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Study of Lipid Profile and Some Renal Parameters in Controlled and Uncontrolled Diabetics

Medical Science

KEYWORDS : UACR, dyslipidemia, microalbuminuria, glycemic control, T2DM.

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ABSTRACT

Background: Diabetes mellitus (DM) is one of the most common chronic diseases in nearly all countries, and continues to increase in numbers and significance, as changing lifestyles lead to reduced physical activity, and increased obesity. Hyperglycemia and hyperlipidaemia are known to be risk factors for the development of micoalbuminuria in patients with diabetes, which leads to progression of end stage renal disease. Therefore assessment and monitoring of blood sugar, lipid profile and microalbuminuria has become standard practice in view of early detection of diabetic nephropathy as well as predicting CVD risk in diabetic patients. Objective: To compare Lipid profile, microalbuminuria (in terms of UACR) and serum creatinine between controlled (controlled DM= FPG≤130mg/dl and/or 2hPG≤180mg/dl) and uncontrolled (uncontrolled DM=FPG>130mg/dl and/or 2hPG>180mg/dl) T2DM patients. Materials and Methods: This was a cross-sectional hospital based study with comparison groups conducted in Indira Gandhi Govt. Medical College, Nagpur during June 2013 to November 2013. Study included 25 controlled and 25 uncontrolled diabetic patients. Results: In this study we observed the higher mean values of UACR (albuminuria), serum creatinine, total cholesterol, TG, VLDL and LDL-C in uncontrolled diabetics compared to that in controlled diabetics. This indicates that glycemic control has got a strong impact on development of endothelial dysfunction, dyslipidemia and nephropathy in diabetic patients. Therefore patients should be educated about the importance of achieving a strict glycemic control along with regular monitoring for microalbuminuria and dyslipidemia so that complications can be detected much earlier and intervention can be applied at the right time.

INTRODUCTION

Diabetes mellitus (DM) today is a growing epidemic that has the potential to cripple health services in all parts of the world[1]. In India itself, the numbers of diabetic patients have increased tremendously over the last decade making her the capital of diabetic patients. It is a major cause of disability and premature death, mainly through cardiovascular disease and other chronic complications.[1-3] There were 285 million diabetics worldwide in 2010 and it is estimated to reach 439 million in 2030.[1,4]

Diabetes mellitus is characterized by hyperglycemia, glycosuria, hyperlipidemia, negative nitrogen balance and sometimes ketonemia.[5] Major consequence of hyperglycemia is excessive non enzymatic glycosylation of various body proteins including hemoglobin, albumin, collagen and elastin. Apart from hyperglycemia, DM is also characterized by oxidative stress, inflammation and insulin resistance. Chronic hyperglycemia from any cause can lead to a number of complications like cardiovascular, renal, neurological or ocular pathology, intercurrent infection and lower extremity complications. After adjusting for age, the death rate of people with T2DM is about twice as high as their non-diabetic peers.[6] Nearly 50-80% of all diabetics die of cardiovascular disease, stroke, or renal failure.[1,6]

Diabetic nephropathy is a clinical syndrome characterized by persistent albuminuria, arterial blood pressure elevation, progressive decline in glomerular filtration rate (GFR), and a high risk of cardiovascular morbidity and mortality.[7] Approximately 40% of people with diabetes will develop nephropathy. Diabetic nephropathy (DN) is a leading cause of end-stage renal disease. However, the decline in GFR is highly variable, ranging from 2 to 20 ml/min/year.[8-11] Chronic kidney disease (CKD) can be quantitatively defined as a GFR <60 ml/min/1.73m2 and the rate of rise in serum creatinine, a well-accepted marker for the progression of DN, (creatinine value 1.4 to 3.0 mg/dl) is the indicator for impaired renal function.[12,13] Several markers have been used for screening. Proteinuria has been known for a long time as an independent significant risk factor for ESRD and cardiovascular disease in diabetic patients.[14,15] However, the focus has moved recently to much earlier stages in renal disease as established by the presence of microalbuminuria. Microalbuminuria is not only established as a significant predictor for the development of overt diabetic nephropathy but is also associated with increased cardiovascular morbidity and mortality risk in both type 1 and type 2 diabetes.[16,17] Some of the Indian studies have shown that the prevalence of microalbuminuria ranged from 19.7% to 28.5% in type 2 DM.[18] The pathological basis of elevated urinary albumin excretion which is caused by protein glycosylation, with advanced glycated end products and their deposition, results in hypertrophy of glomerular and renal systems, which in turn, leads to the leakage of low molecular weight proteins (albumin).[19] The continuous persistent leakage of these proteins into urine results in overt diabetic nephropathy, which results in the gradual development of ESRD and cardiovascular complication.[20] While timed urine collection is considered the gold standard for evaluating albuminuria or proteinuria, it has logistical difficulties. Measurement of albuminuria in a first morning void specimen provides acceptable accuracy and reliability in most circumstances. Random urine specimens are acceptable if first-void specimens are impractical. Investigations have also shown that correction of urinary albumin measurements for urinary creatinine excretion (UACR) accounts for variation in urinary concentration, and results in better correlation with timed urine results.[21]

