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INCIDENCE AND SIGNIFICANTLY ELEVATED LEVELS OF CREATININE AND GRF AMONG DIABETIC KIDNEY DISEASE PATIENTS.

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ABSTRACT
Diabetes mellitus is attaining probably epidemic proportions in India. The level of morbidity and mortality because of diabetes and its ability complications are enormous. The chronic hyperglycemia of diabetes is associated with damage and failure of various organs, especially the eyes, kidneys, nerves, heart, and vascular system. The study therefore was carried out to evaluate levels of Creatinine and GRF among diabetic kidney disease patients.90 Type 2 Diabetes Mellitus patients and 90, age and sex matched healthy controls were included in the study. Routine biochemical markers like FBS, PPBS, Serum urea creatinine, Lipid profile and HbA1c level was measured in all of them. We have found out that creatinine based GFR was significantly reduced in microalbuminuric cases when compared to controls but not significantly reduced in normoalbuminuric diabetics. GFR, and creatinine can serve as a reliable indicator for predicting renal impairment in an early stage in Type 2 Diabetes Mellitus cases.

Key words: Creatinine, Type 2 Diabetes Nephropathy; Glycosylated Hemoglobin, GRF.

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INTRODUCTION

Diabetes mellitus is attaining probably epidemic proportions in India. The level of morbidity and mortality because of diabetes and its ability complications are enormous. The chronic hyperglycemia of diabetes is associated with damage and failure of various organs, especially the eyes, kidneys, nerves, heart, and vascular system. Diabetes is the primary reason of quit-degree renal disorder and diabetic nephropathy which can be also referred to as diabetic kidney disease. It has been suggested that in lifetime 25-45% of the diabetic patients would be developing clinically evident diabetic nephropathy.1

Diabetic Nephropathy is the leading cause of End Stage Renal Disease and affects approximately 40% of Type 2 Diabetic patients and most of the patients entering dialysis are diabetic. In diabetes mellitus, hyperglycemia causes the excess of glucose to combine with free amino acids on circulating. In diabetes mellitus, hyperglycemia reasons the more of glucose to mix with loose amino acids on circulating. This non-enzymatic manner to start with forms reversible early glycosylation merchandise and later irreversible advanced glycosylation end-products (AGEs) via an Amadori rearrangement. The tissue accumulation of AGEs, by cross linking with collagen, can contribute to the associated renal and microvascular complications. Good glycemic manipulate can reduce the prevalence of diabetic nephropathy which is clinically characterized by increasing rates of urinary

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albumin excretion starting from normal albuminuria, which progress to microalbuminuria then macroalbuminuria and eventually to end stage renal disease.[2]

Screening for diabetic nephropathy is currently executed by means of tracking patients for the improvement of microalbuminuria and as adjunct for the estimation of GFR, the determination of serum creatinine (sCr).

The appearance of pathological levels of urinary albumin excretion (UAE) represents the most common clinical sign of early renal involvement in patients affected by diabetes mellitus.[3-4]Moreover, impaired renal function may be present even in patients with normal urinary albumin excretion (UAE) which in addition is tormented by several greater renal factors. In addition, reduced kidney function is associated with increased incidence of cardiovascular morbidity and mortality.[5] the tissue accumulation of AGEs, by crosslinking with collagen, can contribute to the associated renal and microvascular complications. Good glycemic manage can lessen the prevalence of diabetic nephropathy.

The earliest detectable abnormality of nephropathy is microalbuminuria observed by decrease in glomerular filtration charge (GFR) and increase in serum creatinine concentrations. Owing to the increased relevance of early detection and intervention in diabetic nephropathy this study was done to incidence and significantly elevated levels of creatinine and grf among diabetic nephropathy patients.

MATERIAL AND METHODS

This observational study was approved by the local Institutional Ethics Committee and conducted in the Department of Pharmacology and Biochemistry, Sri lakshmi Narayana institute of medical sciences Pondicherry Feb 2019 to July 2019

Ninety patients of type 2 diabetes of age group 35-60 years, attending OPD and indoor in the Department of Medicine, SLIMS in Pondicherry, were included in the study. Patients with Type 2 Diabetes Mellitus were selected and diagnosed on the basis of their history, physical examination, biochemical investigations and according to the Criteria for the diagnosis of Diabetes Mellitus given by WHO.

The control group consisted of 90 age and sex matched healthy adults with normal plasma glucose levels, no symptoms suggestive of diabetes mellitus and no family history of the disease, no history of any kind of kidney disease.3 ml of blood was collected after overnight fasting of 8 hours from all enrolled patients and healthy controls for the assessment of serum creatinine and GRF parameters.

Inclusion Criteria:

- Classic symptoms of diabetes and random plasma glucose concentration ≥ 200 mg/dl
- Fasting plasma glucose ≥ 126 mg/dl
- A1C>6.5%
- 2-hour post load plasma glucose concentration ≥ 200 mg/dl during the OGTT
- The control group consisted of age and sex matched healthy adults with fasting plasma glucose levels ≤ 99 mg/dl and post prandial plasma glucose ≤ 139 mg/dl.

