relative risk of development of diabetic nephropathy and is a risk factor for adverse cardiovascular outcomes.^{12,13}

Diabetes is a major cause of morbidity and mortality throughout the world especially more alarming in developing countries. Diabetes is among the leading causes of kidney failure and screening for early signs of diabetes-related to kidney disease is a cost-saving intervention and feasible for developing countries. Microvascular complications including nephropathy, retinopathy and neuropathy are initiated by chronic hyperglycemia.

MA (microalbumin) is an early marker of reversible nephropathy, can identify very early stages of progressive glomerular disease. Early detection of diabetic nephropathy relies on tests for urinary excretion of albumin. There are two methods used to determine urinary albumin excretion: 24 hours AER (Albumin Excretion Rate) & spot urine ACR.¹⁴ Serum creatinine is primarily a metabolite of creatine, almost all of which is located in skeletal muscle. The normal level of creatinine is 0.8 to 1.4 mg/dL. Females usually have a lower creatinine (0.6 to 1.2 mg/dL) than males, because they usually have less muscle mass.¹⁵ The quantity of creatine per skeletal muscle mass unit is consistent and the creatine breakdown rate is also consistent. Thus, plasma creatinine concentration is very stable and a direct reflection of skeletal muscle mass.¹⁶ Skeletal muscle is a major target tissue of insulin and a lower volume of skeletal muscle would mean fewer target sites for insulin which causes an increase in insulin resistance. This leads to the development of type 2 diabetes.¹⁷

Monitoring for glycemic control & Screening for MA and timely therapeutic intervention has become the standard of diabetic care worldwide. This study was designed to see the association of HbA1c (a marker for glycemic control) & two early markers of renal functional impairments: ACR (reflection of MA) serum creatinine in Type 2DM.

MATERIALS AND METHODS

Study design

This study was a case-control study, conducted in the Medicine Department at DMMC & SMHRC, Nagpur in

collaboration with ABVRH, Sawangi (Meghe) from September 2020 to November 2020.

Study population

In the present study, the total number of subjects included was 100 having an age group between 41-70. The subjects were grouped into the following two types:

- I. Group 1: 50 (control) Healthy Individuals
- II. Group 2: 50 (study) Type 2 diabetes mellitus

Inclusion criteria for Type 2 Diabetes Mellitus

The following criteria were taken into consideration while characterizing the subjects as Type -2 Diabetes as per WHO

1. FBS >126mg/dl on more than one occasion.
2. 2 hours PP level > 200mg/dl.
3. Both fasting and PP levels are above these values on the same occasion.
4. HbA1C levels more than 6.5% of the average three-month assessment.

Exclusion criteria for Type 2 Diabetes Mellitus

Patients suffering from chronic disorders like

1. Tuberculosis
2. HIV.
3. liver Cirrhosis, Acute & chronic kidney failure.

Sample Collection

Blood was collected from each subject by venipuncture with standard blood collection technique in a plain vial for serum separation and EDTA vial for HbA1C estimation. The urine sample was collected in a sterile container with a preservative (Boric Acid).

Biochemical Analysis¹⁸⁻²¹

Glycosylated haemoglobin was estimated by the HPLC method. Urinary Microalbumin was estimated by the immune Turbidometry method. Urine creatinine and serum creatinine was estimated by modified Jaffe's method. Spot Urinary ACR (UACR) calculated by calculation.

Statistical analysis

The data were analyzed using the SPSS software program, version 20.0. The mean and standard deviation were measured. Analyzed and interpreted using descriptive and inferential statistics. The correlations of HbA1c with urinary ACR and serum creatinine were calculated by Pearson's correlation test and the relevant 'p' value was calculated as level of significance. The probability value is less than 0.05 (p <0.05) and it was considered statistically significant.

RESULT

Table 1 shows percentage-wise distribution of control group and study group. The present study includes a total of 100

subjects. Total 100 subjects were divided into two groups: the Control Group consists of 50 (50%) Healthy Individuals and the study group consists of 50 (50%) (T2DM Patients).

