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Association of Urinary 8-Hydroxy-Deoxyguanosine with Albumin Creatinine Ratio and eGFR in Patients with Type 2 Diabetes Mellitus

Dr Sendil G[1], Dr Swathi Thilak[2*], Dr Veluri Ganesh[3]

1. Assistant Professor, Department of General Medicine (Cardiology), Akash Institute of Medical Sciences and Research Centre, Bengaluru, Karnataka, India.

2. Assistant Professor, Department of Obstetrics & Gynaecology, Haveri Institute of Medical Sciences, Haveri, Karnataka, India.

3. Assistant Professor, Department of Biochemistry, PES University Institute of Medical Sciences and Research, Bengaluru, Karnataka, India.

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KEYWORDS

Type 2 Diabetes Mellitus, Nephropathy, Microalbumin and Urinary 8-Hydroxy-Deoxyguanosine

ABSTRACT:

Introduction

Type 2 Diabetes Mellitus with patients are more likely to experience kidney issues. A sensitive and specific marker is required for renal disease detection.

Objectives

In patients with Type 2 Diabetes Mellitus, the current study sought to correlate urine 8-hydroxy-deoxyguanosine with clinical indicators of nephropathy.

Methods

This cross-sectional analytical investigation recruited 100 type 2 diabetes mellitus patients and 50 healthy controls. We examined fasting blood sugar, HbA1c, lipid profile, urine albumin creatinine ratio, eGFR, and urine 8OHdG for each research participant.

Results

Both groups of type 2 diabetes mellitus had considerably high urinary 8-hydroxy-deoxyguanosine levels than in controls. Furthermore, there was a significant and positive correlation between 8-hydroxy-deoxyguanosine and the urine albumin creatinine ratio. Additionally, the 8-hydroxy-deoxyguanosine also had a significant negative correlation with eGFR.

Conclusion

According to research findings, urine 8-hydroxydeoxyguanosine may be utilized as an early predictive and prognostic marker for nephropathy in people with type 2 diabetes mellitus, and advantageous for these patients.

1. Introduction

Type 2 Diabetes mellitus (T2DM) is a chronic condition characterized by high blood sugar levels. Chronic renal disease is the most dangerous of the several outcomes it can cause. Oxidative stress is caused by an imbalance between the body's antioxidants and free radicals, and it plays a significant role in the development of T2DM and its aftereffects (1-2). An excess of free radicals damages cells by disrupting DNA, lipids, and proteins' structure and activity (3-4).

According to recent research, 8 hydroxy-20-deoxyguanosine (8-OHdG) is a more specific indicator of oxidative stress-induced damage than the numerous other oxidative stress indicators (5-6). It is directly linked to DNA damage. In particular, the 8-OHdG assesses the extent of oxidative stress at the DNA level, which is significant in T2DM and related outcomes (7-8). This

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contrasts with other metabolites that reflect the body's overall levels of oxidative stress. Elevated 8 OHdG levels in T2DM patients produce increased oxidative stress and potential genetic damage, which may have long-term repercussions on cellular activity and overall health. This unique characteristic of 8 OHdG provides crucial information about the mechanisms driving oxidative stress-related diabetes consequences such renal impairment (9–10).

When oxidized guanosine is removed from nuclear and mitochondrial DNA by the base excision and repair process, 8-hydroxy-2'-deoxyguanosine (8-OHdG) is produced as a byproduct, causing oxidative DNA damage. Oxidative stress has been established as a prevalent cause of T2DM problems, including nephropathy (11-12). Based on this background the present study aimed to evaluate, the 8-OHdG is therefore a marker for oxidative DNA damage and diabetic nephropathy.

2. Objectives

In patients with Type 2 Diabetes Mellitus, the current study sought to correlate urine 8-hydroxy-deoxyguanosine with clinical indicators of nephropathy.

3. Methods

This cross-sectional analytical study conducted in department of medicine collaborated with biochemistry at Akash Institute of Medical Sciences and Research and Centre, Bangalore, Karnataka, India between March 2023- May 2025. A total 100 patients diagnosed with T2DM according to American Diagnosed Association (ADA) (13), further sub divided into two groups 50 T2DM with normoalbuminuria (Group 2) and remaining 50 T2DM with microalbuminuria (Group 3). Additionally, 50 age, gender and BMI matched healthy controls considered as group 1. The present study conducted after taken approval from Institutional Ethics Committee (IEC) and the subjects recruited after taken written consent forms.

Criteria of the study

According to the kidney disease improving global outcomes (KDIGO) criteria, patients with type 2 diabetes between the ages of 30 and 70 who had varied degrees of nephropathy were included in the current analysis (14). Type 1 diabetes mellitus, non-diabetic renal illness, thyroid and liver disease, macrovascular complications such as peripheral vascular, cardiovascular, and cerebrovascular diseases, active inflammatory disease, or urinary tract infections were all grounds for exclusion from the study.

