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ORIGINAL ARTICLE

ASSOCIATION OF GLYCEMIC CONTROL WITH URINARY PROTENURIA AND PROTEIN: CREATINE RATIO IN TYPE II DIABETIC SUBJECTS

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ABSTRACT: Diabetes has become the most common single cause of end stage renal disease in USA Europe and Asia. Diabetic nephropathy is leading cause of morbidity and premature mortality in diabetic subjects. Glycemic control closely associates with renal involvement in diabetes. Proteinuria is recognized as a independent risk factor of renal disease. Diabetic nephropathy has an insidious onset with increase in glycosylated hemoglobin before the appearance of micro albuminuria.

KEYWORDS: Diabetic nephropathy, Glycosylated Hemoglobin, Protein: Creatinine ratio, 24-hr Urinary Protein.

INTRODUCTION: Diabetes is an ice berg disease. Currently the number of cases of diabetes worldwide is estimated to be around 150 million. This number is predicted to double by 2025 (A prevalence rate of 5.4%) with greatest number of cases being expected in China & India. In India the prevalence of disease in adults is 2.4% in rural and 4.0-11.6% in urban dwellers.[1]

Among the clinically important secondary micro vascular complications of diabetes, Kidney as the target organ represents a health problem of enormous social cost.[2] Nephropathy like other diabetic complications is probably influenced by genetic factors.[3] 35% of NIDDM develop nephropathy.[4] Diabetic nephropathy is duration dependent and extends over many years before clinical evident.[5] Persistent proteinuria appears to predict evidence of kidney damage.[6] Proteinuria is the most widely accepted sign of diabetic nephropathy.[7],[8] Random Urine Protein: Creatinine ratio would be more acceptable and less time consuming. When GFR is stable, Protein: Creatinine ratio remains fairly stable.[9],[10],[11] Hence Protein: Creatinine in single voided Urine sample is accurate, convenient inexpensive and reliable.

Heavy Proteinuria in type-II diabetes was defined by a Urine Protein (g/l) to Creatinine (g/l) ratio of >=1.0 which corresponds to urine excretion rate of about 1gm/day.[12] Glycosylated hemoglobin represents past 6-8 weeks of glucose concentration in blood. Another advantage of Glycosylated hemoglobin value is to assess glucose control,[13],[14],[15] and screening test for uncontrolled diabetes.[16] The risk of Proteinuria in patients with NIDDM increases with increasing Glycosylated hemoglobin.[17] It is difficult to precisely date the onset of type-II diabetes, so screening for micro albuminuria 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.

AIM: The aim of study was firstly to investigate glycosylated hemoglobin and association of urinary Protein in normal and type-II diabetic subjects. Secondly association of 24hr urinary Protein and random Protein: Creatinine ratio in same normal and type-II diabetic subjects. Thirdly comparison of 24 urinary protein and protein:creatinine ratio in diabetic subjects in relation to duration of diabetes.

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METHODS: A Study of estimating Glycosylated hemoglobin, random Urinary Protein: Creatinine ratio and 24hr urinary Protein was conducted in diabetic subjects and controls in Katuri Medical College and Hospital. Each gave an informed consent and study was approved by ethical and research committee of Katuri Medical College and Hospital.

A total of 100 subjects participated 60 were diabetic subjects who were on treatment and 40 controls who were non- diabetic. Study includes both males and females in age group of 40-82 years. Fasting venous blood of about 3ml was collected from selected subjects under aseptic precaution in EDTA vial and 2ml in plain clot activation tube.

24hrs Urine was collected by subjects to begin collection in container having 4ml of 10% thymol in isopropanol as preservative .Total volume was noted and calculation was done for 24hrs.

A random Urine sample of 5ml was collected on the next day just before analysis after completion of 24 hrs collection.

The Biochemical parameters were analyzed by biosystem automated analyzer.

The following parameters are studied:

1. Fasting Blood Glucose.
2. Glycosylated hemoglobin.
3. Random Urine Creatinine.
4. Random Urine Protein.
5. 24hr Urinary Protein.

Statistical analysis was done using SPSS software. Results were expressed as mean, +/- SD. Statistical correlation was done using partial correlation test and significance was expressed in the form of 'p' value. 'p' value of <0.5 was considered statistically significant and 'p' value <0.01 was considered highly significant.

