Association of Glycosylated hemoglobin and Blood pressure with proteinuria in diabetes mellitus patients

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Abstract

Background: Chronic type II diabetes mellitus(T2DM) has profound effects on various organs, contributing to increased morbidity and mortality rates. Diabetic kidney disease typically progresses from a normal level of protein in the urine to end-stage renal disease. The presence of protein in the urine is a sign of kidney damage. Monitoring the levels of urine protein accurately is crucial for managing the disease in diabetic patients. Higher levels of HbA1c are associated with an increased risk of developing proteinuria. High blood pressure can also damage the nephrons in the kidneys, causing proteins to be filtered through the glomerulus and potentially causing nephropathy.

Aim: 1. To measure Blood pressure, glycosylated hemoglobin and urine protein levels in type 2 diabetes mellitus patients. 2. To find out the correlation between glycosylated hemoglobin with Blood pressure and urine protein levels in type 2 diabetes mellitus patients.

Materials and methods: An analytical prospective study was conducted at Kanachur Institute of Medical Sciences, Mangalore, including 70 T2DM patients. Patients with HbA1c > 7.0% were grouped as poor control/ Group 1, while those with HbA1c ≤ 7.0% were considered as good control/ Group 2. Serum levels of Random blood sugar (RBS), HbA1c, Serum Urea, Creatinine, Uric acid and Urine protein levels were estimated. Blood pressure (BP) was recorded manually in supine position. Data were analyzed in SPSS software 21 using independent student t test. $p < 0.05$ was considered significant.

Results: Increased levels of HbA1c, Blood pressure, Serum levels of Urea, Creatinine, and Uric acid levels were found in patients with poor control that is group 1 cases, and they were statistically significant. Urine protein levels were elevated in group 1 cases. Spearman rho correlation showed that HbA1c was positively and highly significantly correlated with Urine protein, Systolic BP and Diastolic BP.

Key words: T2DM, Glycosylated Hemoglobin, Blood pressure, Urine protein, Nephropathy.

Introduction:

Type II diabetes mellitus is a complex, heterogeneous, metabolic disease condition in which the body fails to produce enough insulin and hence characterized by increased blood glucose levels[1]. These metabolic derangements are frequently associated with permanent and irreversible functional changes in the cells, which in turn lead to the development of vascular problems which can cause complications of DM. Diabetes mellitus has become a major non communicable health problem in India. It has been estimated that by the year 2030, 87 million of the Indian population would be suffering from this disease. Long-standing type II DM has significant impact on various organs of the body. It increases morbidity and mortality by decreasing the quality of life[2,3]. Currently, India has the largest number of diabetic subjects and this is expected to increase in the coming years[4]. Studies on diabetes-related complications are, therefore, important to assess the burden of diabetes[1].

Diabetic Nephropathy is the major complication in patients with diabetes mellitus (DM). Diabetic nephropathy usually takes the descending path from normoalbuminuria to end stage renal disease (ESRD) Appearance of proteinuria marks the onset of nephropathy. So, estimating urine protein accurately and precisely, is very much essential in monitoring

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disease activity in patients with DM[5].

For estimation of proteinuria, 24 hours urine protein is considered as gold standard, but it has major limitations like time consumption and error in sample collection. Spot urine protein estimation avoids the 24-hour urine collection and it is favored because it is less time consuming[6].

Glycosylated hemoglobin (HbA1c) represents 3 months of glucose concentration in blood. Another advantage of Glycosylated hemoglobin value is to assess glucose control. The risk of Proteinuria in patients with diabetes mellitus increases with increasing Glycosylated hemoglobin. It is difficult to predict the onset of complications like nephropathy in T2DM, so screening for proteinuria should begin at the time of diagnosis. The onset and course of diabetic nephropathy can be ameliorated to a very significant degree by several interventions at early course and can prevent End stage renal disease[7].

Recent research studies have demonstrated that proteinuria is an independent risk factor for cardiovascular mortality among the patients with diabetes and hypertension. High blood pressure, over many years can lead to renal impairment with the development of proteinuria and may lead to renal disorders. Elevated BP can damage the nephrons and causes filtration of proteins through the glomerulus and will cause nephropathy[8].

Keeping this research evidence as background, this study was initiated and designed to investigate the development of proteinuria, nephropathy, under the influence of glycemic control and elevated BP. Study findings may help us modify clinical guidelines, emphasizing the need for routine monitoring of both HbA1c and blood pressure in diabetic patients to mitigate the risk of developing proteinuria. The findings may help identify patients at higher risk of renal complications earlier, enabling more proactive management of diabetes to prevent progression to more severe kidney disease.