Dyslipidemia is a relatively common problem in patients with poorly controlled diabetes mellitus. Dyslipidemia is a risk factor for CVD as well as microalbuminuria in patients with diabetes.[22,23] Findings from basic and clinical studies strongly suggest that excess amounts of a variety of lipoproteins and lipids worsen diabetes-associated microvascular and macrovascular diseases, promote glomerular and tubulointerstitial injury and contribute to the progression of diabetic nephropathy.

Glycemic control- According to American Diabetic Association (ADA) guidelines-2013[24] glycemic control is defined as 1)HbA1c

<7% OR 2)FPG<130 mg/dl OR 3)2hPG<180 mg/dl. There are ample evidences to show that tight control of diabetes and early management directed towards the affected organs (ARB; angiotensin receptor blocker and ACE inhibitors; angiotensin converting enzyme inhibitor) delays progression of organ failure and probably prolongs life in these patients.

The present study was done to determine and compare lipid parameters, Serum creatinine and microalbuminuria (UACR) between controlled and uncontrolled diabetics.

MATERIALS AND METHODS
This was a cross-sectional study with comparison group conducted in Indira Gandhi Govt. Medical College, Nagpur during June 2013 to November 2013. The study included 50 diagnosed patients of T2DM attending Diabetic clinic of this institute. All diabetic patients with age >20 yrs were included in the study irrespective of their duration of diabetes. The study subjects were divided in two groups. One group included 25 controlled diabetic patients (FPG≤130mg/dl and/or 2hPG≤180mg/dl) while other group included 25 uncontrolled diabetic patients (FPG>130mg/dl and/or 2hPG>180 mg/dl). All details of study were explained to the subjects and informed consent was taken & clinical examination was done as per a predesigned proforma. Dermographic and anthropometric details like age, weight, height and duration of diabetes were recorded for all subjects. Details of diabetes treatment were obtained from medical records.

5 ml of fasting (8-12 hour fasting) venous blood sample by disposable syringe and needle with all aseptic precautions was taken for fasting blood sugar, urea, creatinine and lipid profile estimation. 2 ml of venous blood was taken for postprandial blood sugar estimation and a random urine sample was obtained in a sterile urine container for urinary albumin and creatinine estimation. The blood samples were centrifuged after 30 minutes of collection for separation of plasma and serum. Creatinine and lipid profile were measured in serum while sugar and urea was measured in plasma. Urine was also centrifuged before analysis. Glucose estimation was done by glucose oxidase and peroxidase method, cholesterol by cholesterol esterase, cholesterol oxidase and peroxidase method, Triglyceride by glycerol phosphate oxidase and peroxidase, HDL with precipitation method, Serum and Urine Creatinine by jaffe's method using alkaline picrate, urea by urease method on ERBA XL640 autoanalyzer and VLDL, LDL were estimated by applying Frieldwald's formula. Urine albumin was estimated by pyrogallol red method on semiautoanalyzer.

Statistical analysis: Continuous variables (Age, Duraion of diabetes, Serum creatinine, UACR, BSL[F&PM], CHO, TG, VLDL, HDL and LDL) were presented as Mean ± SD. Wilcoxon Rank sum test was applied for comparing non-normally distributed data (creatinine, UACR and duration of diabetes) while unpaired T test was applied for comparing normally distributed data. p-value<0.05 was considered as statistically significant, and Statistical software STATA version 10.0 was used for statistical analysis.