Exclusion Criteria:

Patients with Uncontrolled hypertensive patients, Thyroid disorders, thyroid medications steroid therapy and Cardiovascular disease patients

Univariate analysis determined the links between nephropathy complications (present/absent) and each independent variable. Independent variables contain model one of personal characteristics which include (gender, race, age, physical activity, level of education, smoking history, alcohol history and family history).

Model two include health characteristics (diabetes duration, waist circumference (WC), body mass index (BMI), diabetic medication) and model three clinical variables include (HbA1c, FPG, PPG, BMI, WC, low density lipoproteins (LDL), high density lipoproteins (HDL), total cholesterol, triglyceride, blood pressure, and creatinine clearance (CrCl)) at four visits. In simple logistic analysis, each independent variable was analysed to look at any significant association with dependent variable (nephropathy) and preceded to multiple logistic regressions to confirm the association after excluding confounders. The results of simple logistic regression analysis were recorded as beta, p-value, crude odds ratio and 95% confidence interval.

Multivariate analysis was done on numerical and categorical analysis variable by using binary logistic regression to eliminate confounding effect as there is more than one independent variable. The first step was to do variable selection.

Second step for further multivariate analysis, and selection step was to do manual backward or forward analysis of each variables was excluded of p value which was more than 0.05. The third step was to find a model when all variables have a p value of less than 0.05

Table 1: Characteristics of control group and study group

S.no	Parameters	Control group	Study group	
		Mean ± SD	Normoalbuminuic Mean ± SD	Microalbunuric Mean ± SD
1	Age	76.46 ±9.74	70.24 ± 6.75	66.68 ± 6.64**
2	BMI	26.29 ±4.36	42.74 ± 6.42*	52.90 ± 2.37**
3	Duration of diabetes (in yesr)	-	9.10 ± 4.55	12.52 ± 5.60

***statistically non-significant as compared to controls. **Statistically significant (p<0.01) as compared to control and normoalbuminurics.**

Table 2: Comparision of FPG, PPPG and HbA1C % of the control and study group.

S.no	Parameters	Control group (90)	Study group (90)	
		Mean ± SD	Normoalbuminuic Mean ± SD	Microalbunuric Mean ± SD
1	FPG(mg/dl)	93.74 ± 9.35	156.65 ± 42.34*	186.88 ± 34.69**
2	PPPG(mg/dl)	113.77 ±22.18	309.97 ± 35.41*	266.75 ± 43.27**
3	HbA1C(%)	6.57 ± 0.46	8.3 ± 1.5*	8.9 ± 1.3**

***Statistically significant (p<0.01) compared to controls.**
****Statistically significant (p<0.01) compared to controls and normoalbuminuric cases.**

Table 3:Serum urea and creatinine in control group and study group

S.no	Parameters	Control group(90)	Study group(90)	
		Mean ± SD	Mean ± SD	Mean ± SD
1	Serum urea (mg/dl)	25.86 ± 9.03	31.72 ± 5.61	36.32 ± 19.15
2	Serum Creatinine(mg/dl)	0.60 ± 0.76	0.95 ± 0.19	2.10 ± 0.31

There was no significant increase in either urea or creatinine in cases when compared to controls

Table 4: Lipid Profile of Control Group and Study Group

S.no	Parameters	Control group(90)	Study group(90)	
		Mean ± SD	Normoalbuminuic Mean ± SD	Microalbunuric Mean ± SD
1	Total Cholesterol	183.82 ±14.50	197.61 ±25.98*	197.81 ±39.33*
2	Triglycerides (TG)	138.78 ±39.89	187.90 ±25.33*	225.13 ± 36.13
3	HDLc	49.54 ± 5.32	49.35 ± 5.58	42.61 ± 5.70
4	LDLc	90.62 ±20.73	119.82 ± 19.33*	153.35 ± 39.75
5	VLDLc	29.26 ± 4.19	29.91 ± 4.98*	36.49 ± 9.64

***Statistically significant (p<0.05) as compared to control group.**
#Statistically non significant (p=0.16) as compared to normoalbuminuric.
Statistically significant as compared to normoalbuminuric (p<0.05).

Table 5: Comparison of albuminuria and glomerular filtration rate grading among the studied patients.

GRF grade	Normoalbuminuria (N=46)	Microalbuminuria (N=32)	Macroalbuminuria (N=12)	P
G1 (GFR ≥90 ml/min)	17(36.9%)	1(3.1%)	**0**	**<0**
G2(GFR60–89ml/min)	23(50%)	1(3.1%)	**0**	**.0**
G3a(GFR59-45ml/min)	6(13%)	7(21.8%)	**0**	**01**
G3b(GFR30-44ml/min)	1(2.1%)	19(59%)	**2(16.6%)**	
G4(GFR15–29ml/min)	0	4(12.5%)	**7(58.3%)**	
G5 (GFR <15 ml/min)	0	0	**3(25%)**	

GFR (Glomerular filtration rate) P value less than 0.05 is significant.

DISCUSSION

Diabetes mellitus is a clinically and genetically heterogeneous group of disorders. It is characterized via abnormally high degrees of glucose inside the blood. It is the maximum not unusual endocrine ailment, described via metabolic abnormalities and long-term headaches regarding the eyes, kidneys, nerves, and blood vessels.