Collection of samples

Every research participant had a fasting venous blood sample taken in six milliliters. A simple tube held four milliliters of the blood sample, a fluoride tube held one milliliter, and an Ethelin Diamino Tetra Acetic acid tube held one milliliter. A spot urine sample was also taken. Centrifugation was used to separate all obtained samples for ten minutes at 3000 rpm. All of the separated samples were put into aliquots with the proper labels. Prior to analysis, the samples were kept at -800 C.

Methods

Blood sugar, total cholesterol, triglycerides, high density lipoprotein, urine albumin, urine creatinine, and HbA1c were among the standard biochemical markers that were measured in a lab. The urinary 8-OHdG levels were measured using the enzyme-linked immunosorbent assay. The very low-density lipoprotein and very low-density lipoprotein were calculated using friedewald's formula. The estimated glomerular filtration rate was calculated by using modification of diet in renal diseases.

Statistical analysis

The mean ± standard deviation was used to express the data. The analysis of variance (ANOVA) was used to compare the groups. The pearson correlation analysis was used to determine the relationship between the study's other measures, including urinary 8-OHdG. The receivers operating characteristics (ROC) curve study was performed on T2DM patients with normo albuminuria and controls in order to diagnose and track the evolution of nephropathy. The statistical analysis was done by SPSS version 20 and Microsoft Excel Spreadsheets. A P value is less than 0.05 were consider as significant.

4. Results

Age, BMI, blood sugar, and lipid profiles, including total cholesterol, TGL, VLDL, and LDL HbA1c, are all significantly higher in patients with type 2 diabetes mellitus than in the controls ($P<0.05$). The Urinary 8-OHdG and albumin creatinine ratios were

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considerably higher in T2DM patients (P=0.001**) (Table 1).

Table 2 displays blood sugar levels, age, BMI, and lipid profiles, including total cholesterol, TGL, VLDL, LDL, and HbA1c, all of which are significantly higher in both groups of type 2 diabetes mellitus than in the controls (P<0.05). When compared to T2DM patients with normo albuminuria and controls, those with micro albuminuria have significantly higher urine albumin creatinine ratios (P=0.001**). The T2DM patients with micro albuminuria shown significant drop in both eGFR, to those T2DM patients with normo albuminuria and controls, (P=0.001**). The Urinary 8-OHdG levels were considerably greater in T2DM patients with normo, micro albuminuria than in controls (P=0.001**).

A significant and positive correlation between urinary 8-OHdG and FBS, total cholesterol, TGL, VLDL, LDL, HbA1c, and albumin creatinine ratio (P=0.001**). Additionally, the urinary 8-OHdG, shown significant and negatively correlated with HDL, and eGFR were significantly (P=0.001**) (Table 3).

The albumin creatine ratio and eGFR were not found to be significant at area under the curve (P=0.671,0.727) with sensitivity (52.19,53.19) and specificity (61.23,73.50) where the P value was more than 0.05. Additionally, the urinary 8-OHdG has very high significant area under the curve (P=0.0001**) with sensitivity (95.00) and specificity (97.50) (Table 4).

5. Discussion

This study emphasises the significance of 8 hydroxy-20-deoxyguanosine (8-OHdG) as a biomarker for oxidative stress and DNA damage in T2DM patients, as well as the fact that the same biomarker has a respectable level of discriminatory power for identifying kidney disease in T2DM patients (15-16). Similarly, patients with type 2 diabetic nephropathy were found to have greater levels of oxidative stress in earlier research. The greater 8-OHdG levels in DKD patients compared to those without kidney dysfunction indicate increased oxidative DNA damage, which is linked to kidney failure in this population (17).

In the current investigation, we discovered a positive association between 8-OHdG and HbA1c. According to the new research, elevated 8-OHdG levels have also been connected to the severity of T2DM sequelae, including nephropathy, cardiovascular diseases, and the risk of death in individuals with T2DM (18-19). Similar to these results, earlier research has found that glycated haemoglobin levels have an impact on the likelihood of DKD in the diabetic population. Hyperglycemia itself is known to increase the formation of reactive oxygen species (ROS) through a variety of mechanisms, including the polyol pathway, the creation of advanced glycation end products (AGEs), and mitochondrial dysfunction. DNA and other biological components can be severely damaged by these ROS (20-21).

Chronic kidney disease can worsen due to tubular and glomerular damage brought on by ROS in the kidneys caused by hyperglycemia. The kidneys' high oxygen consumption and metabolic activity make them especially vulnerable to oxidative stress. Diabetes patients' kidneys are more vulnerable to oxidative stress, which can increase fibrosis, apoptosis, and inflammation, further decreasing renal function. High 8-OHdG levels can occur in CKD patients with type-2 diabetes for several causes (22-23). The degree of kidney impairment in patients with Type 2 diabetes mellitus is indicated by the considerable excretion of urine 8OHdG levels.

