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Determine the Relation between Duration of Type 2 Diabetes Mellitus and Its Complication - Diabetic Nephropathy

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Abstract: *Diabetes is a chronic disease in which the body cannot regulate the amount of sugar in the blood. It is a disease caused by deficiency or diminished effectiveness of endogenous insulin. It is characterized by hyperglycemia leading to defect in metabolism which predominantly affect vasculature. This consistent hyperglycemia is associated with long term complications like diabetic nephropathy, Cardiovascular diseases, Retinopathy, Neuropathy, etc. Diabetic nephropathy is the largest cause of chronic kidney disease. The purpose of this study is to determine the relation between type 2 Diabetes Mellitus and its complication - Diabetic Nephropathy. The study also tries to find the correlation between duration of diabetes mellitus and Diabetic nephropathy.*

Keywords: *Diabetes mellitus, nephropathy, hyperglycemia, insulin*

I. Introduction

"Diabetes" is derived from Greek word "diabainein". It means the discharge of excess amount of urine. It is a metabolic disorder of multiple etiology. It is characterized by Chronic Hyperglycemia due to defects in insulin secretion / action or both.

The main symptoms of diabetes are 3 Ps

1. Polyuria
2. Polydypsia
3. Ploy phagia

Epidemiology of Diabetes Mellitus:-

WHO estimates that 220 million people worldwide have diabetes. In the year 2000 estimated population to have diabetes around the world was around 171 million which is projected to increase to 366 million by 2030.

The top three countries in number of people with diabetes are India, China and U.S.A. [1-3]

There is a rising pattern in prevalence of type 2 diabetes in India both in urban and rural areas although it is 3 times higher among urban population[4].

Classification:-

1. Type I
   - Immune mediated
   - Idiopathic
2. Type II – (Impaired insulin secretion/ insulin resistance)
3. Other Specific types

a. Genetic defects of islet β cell function
b. Genetic defects of insulin action
c. Diseases of exocrine pancreas
d. Endocrinopathies
e. Drug or chemical induced diabetes
f. Infections
g. Uncommon forms of immune mediated diabetes
h. Other genetic syndromes

4. Gestational diabetes mellitus

Some patients with Type 2 diabetes mellitus require insulin so old terms of Insulin Dependent Diabetes Mellitus (IDDM) for type I and Non Insulin Dependent Diabetes Mellitus (NIDDM) for type 2 are inappropriate.

Diabetic Nephropathy

Nearly 50% of the prevalence of chronic kidney disease is attributed to diabetes and hypertension[5-6]. Approximately 40% of the patients with type 2 diabetes will develop diabetic kidney disease[7]. In the United

States, diabetes has become the most common single cause of end stage renal disease defined by the need for dialysis or transplantation[8-9]. Clinical features are usually absent until advance chronic Kidney disease develops.

Diabetic Nephropathy may be diffused or nodular. In early stages Glomerular Filtration Rate (GFR) is increased leading to enlarged Kidney but principle feature of Diabetic Nephropathy is proteinuria. This develops insidiously starting as intermittent micro albuminuria before progressing to constant proteinuria. The earliest clinical evidence of nephropathy is the appearance of low but abnormal levels (≥ 30 mg/day) of albumin in urine, referred to as microalbuminuria.[10]

In addition to being the earliest manifestation of nephropathy albuminuria is a marker of increased cardiovascular morbidity and mortality. Three types of lesions are encountered in diabetic nephropathy[11-12].

i. Glomerular lesions
ii. Renal vascular lesions, principally arteriosclerosis
iii. Pyelonephritis including necrotizing papillitis.

Optimal control of blood Glucose and blood pressure is necessary for primary prevention.Screening for microalbuminuria can be performed by three methods[13] –

(1) Measurement of ACR in a random spot collection.
(2) 24-hour collection with creatinine, allowing the simultaneous measurement of creatinine clearance.
(3) Timed (e.g. 4 hours or overnight) collection.

The first method is easy, more accurate and so is therefore preferred.