RESULTS
Table1: Comparison of mean values of various parameters between controlled and uncontrolled diabetics

Parameter (mean±SD)	Controlled Diabetics (n=25)	Uncontrolled diabetics (n=25)	p value
Age in years	56.42±8.52	57.64±9.43	0.845,NS
Duration of diabetes in years	2.88±3.05 *2(0.1-10)	5.08±3.54 *5(0.1-11)	0.022,S
BSL(F) mg%	102.72±19.88	198.96±88.35	
BSL(PM) mg%	155.24±24.68	275.72±86.51	
Sr. Creat. mg%	0.98±0.21 *0.9(0.6-1.5)	1.13±0.46 *1.1(0.5-2.5)	0.511,NS
UACR mg/g	252.12±315.39 *185(0-1250)	797.92±882.49 *404(0-2985)	0.001,HS
Total Cholesterol mg%	167.44±43.04	181.32±34.68	0.215,NS
Triglycerides mg%	126.88±41.23	151.88±41.11	0.026,S
VLDL mg%	25.32±8.18	30.40±8.06	0.031,S
HDL mg%	43.44±9.06	43.92±11.90	0.873,NS
LDL mg%	98.84±34.83	105.80±27.74	0.438,NS

Where, SD-Standard deviation; S-Significant; NS-Nonsignificant; HS-Highly significant; *Median & range.

All patients were diagnosed cases of T2DM having age in the range of 42-75 years. Among patients in the controlled diabetics group, mean age was 56.42±8.52 with a range of 42-70 years. Mean age of patients in the uncontrolled diabetics group was 57.64±9.43 with a range of 45-75 years. There were 15 (30%) male patients in the study of which 8 were in the controlled group and 7 in uncontrolled group. The mean duration of diabetes in controlled diabetics group was 2.88±3.05 years while that of in uncontrolled diabetic group was 5.08±3.54 and this difference was statistically significant. The mean fasting blood sugar in controlled and uncontrolled group was 102.72±19.88 and 198.96±88.35 mg% respectively. The mean postmeal blood sugar in controlled and uncontrolled group was 155.24±24.68 and 275.72±86.51 mg% respectively. The mean serum creatinine level in controlled and uncontrolled group was 0.98±0.21 and 1.13±0.46 mg% respectively but this difference was statistically nonsignificant. The mean UACR in controlled and uncontrolled group was 252.12±315.39 and 797.92±882.49 mg/g respectively and this difference was found to be statistically highly significant. Among lipid parameters, mean total cholesterol in controlled and uncontrolled group was 167.44±43.04 and 181.32±34.68 mg% respectively; mean TG in controlled and uncontrolled group was 126.88±41.23 and 151.88±41.11 mg% respectively; mean VLDL in controlled and uncontrolled group was 25.32±8.18 and 30.40±8.06 mg% respectively; mean HDL in controlled and uncontrolled group was 43.44±9.06 and 43.92±11.90 mg% respectively and mean LDL in controlled and uncontrolled group was 98.84±34.83 and 105.80±27.74 mg% respectively.

Figure 1: Comparision of creatinine, CHO, TG and LDL between controlled and uncontrolled diabetics

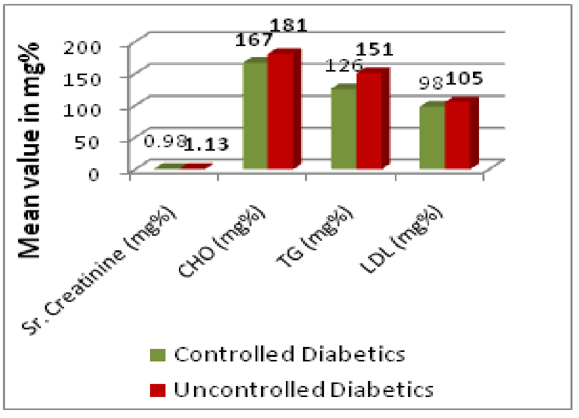

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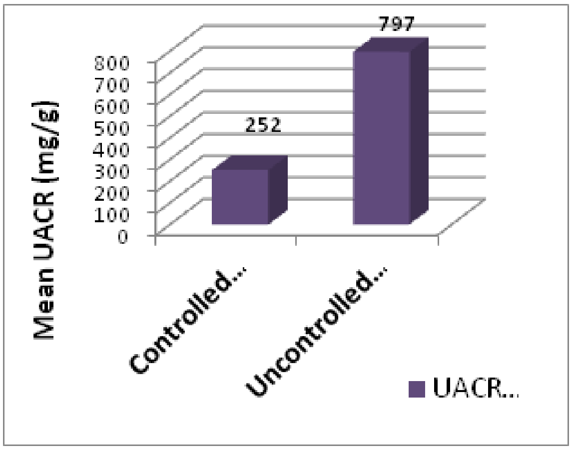
Figure 2: Comparision of UACR between controlled and uncontrolled diabetics



DISCUSSION

Management of T2DM involves a vast array of lifestyle modifications and pharmaceutical interventions, majorly aimed at preventing and controlling the primary pathogenic feature of hyperglycemia & its harmful effects on various tissues. As glycemic control in a diabetic patient is the basic deciding factor which predicts the development and progression of various complications of diabetes, we have tried to compare the markers of diabetes associated complications between controlled and uncontrolled diabetics.

