Correlation between Microalbuminuria and Glycated Hemoglobin in Type 2 Diabetes Mellitus

Dr. Ratna Priya¹, Dr. Chandan Kishore²

¹Assistant Professor, Department of Biochemistry, Patna Medical College, Patna

²Professor, Department of Radiology, Narayan Medical College, Jamuhar, Sasaram

Abstract: <u>Background</u>: DM is a worldwide public health problem and puts a substantial burden on health care resources. The chronic hyperglycemia of DM type 2 is associated with end-organ damage, dysfunction, and failure, including the retina, kidney, nervous system, heart, and blood vessels. Diabetic Nephropathy (DN) is the leading cause of premature deaths in diabetic patients due to renal failure. Mortality in diabetic patients with proteinuria is about 40 times higher than in diabetes without proteinuria. Glycated hemoglobin is the perfect and widely utilized biomarker of glycemic control in subjects with DM with higher concentration of glucose. The formation of the sugar-hemoglobin linkage indicates the presence of excessive sugar in the bloodstream, often indicative of diabetes in high concentration (HbA1c >6.4%). (11) A1C is of particular interest because it is easy to detect. Objective: Present study was aimed to estimate microalbuminuria, HbA1c in patients with type 2 DM and to find out the correlation of glycemic control with microalbuminuria. Materials and methods: A cross-sectional study is conducted at the Department of Medicine, Patna medical college, Patna. The duration of the study was from September 2021 to March 2022. A sample size of a total of 150 patients of type 2 DM was selected. A total of 150 patients fulfilling selection criteria was included by their consent in the study. Venous blood was collected after 12 hours of fasting in a test tube with ethylene diamine tetraacetic acid (EDTA) anticoagulant for HbA1c. The blood samples were analyzed for HbA1c, fasting blood glucose and postprandial blood glucose, serum urea and serum creatinine. Urine sample was analyzed for microalbumin. <u>Result</u>: In the present study, levels of HbA1c and microalbuminuria are higher in diabetics than in controls, and the elevations are of high statistical significance (P < 0.0001). In this study, it is found that diabetics with poor glycemic control had higher microalbumin levels compared with those of diabetics with good glycemic control. Conclusion: it is seen that there is an association of microalbumin levels with poor glycemic control (HbA1c). Similarly, this study also reveals that the diabetics' subjects having poor metabolic control are more prone to renal damage, and thus elevated microalbumin levels.

Keywords: microalbumin, HbA1c, glycated hemoglobin, diabetes mellitus, nephropathy

1. Introduction

DM is a worldwide public health problem and puts a substantial burden on health care resources. Diabetes mellitus, often known simply as diabetes, is a group of common endocrine diseases characterized by sustained high blood sugar levels. (1, 2) Diabetes is due to either the pancreas not producing enough insulin, or the cells of the body becoming unresponsive to the hormone's effects. (3)The prevalence of diabetes for all age-groups worldwide was estimated to be 2.8% in 2000 and 4.4% in 2030. The total number of people with diabetes is projected to rise from 171 million in 2000 to 366 million in 2030. The urban population in developing countries is projected to double between 2000 and 2030 (4).

Diabetes Mellitus (DM) is a chronic illness characterized by hyperglycemia, insulin resistance, or relative insulin deficiency (5). People having type 2 DM are more vulnerable to various forms of both short-and long-term complications, which often lead to their premature death. The major long-term complications of diabetes relate to damage to blood vessels at both macrovascular and microvascular levels. (6, 7)

The chronic hyperglycemia of DM type 2 is associated with end-organ damage, dysfunction, and failure, including the retina, kidney, nervous system, heart, and blood vessels (8). This tendency of increased morbidity and mortality is seen because of its insidious onset and late recognition [9]. Mortality in diabetic patients with

proteinuria is about 40 times higher than in diabetes without proteinuria. Kidney damage is a proportionately grave complication of diabetes. Estimation explored the death rate due to kidney damage is 17 times more common in diabetics than nondiabetics (10). The formation of the sugar-hemoglobin linkage indicates the presence of excessive sugar in the bloodstream, often indicative of diabetes in high concentration (HbA1c >6.4%). (11) A1C is of particular interest because it is easy to detect. The process by which sugars attach to hemoglobin is called glycation and the reference system is based on HbA1c, defined as beta-N-1-deoxy fructosyl hemoglobin as component (12). In diabetes, higher amounts of glycated hemoglobin, indicating poorer control of blood glucose levels, have been associated with cardiovascular disease, nephropathy, neuropathy, and retinopathy. HbA1c is highly prognostic for long term diabetes related complications such as microalbuminuria. (14).

2. Methodology

A cross-sectional study is conducted at the Department of Medicine, Patna medical college, Patna. The duration of the study was from September 2021 to march 2022. A sample size of a total of 150 patients of type 2 DM was selected with a 95% confidence interval. Diabetic patients (Type 2 DM) with good glycemic control, with either gender having age in the range of 30-60 years, were enrolled in the study. Patients with Urinary Tract Infection, previous cardiac disease, Hypertension,

DOI: https://dx.doi.org/10.21275/SR231201103855

Hematuria, any Urinary tract tumor, or had plasma creatinine of >1.2 mg/dl were excluded from the study.