Objectives:

- To measure Blood pressure, glycosylated hemoglobin and urine protein levels in type 2 diabetes mellitus patients.
- To find out the correlation between glycosylated hemoglobin with Blood pressure and urine protein levels in type 2 diabetes mellitus patients.

Materials and Methodology:

An analytical prospective study was conducted on randomly selected 70 type 2 diabetes mellitus patients attending as out-patients in the department of medicine at Kanachur Institute of Medical Sciences. The patients were grouped into 2, based on the glycemic control. Patients with HbA1c > 7.0% were grouped as (poor control) Cases/ Group 1, while those with 1HbA1c ≤ 7.0% were considered as (good control) Controls/ Group 2. The sample size was calculated by the formula

n=(Zα/2)2 σ2 / E2, where E is margin of error (0.3), σ is standard deviation (1.28), (Zα/2)2 is 1.96 of 95% confidence interval[7]. Sampling procedure was done by simple random sampling. Ethical clearance was obtained from the Institutional Ethical Committee before commencing the study.

Inclusion Criteria:

Seventy Diagnosed cases of T2DM patients, diagnosed by American Diabetes Association, aged between 30 years to 60 years, who are on oral hypoglycemic, not on insulin and willing to participate in the study were included in the study.

Exclusion criteria:

Patients with urinary tract infection, chronic renal failure, glomerular nephritis due to other systemic conditions will be excluded from the study. Pregnant women will also be excluded from the study.

Methodology:

Blood sample which is sent to lab for renal function tests, blood sugar estimation and HbA1c by treating physician was used. Urine sample sent for urine protein estimation was also used. No separate blood and urine samples were collected exclusively for this study purpose. Written informed consent was taken from the study participants after explaining the procedure. Detailed history was taken and a systematic general, systemic examination was done. Blood pressure was recorded manually by using sphygmomanometer on subject lying in supine position.

Routine procedure for collection of blood Sample in laboratory:

As per treating physician's request, 5ml of venous blood sample was collected, after overnight fasting, from antecubital vein under all aseptic precautions. It was allowed to clot and then centrifuged for serum separation. Serum was used for the analysis of all the pre mentioned investigations. The tests were done on the same day after serum separation. EDTA blood was collected for HbA1c estimation in cases. All the investigations except HbA1c were carried out in auto analyzer Vitros 5600. 30 ml spot urine was collected in a sterile container with all aseptic precautions for urine protein estimation.

1. Blood glucose was estimated by glucose oxidase - peroxidase method[9].

2. Serum creatinine was estimated by enzymatic method [10].
3. HbA1c was estimated by fluorescence immunoassay method [11].
4. Serum urea was estimated by enzymatic method [12].
5. Serum uric acid was estimated by uricase method[13].
6. Urine protein levels was estimated by pyrocatechol violet dye method[14].

Statistical analysis:

Data was analyzed using statistical software SPSS version 21. Values were expressed as mean ± SD (standard deviation). Comparison of values between cases and controls was done by using independent Student's t test. Correlation between two parameters was done using Spearman rho correlation test. p value of less than 0.05 was considered as statistically significant.

Results:

Table 1: Comparison of RBS, Urea, Creatinine, Uric acid, HbA1c, SBP, DBP and Urine protein levels in both the groups.

				Percentile			
	Group	Mean	SD	25th	50th	75th	p Value
RBS (mg/dl)	Cases	236.8	42.97	202	234	259	<0.001**
	Controls	153.14	14.55	145	152	164.5	
Urea (mg/dl)	Cases	61.94	12.31	52.5	62	68.5	<0.001**
	Controls	23.49	4.74	20	23.5	26	
Creatinine (mg/dl)	Cases	2.81	0.71	2.4	2.8	3.25	<0.001**
	Controls	1.04	0.2	0.85	1.10	1.2	
Uric acid (mg/dl)	Cases	7.04	0.92	6.52	7.2	7.63	<0.001**
	Controls	5.65	0.59	5.23	5.71	5.96	
HbA1c(%)	Cases	10.9	1.53	9.8	10.8	12.2	<0.001**
	Controls	5.78	0.45	5.35	5.8	6.1	
SBP (mm Hg)	Cases	153.77	14.57	140	150	160	<0.001**
	Controls	113.66	4.78	110	114	118	
DBP (mm Hg)	Cases	91.77	4.79	90	92	96	<0.001**
	Controls	75.77	4.38	70	76	80	
Urine protein (mg/dl)	Cases	185.67	336.45	13	33	163	0.003
	Controls	15.97	6.46	10.5	17	19.5	

p value <0.001** is highly significant.

