

Prevention of Complications in Type II Diabetes Mellitus by Measuring Glycated Hemoglobin, 24 Hours Urinary Protein and Protein Creatinine Ratio and Fundus Examination.

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Abstract: The measurement of glycated hemoglobin, 24 hours urinary protein and protein creatinine ratio serves as an important index in the monitoring of diabetes patients to prevent the complications. Screening patients for Retinopathy is again very important. The cause of diabetic complication is not known. Major emphasis has been placed on the polyol pathway where in glucose is reduced to sorbitol by the enzyme aldolase reductase with reduced NADPH as the electron donating coenzyme. Sorbitol molecule is oxidized to fructose by the enzyme Sorbitol dehydrogenase and reduced NAD⁺. Sorbitol appears to function as a tissue toxin and has been implicated in the pathogenicity of retinopathy, neuropathy and cataract. Among the clinically important secondary microvascular complications of diabetes, kidney as the target organ represents a health problem of enormous social cost. Nephropathy like other diabetic complications is probably influenced by genetic factors. 35% of NIDDM patients develop nephropathy. Diabetic nephropathy is duration dependent and extends over many years before becoming clinically evident. Persistent proteinuria appears to predict evidence of kidney damage. Proteinuria is the most widely accepted sign of diabetic nephropathy. Spot protein, creatinine ratio would be more accurate and less time consuming. Diabetic nephropathy is leading cause of morbidity and premature mortality in diabetes subjects. Diabetic nephropathy has an insidious onset with increase in glycated hemoglobin before the appearance of microalbuminuria.

Keywords: Diabetic nephropathy, Glycosylated hemoglobin, Spot Urine Protein:Creatinine Ratio, 24 hours urinary protein.

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I. Introduction

It has been estimated that on the average the expected life span of diabetics is 2/3rd that of non diabetics. In the past, knowledge about diabetic complications was largely limited to description of morphological changes and clinical manifestations. However in the last decade, physiological and biochemical studies have provided a great deal of new information about micro-angiopathy and diabetic complication (Brownlee, 1981; Albert 1982).

Renal capillary damage resulting in edema, new vessel formation and hemorrhage makes blindness 25 times more prevalent than in normal population. Cataract appears early in life and seems to progress more rapidly in diabetics than in non diabetics. Chronic renal failure with proteinuria resulting from glomerular capillary damage secondary to basement membrane thickening is 17 times more prevalent (Crafford, 1977). Focussing on prevalence of CAD amongst diabetics in India starting with data of multicentric study conducted by ICMR (1984-1987) to recent publication from Ahmedabad, there has been visible rise of prevalence from 5-8% to 20-30% amongst diabetics over the period of time. This is an alarming situation and needs introspection with reference to quantum increase in prevalence as well as risk factors.

Severe proteinuria in Type II diabetes was defined by a urine Protein:Creatinine ratio >5.0. Glycosylated hemoglobin represents past 6-8 weeks of glucose concentration in blood; a period approximately equal to the half life of the average RBC. Normal glucose produces a normal amount of glycated hemoglobin. In diabetes mellitus, higher amount of glycated hemoglobin indicates poorer control of blood glucose level.

II. Aim

The aim of the study was to investigate patients with diabetes mellitus developing complications by measuring glycosylated hemoglobin, spot protein:creatinine ratio, 24 hours urinary protein in normal and Type II diabetes patients. Patients were also screened for neurological complications and for retinopathy and cataract formation.

III. Methods

The present study was conducted at Princess Esra Hospital, Deccan College of Medical Sciences.

The following parameters were analysed

1. Fasting Blood Glucose: In automated analyzer Cobas c 311 by Glucose Oxidase Peroxidase method. Blood was collected in grey cap vacutainer with NaF/Na₂EDTA
2. Glycosylated hemoglobin: Done in semiauto analyser Stat Fax (Direct with calibrator) by Immunoturbidimetry method using Beacon reagent. Blood was collected in a lavender cap vacutainer with K₂EDTA
3. Spot Protein:Creatinine Ratio: Done in semi auto analyzer Merck-Microlab 300. Protein measured by 3% Sulphosalicylic acid method. Creatinine measured by Modified Jaffe Method. Finally, the ratio was calculated.
4. 24 Hours Urinary Protein: Done in semi auto analyzer Merck Microlab 300 by Sulphosalicylic acid method and the value was calculated

S.No.	Parameter	Units	Reference ranges
1.	Fasting Blood Sugar	mg/dl	80-110
2.	HbA1c	%	Non Diabetic <5.7 Pre Diabetes 5.7 - 6.4 Diabetes >6.5
3.	24 Hours Urinary Proteins	mg/day	<150
4.	Spot Urine Protein/Creatinine Ratio	-	Normal <0.2 Low Grade Proteinuria 0.2 - 1.0 Moderate Proteinuria 1.0 - 5.0 Severe Proteinuria > 5.0

Table showing comparison of FBS, HbA_{1c}, 24 hour urinary protein and spot urine protein:creatinine ratio between controls and diabetic subjects

S.No.	Parameter	No of subjects	Mean ± SD	P value Cases vs Control	
1.	FBS	Control	20	91 ± 11.0	<0.001
		Cases	30	193 ± 78.8	
2.	HbA1c	Control	20	5.21 ± 0.73	<0.001
		Cases	30	7.92 ± 1.48	
3.	24 Hour Urinary Protein	Control	20	124 ± 1.33	<0.001
		Cases	30	2619 ± 1.96	
4.	Spot Urine Protein/Creatinine Ratio	Control	20	0.12 ± 0.61	<0.001
		Cases	30	3.11 ± 1.22	

IV. Results And Discussion

Diabetes mellitus is a complex disorder affecting the metabolism of carbohydrates, proteins and lipids. The early detection and treatment of this condition prevents complications and further decreases the morbidity and mortality. Persistent elevation in blood sugar (and therefore HbA_{1c}) increases the risk of long term complications of diabetes such as coronary artery disease, stroke, heart failure, kidney failure, blindness, erectile dysfunction, neuropathy (loss of sensation, especially in the feet) gangrene and gastroparesis. Screening and early diagnosis for renal involvement has to be done. It is well documented that glycemic control correlates with levels of glycosylated hemoglobin (Koenig RJ) (Jovanovic) (Le-Ran A). It is observed that glycosylated hemoglobin values positively correlated with 24 hours urinary protein and spot urine protein:creatinine ratio (Mogensen CE) (Townsend JC) (Banerjee). Highly significant increase in 24 hour urinary protein concentration in diabetic subjects is observed when compared to controls (Nathan DM) (Nelson RG). There is a significant increase in Spot urine protein:creatinine ratio in diabetic subjects when compared to controls (Nathan DM) (Nelson RG)

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