Table 1.Definitions of abnormalities in albumin excretion

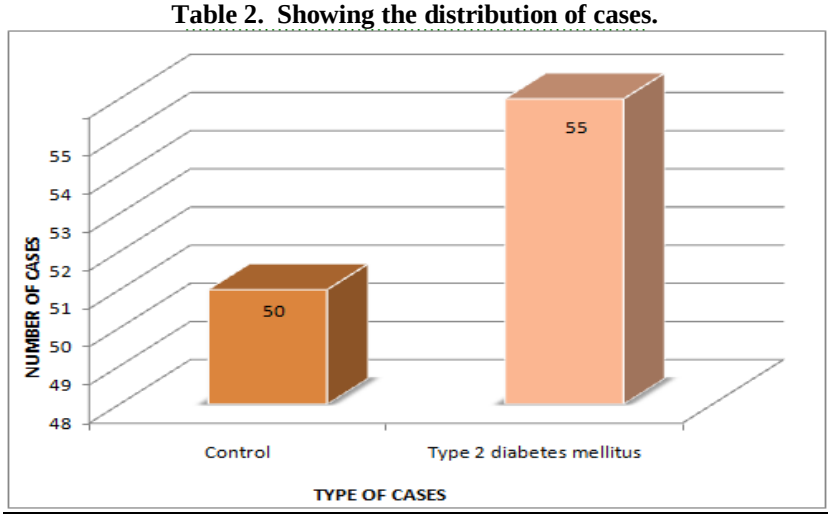
Category	Spot collection (µg/mg creatinine)	24h collection (mg/24 h)	Timed collection (µg/min)
Normal	<30	<30	<20
Microalbuminuria	30-299	30-299	20-199
Clinical albuminuria	>300	>300	>200

'Microalbuminuria' refers to the excretion of albumin in the urine at a rate that exceeds normal range, but below the detection level by test for total protein[14].

II. Material And Methods

Present study was conducted in the Department of Biochemistry, Mata Gujri Medical College & LSK Hospital, Kishanganj. Total number of 105 patients were enrolled and divided into two groups.

Table 2. Showing the distribution of cases.



Group I (Control Group): - Out of 105, 50 patients (30 males and 20 females) were in group I who were normal healthy individual. Each patient was clinically examined and was included in study after finding then as normal individual. They were selected from postgraduate students, teachers, undergraduate students, paramedical staff, attendants of patients admitted in Indoor of Mata Gujri Medical College & LSK Hospital, Kishanganj, Bihar (INDIA).

Group II (Type 2 Diabetes Mellitus): - This group included 55 cases (31 males and 24 females) of type 2 diabetes mellitus. These cases were taken from Medical Outdoor and admitted patients in the Indoor Department of Medicine, Mata Gujri Medical College & LSK Hospital, Kishanganj, Bihar (INDIA).

Patients:
Before inclusion in study patients were informed and consent was taken. Patients included in the study (Group II) were having:
(i) History of diabetes mellitus for 10 years or more and undergoing treatment for diabetes.
(ii) Normotensives (B.P. <130/80 mm of Hg)
(iii) Age 20 – 50 years.

Exclusion Criteria:
(i) Cases having proteinuria detectable by dipstick tests.
(ii) Cases having any evidence of infection.

III. Methodology

Following estimations were done in the Department of Biochemistry, Mata Gujri Medical College & LSK Hospital, Kishanganj.
1. Estimation of micro-albumin in urine.
2. Estimation of serum creatinine
3. Estimation of fasting and postprandial blood glucose to select the diabetic patients.

Sample collection

Urine samples were collected and tested by dipsticks for the presence of frank proteinuria. Dipstick negative urine samples were included in the study.

Blood samples were collected for fasting and postprandial blood glucose estimation.

Urinary albumin was estimated by immunoturbidimetric method and Urinary creatinine was estimated by Modified Jaffe's method

The blood glucose level was estimated by Glucose Oxidase & Peroxidase (GOD-POD enzymatic) method. All the estimations were performed on ERBA Chem-7 semi auto-analyzer.

Observation
The results are tabulated and represent in tables.