Diabetic nephropathy is one of the important long-term headaches of diabetes and the main motive of death and disability in diabetes. Diabetic nephropathy is a kidney ailment that happens as a result of diabetes. Both microalbuminuria and macroalbuminuria in people with DM are related to the multiplied threat of cardiovascular disease. Individuals with diabetic nephropathy usually have diabetic retinopathy.

In diabetic nephropathy glomerular hyperperfusion and renal hypertrophy happen at the early degrees of DM and are related to growth in GFR During the first five yrs of DM, thickening of the glomerular basement membrane, glomerular hypertrophy takes place because the GFR returns to normal. After 5-10 years 40% of people begin to excrete small volumes of albumin in the urine. Although the appearance of microalbuminuria (30-299 mg/day albumin in the urine) is a vital danger element for progression to macroalbuminuria (>three hundred mg/day albumin in the urine), only 50% of individuals development to macroalbuminuria over the next 10 years. Once macroalbuminuria is present, there is a steady decline in GFR, and 50% of people attain ESRD in 7-10 years.

Our observations become undertaken to estimate the serum tiers of creatinine in normal and microalbuminuric kind 2 diabetics. It has tried to explore the usefulness of creatinine and C-G GFR as a marker of early renal involvement in diabetic sufferers which in flip can assist in their well-timed intervention. The suggested age in the microalbuminuric DM instances changed to drastically higher (p<zero.01) than the controls as nicely normoalbuminuric DM instances.

In normoalbuminuric DM cases imply BMI was 52.90 ± 2.37and in microalbuminuria mean BMI becomes forty-two. Seventy-four ± 6.42which turned into drastically raised compared to normoalbuminuric institutions and controls. This declares that higher BMI is a threat element for diabetes.6 Conversely the BMI of normoalbuminuric instances as compared to healthful controls did no longer show any huge distinction. (p=zero.12)

The gift observes consequences imply values PPPG turned into determined to be considerably raised ($p \leq$ zero.01) in each normoalbuminuric case and microalbuminuric case while as compared to wholesome controls. FPG was found to be substantially raised ($p \leq 0.01$) in both normoalbuminuric and microalbuminuric cases compared to healthy controls. Is can being because of insulin resistance, impaired insulin secretion, and accelerated hepatic glucose manufacturing.

Monnier, et al. 20037demonstrated the significance of PPBS to growth in HbAIC% level this take a look at resembling to our look at HbA1C (%) on top of things was substantially raised (p<0.01) in normoalbuminuric and microalbuminuric cases. This caused by better PPBS will produce extended superior glycation giving up merchandise and oxidative strain thereby producing microvascular difficulties like diabetic nephropathy.

Serum urea was not notably improved in instances in comparison to controls which can be urea attention within the blood can vary with weight-reduction plan, hepatic feature, and severe disease states and also freely filtered by using the glomerulus and now not secreted with the aid of the tubules, but up to (forty–70% is passively reabsorbed from the renal tubules that is similar to observe of Newman DJ, et al8 Serum creatinine stage turned into increase significantly when in comparison to governing until the GFR is decreased to much less than 50% of its regular cost due to improved tubular secretion of creatinine which ends correlated to Arindam Sur et al study9.

Our results display that 36% of sufferers had MA and thirteen. Three % had macroalbuminuria. These outcomes agree with that of Farahat TM et al 10study which reported that during type 2 diabetic patients, MA and macroalbuminuria changed to 34.2 and 12.8% respectively.

Lipids profile extended (Elevated triglycerides, reduced excessive-density lipoprotein (HDL), and accelerated small dense low-density lipoprotein (LDL) debris) in the present study that is coincided with the Mahato RV, et al look at those raised lipid levels are involved inside the pathogenesis and development of renal illnesses.11Which may be due to insulin resistance in adipose tissue as a result of which loose fatty acid (FFA) flux from adipocytes is elevated, leading to extended lipid synthesis in hepatocytes.

GFR is commonly regular because of the nice ordinary estimate of kidney features. The suggested C-G e-GFR (ml/min/1.73m²) calculated inside the controls, normoalbuminuric and microalbuminuric diabetes mellitus instances were 126.36 ± 14. Fifty-five; 109.37 ± 17.10; and 82. Seventy three±thirteen.39 respectively. C-G e-GFR is drastically decreased (p<zero.05) most effective within the microalbuminuric cases compared to controls.

Concurrence of glomerulosclerosis and basement membrane thickening causes decreased filtration characteristic of a kidney. Therefore, upward push inside the serum stages creatinine as it's far solely filtered by means of the glomerulus with catabolism in tubules without tubular secretion.

Conclusion

It is already set up that creatinine is a touchy marker for predicting renal harm in Type 2 DM cases. Our examine GFR became determined to be less considerably decreased in type 2 DM instances with microalbuminuria. Therefore, according to our examine, GFR, and creatinine can serve as a dependable indicator for predicting renal impairment in an early level in Type 2 Diabetes Mellitus cases.

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