6. Conclusion

According to research findings, urine 8-hydroxydeoxyguanosine may be utilised as an early predictive and prognostic marker for nephropathy in patients with type 2 diabetes mellitus, and magnesium is advantageous for these patients.

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Table 1: comparison of baseline features of T2DM patients and controls

Parameter	Control			T2DM Cases			P-Value
	Mean ± SD			Mean ± SD			
Age (years)	46.05	±	7.59	52.16	±	9.21	0.001**
BMI (kg/m2)	20.54	±	0.56	31.24	±	1.17	0.001**
FBS (mg/dL)	77.43	±	7.25	184.16	±	19.02	0.001**
HbA1c (%)	5.04	±	0.12	9.54	±	1.98	0.001**
Total Cholesterol (mg/dL)	166.32	±	16.37	287.43	±	7.01	0.001**
Triglycerides (mg/dL)	105.21	±	20.46	206.67	±	18.32	0.001**
HDL (mg/dL)	38.11	±	7.16	27.31	±	2.98	0.001**
VLDL (mg/dL)	20.17	±	4.22	44.78	±	15.41	0.001**
LDL (mg/dL)	60.34	±	4.53	207.35	±	34.43	0.001**
eGFR (ml/min)	99.24	±	10.42	56.78	±	12.32	0.001**
Albumin Creatinine Ratio (mg/g creatinine)	10.22	±	2.21	194.67	±	60.31	0.001**
Urinary 8-Hydroxydeoxyguanosine (ng/mL)	1.79	±	0.12	8.98	±	7.24	0.001**

Table 2: Study variable comparisons between both groups of T2DM patient and control

Parameter	Control			T2DM with Normo albuminuria			T2DM with Micro albuminuria			P-Value
	Mean ± SD			Mean ± SD			Mean ± SD			
Age (years)	46.05	±	7.59	44.12	±	4.46	54.21	±	7.31	0.001**
BMI (kg/m2)	20.54	±	0.56	21.34	±	1.94	34.35	±	3.61	0.001**
FBS (mg/dL)	77.43	±	7.25	156.01	±	8.01	194.88	±	24.22	0.001**
HbA1c (%)	5.04	±	0.12	7.56	±	1.29	11.24	±	1.89	0.001**
Total cholesterol (mg/dL)	166.32	±	16.37	147.32	±	12.21	346.38	±	41.12	0.001**
TGL (mg/dL)	105.21	±	20.46	114.73	±	9.88	266.00	±	26.03	0.001**

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HDL (mg/dL)	38.11	±	7.16	32.55	±	5.29	27.48	±	4.33	0.001**
VLDL (mg/dL)	20.17	±	4.22	24.32	±	1.00	53.20	±	5.21	0.001**
LDL (mg/dL)	60.34	±	4.53	79.34	±	8.22	265.70	±	41.16	0.001**
eGFR (ml/min)	99.24	±	10.42	91.17	±	14.31	11.31	±	3.45	0.001**
Albumin Creatinine Ratio (mg/g creatinine)	10.22	±	2.21	15.78	±	1.09	801.52	±	107.83	0.001**
Urinary 8-Hydroxydeoxyguanosine (ng/mL)	1.79	±	0.12	4.23	±	2.13	7.49	±	1.85	0.001**

Table 3: Association between urinary 8-hydroxydeoxyguanosine, and other research variables

Parameter	Urinary 8-Hydroxydeoxyguanosine	
	r	P-value
BMI (kg/m2)	0.66	0.001**
FBS (mg/dL)	0.72	0.001**
HbA1c (%)	0.74	0.001**
Total cholesterol (mg/dL)	0.70	0.001**
TGL (mg/dl)	0.68	0.001**
HDL (mg/dl)	-0.61	0.001**
VLDL (mg/dl)	0.68	0.001**
LDL (mg/dl)	0.70	0.001**
eGFR (ml/min)	-0.68	0.001**
Albumin Creatinine Ratio (mg/g creatinine)	0.69	0.001**

Table 4: ROC curve analysis for T2DM nephropathy prediction Individuals with normoalbuminuria and controls

Parameter	AUC	95% CI for Value	Sensitivity	Specificity	P-Value
Albumin Creatinine Ratio (mg/g creatinine)	0.744	0.544 to 0.596	52.19	61.23	0.671
eGFR (ml/min)	0.518	0.623 to 0.819	53.19	73.50	0.727
Urinary 8-Hydroxydeoxyguanosine (ng/mL)	0.988	0.934 to 1.000	95.00	97.50	<0.0001