Table 1 shows Comparison of RBS, Urea, Creatinine, Uric acid, HbA1c, SBP, DBP and Urine protein levels in both the groups. Group 1 (poor control) cases had significant increase in RBS, Urea, Creatinine, Uric acid, HbA1c, SBP, DBP and Urine protein levels compared to group 2 good control patients.

Table 2: Correlation of HbA1c with Urine protein, SBP and DBP.

HbA1c	Urine protein	SBP	DBP
Spearman's rho correlation	0.420	0.752	0.742
p value	<0.001**	<0.001**	<0.001**

p value <0.001** is highly significant.

Table 2 shows positive and highly significant correlation of HbA1c with Urine protein, SBP and DBP.

Table 3: Correlation of Urine protein with RBS, Urea, Creatinine, Uric acid, SBP and DBP.

Urine protein	RBS	Urea	Creatinine	Uric acid	SBP	DBP
Spearman's rho correlation	0.364	0.374	0.301	0.190	0.280	0.351
p value	0.002*	0.002*	0.011*	0.114	0.019*	0.003*

p value < 0.05 statistically significant.

Table 3 shows significant correlation of Urine protein with RBS, Urea, Creatinine, Uric acid, SBP and DBP.

Discussion:

Type 2 Diabetes mellitus is a most common metabolic disease. If the glycemic control is not adequate, major and minor complications can set in gradually. Renal involvement is one of the major complications of uncontrolled T2DM.Early diagnosis of renal involvement is necessary to prevent development of Diabetic nephropathy and End stage renal disease.

This study estimated glycemic control, blood glucose values, serum urea, creatinine and uric acid levels, Blood pressure levels in T2DM with good glycemic control (HbA1c< 7%) and T2DM with poor glycemic control(HbA1c> 7%).

It is a well-known factor that HbA1c measures glycemic control in T2DM. Our study showed increase in HbA1c in group 1 patients. Studies have shown that strict glycemic control can lead to decrease in microvascular complications of diabetes [15,16].

Increased level of BP is a risk factor for renal damage in T2DM and can lead to excretion of protein in urine. Proteinuria is known as the early marker of nephropathy. In our study, group 1 cases had increased blood pressure values and urine protein compared to group 2. Similar result was obtained in many other studies [17].

Elevated glucose levels in T2DM give rise to advanced glycation end products. These products deposit on glomerulus resulting in hypertrophy of glomerular membrane, which leads to proteinuria [1].

Results of our study showed that urine protein levels and BP levels were high in Group 1 cases. This shows that achieving good glycemic control, HbA1c <7% will help in reducing the risk of proteinuria and also hypertension. This is in accordance with results of many other studies [16,18,15,19].

Among the 2 groups, Serum Urea, Creatinine, Uric acid, HbA1c, BP and Urine protein levels were statistically higher in T2DM with HbA1c > 7% group 1 patients. Spearman rho correlation showed HbA1c positively and significantly correlating with urine protein levels and blood pressure. This result is supported by many articles [19,20].

Spearman rho correlation of Urine protein levels in poor control group showed significant and positive correlation with RBS, Urea, Creatinine and Blood pressure. This finding is also seen in other studies[5,8,16,19].

Poor glycemic control results in hemodynamic and some metabolic changes in the glomerulus which damage the endothelial cells and podocytes. These changes induce variation in the glomerular basement membrane and glomerular filtration gets affected. Slowly negative ionic charge on basement membrane is lost. Size of the pores in glomerulus increase because of podocyte and endothelial cell damage. This causes loss of glomerular filtration selectivity and leads to proteinuria [1,19].

Conclusions: Our study demonstrated high levels of RBS, Urea, Creatinine, Uric acid, SBP, DBP and Urine protein levels in T2DM with HbA1c > 7% group. Urine protein levels were positively and significantly correlated with HbA1c, SBP and DBP.

Blood pressure control is essential to prevent kidney damage in the diabetic state, and to slow down the progression of kidney disease. Diabetes management requires proper control over glycemic status and Blood pressure. Diabetic nephropathy is an important micro vascular complication of diabetes mellitus. Glycemic control and renal involvement are closely associated in diabetes. Proteinuria is an important clinical sign of diabetic nephropathy. Proteinuria can be used as a tool for screening diabetic patients with renal involvement in out-patient clinics. Physicians should emphasize the importance of glycemic control. Periodic estimation of urine protein in T2DM might help in identifying the early stages of renal impairment.

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