Table III. Showing number of cases, range, mean, standard deviation & standard error of mean values of albumin creatinine ratio in healthy controls.

Group	No. of cases	Albumin creatinine ratio in µgm/mg of creatinine			
		Range	Mean	SD	SEM
Control	50	8 – 28 (µgm/mg of creatinine)	18.98	5.94	0.84

SD – Standard Deviation
SEM – standard Error of Mean
Table shows that albumin-creatinine ratio in normal healthy subjects varied from 8 µgm/mg of creatinine to 28 µgm/mg of creatinine with a mean value of 18.98 µgm/mg of creatinine.

Table – IV. Showing number of cases, range, mean, standard deviation and standard error of mean values of albumin creatinine ratio in cases of type 2 diabetes mellitus.

Group	No. of cases	Albumin creatinine ratio in µgm/mg of creatinine			
		Range	Mean	SD	SEM (±)
Type 2 Diabetes mellitus	55	16 – 124 µgm/mg of creatinine	49.27	32.00	4.31

Table shows that in cases of type 2 diabetes mellitus, albumin-creatinine ratio ranged from 16 µgm/mg of creatinine to 124 µgm/mg of creatinine with the mean value of 49.27 µgm/mg of creatinine.

Table – V. Showing difference in mean albumin creatinine ratio of control group with mean value of type 2 diabetes mellitus group respectively and its statistical significance.

Group	Difference in albumin creatinine ratio in µgm/mg of creatinine	't' value	'p' value	Remarks
Type 2 diabetes mellitus and Control	32.34	7.13	<0.001	S

S = Significant;

Table shows a statistically significant (P<0.001) difference in mean albumin – creatinine ratio values of type 2 diabetes mellitus with control, it also shows a statistically significant (P<0.001) difference in mean albumin creatinine ratio values of type 2 diabetes mellitus and control.

Table – VI. Showing percentage of cases in type 2 diabetes mellitus according to albumin-creatinine ratio (ACR).

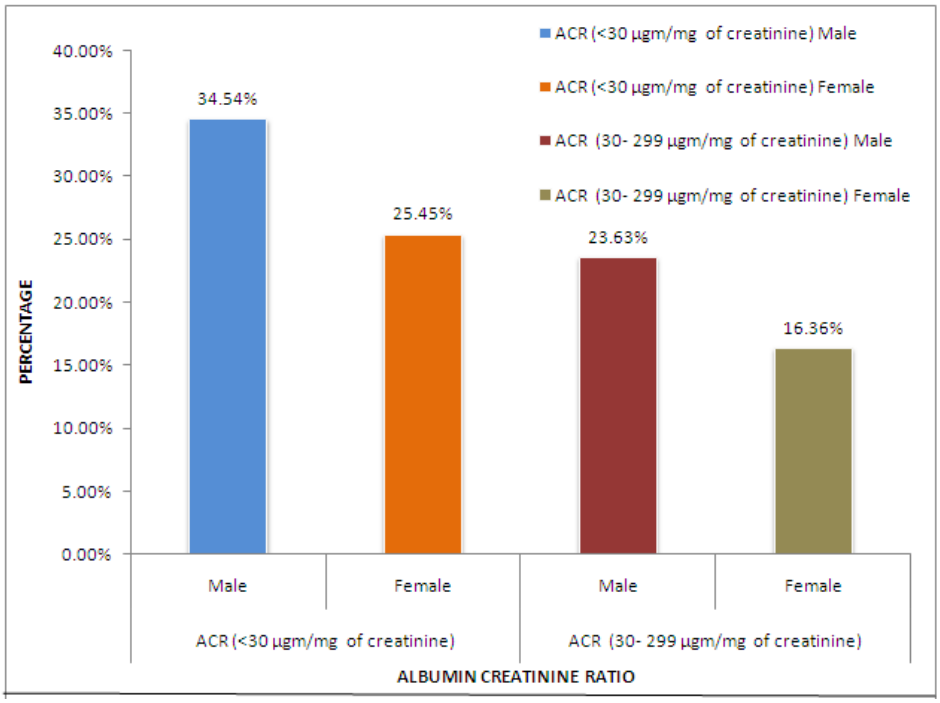


Table shows that 55 cases of type 2 diabetes mellitus, of which 13 are males and 9 are females are having microalbuminuria and 33 cases of type 2 diabetes mellitus, of which 19 are males and 14 are females are in normoalbuminuric range.