Table 1: Percentage-wise distribution of subjects in Control Group & Study Group

Sr. No.	Groups	No. of patients	Percentage (%)
1	Control group (Healthy Individuals)	50	50
2.	Study group (T2DM Patients)	50	50
Total		100	100

Table 2 shows the gender-wise distribution of healthy control and study group. The present study includes a total of 100 subjects. The Control group consists of 18 males (36%) and 32 female (64%). The study group consists of 25 males (50%) and 25 females (50 %)

Table 2: Gender wise distribution of subjects in Control group (Healthy individuals), Study group (T2DM patients)

Groups	Male	Percentage	Female	Percentage	Total	Percentage
Control group (Healthy Individuals)	18	(36%)	32	(64%)	50	(100%)
Study group (T2DM Patients)	25	(50%)	25	(50%)	50	(100%)

Table 3 shows that the mean levels of HbA1c, microalbumin, serum creatinine and UACR were significantly increased in the study group as compared to the control group.

Table 3: Comparison of Mean levels of HbA1c, Microalbumin serum creatinine &UACR in control group (Healthy Controls) and study group (T2DM)

Parameter	Control Group Healthy Individuals Mean ±SD	Study Group (Diabetes Mellitus) Mean ±SD
HbA _{1c} (%)	5.27 ± 0.87	7.30 ± 0.61**
Microalbumin mg /l	16.27 ± 12.10	102.72 ± 81.90**
Serum Creatinine (mg/dl)	0.91 ± 0.40	1.20 ± 0.60*
UACR mg/g	18.20±10.88	163.30±110.0**

*p<0.05 (significant), **p<0.001 (highly significant)

Table 4: Correlation between HbA1c with Microalbumin, serum creatinine & UACR in the study group (T2DM)

Sr. No.	Parameters	Group 2 (r-value)
01	HbA1c with Microalbumin	0.62**
02	HbA1c with serum creatinine	0.41*
03	HbA1c with UACR	0.44*

*p ≤ 0.05 significant, **p ≤ 0.001 highly significant

DISCUSSION

The present study aim was to assess levels of HbA1c, microalbumin, and urine and serum creatinine in diabetes patients and healthy individual and also find an association of glycosylated Hb with UACR and serum creatinine levels in type 2 diabetes mellitus patient. In the present study, we found

mean levels of HbA1c, microalbumin and serum creatinine levels were significantly increased in study groups as compared to the control group. In the present study mean levels of urinary ACR were significantly increased in diabetes patient compared to control & We found a significant positive correlation of UACR with HbA1c in Diabetic patients (r =0.44).

Haque N et al. has also reported a significant positive correlation of HbA1c with S. creatinine and urinary ACR in type 2 diabetic patients (p values are 0.008 and <0.001) respectively.²² Similar studies were reported by Sheik et al. They have found a significant positive correlation of HbA1c with microalbuminuria (p<0.05) and serum creatinine (p<0.001) in type 2 DM patients.²³ Several interesting studies about Diabetes were reported.²⁴⁻²⁷ Khanna et. al. reported a study of serum uric acid levels in acute stroke.²⁸ Sanyukta et al. reported on the association of Spot Urinary Albumin Creatinine Ratio (UACR) with Coronary Artery Disease.²⁹ Ambad et al. reported about the Relationship between Uric Acid and Creatinine in Pre-Diabetic and Diabetic Patients.³⁰ Few of the diabetes-related studies were reviewed.³¹⁻³⁴ Walinjar et al. studied platelet indices as a predictor of microvascular complications in type 2 diabetes.³⁵ Warjekar et al. conducted a study of microalbuminuria and uric acid in type 2 diabetes mellitus.³⁶ Study of Carotid Intima-Media Thickness in Pre-diabetes and Its Correlation with Cardiovascular Risk Factors was done by Bhinder et al.³⁷

The present study shows a statistically significant positive correlation of HbA1c with urinary microalbumin, Serum Creatinine & albumin to creatinine ratio. It indicates as the level of glycosylated haemoglobin increases, it causes increased urinary microalbumin excretion. Hyperglycemia increases glycation of proteins and that may lead to the formation and accumulation of harmful advanced glycation end products and oxidative stress, which might be related to early kidney function impairment and increased urine albumin-to-creatinine ratio in type 2 diabetes mellitus patients.

CONCLUSION

The present study shows a statistically significant positive correlation of HbA1c with urinary microalbumin, S.Cr & UACR. It indicates as the level of glycosylated haemoglobin increases; it causes increased urinary microalbumin excretion. Hyperglycemia increases glycation of proteins and that may lead to the formation and accumulation of harmful advanced glycation end products and oxidative stress, which might be related to early kidney function impairment.

Conflict of interest: Nil

Source of funding: Nil

Ethical clearance: Taken from the institutional ethics committee

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