A total of 150 patients fulfilling selection criteria was included by their consent in the study. Venous blood was collected after 12 hours of fasting in a test tube with ethylene diamine tetraacetic acid (EDTA) anticoagulant for HbA1c. The blood samples were analyzed for HbA1c (immuno-inhibition method), [15] fasting blood glucose and postprandial blood glucose (GOD-POD), [16] serum urea (urease method) [17] and serum creatinine (Jaffe's Kinetic). [18] Urine sample was analyzed for microalbumin (immunoturbidimetric method). (19). Data were analyzed using SPSS version 20. Microsoft Word and Excel have been used to generate graphs and tables.

3. Result

Mean levels of biochemical parameters with P value are shown in Table 1. Levels of Fasting Blood Glucose (FBS), Post-prandial Blood Glucose (PPBS), Glycosylated Hemoglobin (HbA1c), Microalbumin, Serum Urea and Serum Creatinine were found to be higher in cases compared with controls and considered to be extremely statistically significant (P < 0.001).

Table 1: Mean levels of parameters with P value

Parameter	Controls	Cases	P value
FBS (mg/dl)	87.05±9.07	193.15±68.74	0.0001
PPBS (mg/dl)	107.67±22.15	245.98 ± 78.34	0.0001
HbA1c %	5.12±0.58	8.52±2.01	0.0001
Microalbumin (mg/day)	4.65±2.01	283.87 ± 145.98	0.0001
Urea (mg/dl)	26.23±9.21	47.06±25.78	0.0001
Creatinine (mg/dl)	0.87±0.43	2.12±0.67	0.0001

Results of all biochemical analytes from patients with type 2 DM were compared with standard normal values of respective analytes using unpaired t tests analysis. There was a highly significant difference (p<0.0001) between values of all the analytes of the two groups. These results for microalbuminuria of our study are in agreement with Jayprakash (20). Urinary microalbumin, HbA 1c levels

were significantly higher in the cases. Microalbumin levels were linearly correlated to the duration of diabetes and HbA1c (21) as shown in the graph 1.



Microalbumin levels in relation to duration of type 2 diabetes were represented in Table 2. Microalbumin levels (mg/day) were found to be highest i.e., 0.526 ± 0.180 g/ day in diabetic subjects with duration of diabetes more than five years and this difference is considered to be extremely statistically significant (0.0001).

Table 2: Relationship	of microalbumir	with the	duration
	ofdiagona		

of disease					
Duration of disease in years	Microalbumin mg/day	P value			
1-2	0.136±0.06				
2-3	0.183±0.12				
3-4	0.285 ± 0.08	0.0001			
4-5	0.438±0.112				
>5	0.526±0.180				

The relationship of microalbumin with the duration of disease is shown in graph 2. The correlation between microalbumin levels to HbA1c is depicted in Graphs3.



Graph 2: Relationship of microalbumin with the duration of disease

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Paper ID: SR231201103855

DOI: https://dx.doi.org/10.21275/SR231201103855

International Journal of Science and Research (IJSR) ISSN: 2319-7064 SJIF (2022): 7.942



Graph 3: Correlation between HbA1c and microalbumin

4. Discussion

Diabetes mellitus (DM) has long been recognized as a major public health problem for its adverse health impact on individuals and for its economic burden on the health care system and the society at large (22). The International Diabetes Federation (IDF) in 2005 confirmed that diabetes is one of the most common noncommunicable diseases globally and constitutes a major cause of death in most developed countries as well as many developing and newly industrialized countries. (23). In the present study, levels of HbA1c are higher in diabetics than in controls, and the elevations are of high statistical significance (P < 0.0001). In this study, it is found that diabetics with poor glycemic control had higher microalbumin levels compared with those of diabetics with good glycemic control, and this finding is in agreement with several other studies (24). This study also shows that there is a significant correlation between microalbumin levels and HbA1c in cases. Our findings are in correlation with the findings of several other studies. The increased microalbumin levels in diabetic subjects may be due to an altered glomerular filtration barrier, at the podocyte level. Damage to the podocyte may be explained by the fact that there is an increase in the extracellular release of reactive oxygen species. Minimizing microalbuminuria and having a tight glycaemic control is an important treatment goal for patients with diabetes (26). HbA1c is an index of mean blood glucose in fasting and post-prandial state and is well established and widely used as a clinical measure of chronic glycaemia (27). Microalbuminuria has a significant correlation with HbA1c, similar to the study reported by Kassab (32).] A rapid decline in renal function can be predicted for patients having poor glycaemic control and micro-albuminuria (37). In adults, a diagnosis of microalbuminuria can precede Type 2 diabetes and is a component of the World Health Organization's definition of the metabolic syndrome (38). We found a linear continuous relationship of HbA1c with microalbuminuria. Despite the many advantages to using HbA1c over other glycaemic measures such as less intraindividual variation, good ability to detect undiagnosed diabetes, (39) and predict risk of developing microvascular complications both in type 1 and type 2 diabetes, (41) and widespread acceptance as a common endpoint in clinical trials.). It is concluded from this study that screening for microalbuminuria in diabetic patients is necessary in order to reduce future kidney disease. This study shows that if good glycemic control is maintained at early stages of diabetes, chances of microalbuminuria is less. There are no large trials that have studied appropriate glycemic targets to prevent DKD. In type 2 diabetic patients, the duration of diabetes was the strongest predictor and elevated glycemic control (HbA1c) as well predicted increased microalbumin excretion rate. So, it may be suggested that determination of microalbumin levels in urine is an easy method of screening diabetic patients, especially diabetic patients with long-term diabetes.

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Volume 12 Issue 12, December 2023

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