RESULTS:

Comparison of fasting blood glucose and glycosylated hemoglobin, 24 hrs urinary protein and protein: creatinine ratio in random urine sample levels between controls and diabetic subjects.
P<0.001 (Highly Significant).

	No. of Subjects	**Particulars**	**Fasting blood Glucose (mg/dl)**	**Glycosylated Hb (%)**	**24-hr Urinary Protein (g/day)**	**Protein: Creatinine Ratio in random sample**
Controls	40	Mean±S.D	93.0±12.0	6.18±0.63	0.10±0.09	0.09±0.08
Cases	60	Mean±S.D	197±89.5	7.85±1.59	1.79±1.07	1.80±1.28
Cases vs Controls		P- Value	<0.001	<0.001	<0.001	<0.001

Comparison of 24hrs Urine Protein Concentrations and Protein: Creatinine Ratio in Random Urine Sample Level In Diabetic Subjects In Relation To Duration Of Diabetics.

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Duration	No. of Cases	24 Hour Urinary Protein (g/day)	Protein: Creatinine Ratio in Random Sample
<5 Years	27	1.23±0.66	1.34±0.71
>5 Years	33	2.10±1.47	2.06±1.53
	P-Value	<0.025, S	< 0.05, S

P<0.05 (Significant)

DISCUSSION: Type-II Diabetes Mellitus is commonest endocrine diseases. Lack of glycemic control leads to various acute and long term complications. The long term complications of Diabetes cause morbidity and premature mortality. Renal involvement is one such complication. Screening and early diagnosis for renal involvement has to be done. It is well documented that glycemic control correlate with levels of glycosylated hemoglobin.[18],[19],[20],[21],[22]

The mean values of Glycosylated hemoglobin in diabetic subjects are higher when compared to controls. This is in accordance with study of Trivelli LA et al,[23] Gonen B et al,[19] Nathan DM et al,[14] Koenig RJ et al,[24] and Bunn HF.[25]

It is observed that glycosylated hemoglobin values positively correlate with 24hr Urinary Protein and Urine Protein: Creatinine ratio in random urine sample. This is in accordance with the study of viberti GC et al,[26] Kroc collaborative study group[27] and Krolewski AS et al.[7]

Renal involvement in poor glycemic states appears after few years of metabolic abnormality.[28] The development of Proteinuria in diabetes mellitus is due to increase in vascular permeability which is related to degree of poor metabolic control represented by fluctuations in Glycosylated hemoglobin.

Highly significant increase in 24-hr Urinary Protein concentration in diabetic subjects is observed when compared to controls. This is in accordance with Nathan DM et al,[14] Nelson RG et al,[28] Zelmanovitz T et al.[15]

Metabolic disturbance of diabetes initiates Nephropathy due to disturbance in glomerular haemodynamic factors, glomerular basement thickening and expansion of mesangium.[29],[30] These predominantly associated with level of Glycosylated hemoglobin and duration of diabetes.

The reference method for estimating urine protein concentration accurately is timed 24hr Urine specimen. But for most practical purposes the random urine Protein: Creatinine ratio specimen is considered.[27],[7]

There is significant increase in Protein: Creatinine ratio in diabetic subjects when compared to controls. This is in accordance with study of Kunzelman CL et al,[30] Nathan DM et al,[14] Nelson RG et al,[28] Zelmanovizt T et al.[15]

There is a Significant correlation in 24hr Urinary Protein and random Protein: Creatinine ratio in Diabetic subjects in relation to duration of onset of Diabetes.[29]

The present study suggests estimating glycosylated haemoglobin as an indicator of glycemic control and protein: creatinine ratio in random urine sample for renal involvement in diabetic subjects provide a reliable method for early diagnosis and intervention. The possibility to prevent, delay or reverse the progression of diabetic nephropathy can be achieved only by perfect long term metabolic control.

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CONCLUSION: Glycosylated hemoglobin provides a retrospective index of glucose control over a time in diabetic subjects. 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. 24 hrs urinary Protein is definitive method but it is time consuming and inaccurate. Urinary Protein: Creatinine ratio in random urine sample correlated with 24 hrs urinary protein concentration. This serves as an early, accurate, convenient and reliable method to estimate Proteinuria and so can be used as a tool for screening diabetic patients with renal involvement in out-patient clinics and also in health camps.

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