Table – VII Showing number of cases and mean values of albumin creatinine ratio with duration of diabetes in cases of type 2 diabetes mellitus.

Group	Duration of DM (in yrs.)	No. of cases (55)	Mean of ACR
Group 1	10 - 14	45	41.62
Group 2	15 – 19	6	64.00
Group 3	≥20 yrs.	4	113.25

Table shows that albumin creatinine ratio increases with the duration of disease in cases of type II diabetes mellitus and this increase in albumin creatinine ratio is significant in all the three groups. The mean albumin creatinine ratio found for (≥ 20 years duration) to be 113.25 µgm/mg of creatinine justifies the above statement.

IV. Discussion

Diabetes is a costly disease in individual, social and economic terms, and the global burden of diabetes is increasing day by day. It is associated with premature morbidity and mortality, and so should not be thought of as a 'mild' condition. In many people it presents as an asymptomatic disease. With improved screening procedures and better treatments, the long-term outlook for these individuals will be greatly improved.[15]

It is a global problem with India being described as the diabetes capital of the world[16]. It has been reported that nearly 30% of chronic renal failures in India are due to diabetic nephropathy.[17]

The present study was undertaken to study the relationship of albumin creatinine ratio in patients of diabetes mellitus suffering from the disease for 10 years to 24 years. The increased morbidity and mortality in diabetes mellitus lead to search for marker for early detection of renal complications. This study also shows that microalbuminuria is an early marker of renal complications in diabetes mellitus. In this study, randomly selected patients went for spot urinary albumin estimation and spot urinary creatinine estimation to detect microalbuminuria by measuring albumin creatinine ration.

Fasting plasma glucose estimation was done to see the relationship of hyperglycemia with microalbuminuria.

The albumin creatinine ratio in 50 normal healthy subjects of which 30 were male and 20 female ranged from 8 µgm/mg of creatinine to 28 µgm/mg of creatinine with the mean value of 18.98 µgm/mg of creatinine (Table III). While ratio in 55 cases of type 2 diabetes ranged from 16 µgm/mg of creatinine to 124 µgm/mg of creatinine with the mean value of 49.27 µgm/mg of creatinine (Table IV).

So from the above statistical analysis, it is evident that in comparison to control group, there is marked increase in the albumin creatinine ratio and it is significant ($P < 0.001$) for type 2 diabetes mellitus.

V. Summary And Conclusion

The above study shows that albumin creatinine ratio was raised in cases of type 2 diabetes mellitus and has positive correlation with the duration of the disease.

Hyperglycemia is the major factor initiating the changes in the kidney. The tissue damage caused by hyperglycemia can be attributed to the hemodynamic factor, glycosylation of tissue proteins and increase activity of the polyol pathway.

Microvascular pressure and flow are increased in early diabetes. Elevated hydrostatic pressure is partly responsible for the leakage of protein and their deposition in the walls of arterioles and capillaries in the kidney. Glycosylation results in change in physical and chemical structure and causes alteration in function of tissue proteins.

Hyperglycemia increases the expression of transforming growth factor beta (TGF β) in the glomeruli and of matrix proteins. TGF β contributes to both cellular hypertrophy and enhanced collagen synthesis seen in diabetic nephropathy.

Finally it can be concluded that a microalbuminuria can be considered as an early marker of renal involvement in type 2 diabetes mellitus and its early detection can significantly reduce the progression of renal complications associated with type 2 diabetes mellitus.

It is essential to access for the diabetic Nephropathy through

- Annual review for people with Type 1 and Type 2 diabetes mellitus
- Measuring urinary ACR and albumin concentration annually.
- Repeat test of abnormal ACR is obtained in absence of proteinuria or a UTI.
- Measure serum Creatinine Annually.

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