The present study was conducted in 50 diagnosed cases of diabetes. The patients were grouped as controlled and uncontrolled on the basis of their fasting and/or postmeal blood sugar status.

In the present study there were 15 (30%) male patients and 35 (70%) female patients. Female dominancy has also been noted by other studies[25,26,27].

Nephropathy is a well known complication of T2DM and about 40% of diabetic patients will have nephropathy in the course of their disease. The measurement of serum creatinine concentration is widely used clinically as an index of renal function.[28] But, as serum creatinine is a less sensitive marker to diagnose early renal disease, microalbuminuria was proposed as another marker to diagnose nephropathy in early stage and several studies have established the role of microalbuminuria in diagnosing early nephropathy.[28]In the present study mean creatinine level was also higher in uncontrolled group (1.13±0.46 mg%) as compared to the controlled group (0.98±0.21 mg%) but the difference was not statistically significant. The prevalence of microalbuminuria in all 50 patients was 36% which was in accordance with findings observed by some other authors.[25,29,] In our study we observed a transition from normoalbuminuria to microalbuminuria to macroalbuminuria as the duration of diabetes increased which is consistent with findings observed by Kondaveeti et al.[29] The mean UACR in uncontrolled group was higher (797.92±882.49 mg/g) as compared to the controlled group (252.12±315.39 mg/g) and this difference was statistically highly significant (p=0.0015).

Patients with type 2 diabetes often exhibit an atherogenic lipid profile, which greatly increases their risk of CVD compared with people without diabetes. An early intervention to normalize circulating lipids has been shown to reduce cardiovascular complications and mortality.[30,31] The lipid changes in diabetes mellitus are attributed to the associated hyperinsulinemia and insulin resistance. Diabetes is associated with characteristic triad of lipid alteration: hypertriglyceridemia, low HDL-C and increased concentration of small dense LDL-cholesterol particles. This occurs due to (1) increase in the release of free fatty acid from the insulin resistant adipose tissue, (2) increase in fatty acid synthesis in the liver, (3) increase in hepatic VLDL production, and (4) decrease in LPL activity resulting in reduced catabolism of chylomicrons and VLDLs.[32,33] In the present study we compared lipid parameters between controlled and uncontrolled diabetic patients. We compared the mean values of lipid parameters between controlled and uncontrolled diabetics. The mean values of total cholesterol, TG, VLDL-C and LDL-C were comparatively higher in uncontrolled group (181.32, 151.88, 30.4 and 105.8 mg% respectively) as compared to the controlled group (167.44, 126.28, 25.32 and 98.84 mg% respectively) but the difference was statistically significant only with TG and VLDL. The mean values of HDL-C were almost similar in both groups. These findings correlate to some extent with a study done by Mahato RV et al,[23] except that the difference was statistically significant in total cholesterol and LDL-C also in their study.

ADA (American Diabetic association) has reported that well controlled type 2 diabetics have a mixed hyperlipidemia with high triglycerides, low HDL-C and high LDL-C levels.[34] On the other hand in poorly controlled type 2 diabetics have a mixed dyslipidemia resulting in high cholesterol and triglyceride level. It has also been reported that controlling dyslipidemia and good glycemic control delays atherosclerosis and prevent CHD.[35]

In view of these results, the aim is to achieve very tight glycemic control especially in uncontrolled type 2 diabetics to delay or retard the progression of various complications. UKPDS[36] and DCCT[37] study group have all concluded that intensive glycemic control with either suphonylureas or insulin initiated early in the course of DM significantly reduces microvascular and macrovascular end points.

CONCLUSION

In this study we observed the higher mean values of UACR (albuminuria), serum creatinine, total cholesterol, TG, VLDL and LDL-C in uncontrolled diabetics compared to that in controlled diabetics. This indicates that glycemic control has got a strong impact on development of dyslipidemia and nephropathy in diabetic patients. Therefore patients should be educated about the importance of achieving a strict glycemic control along with regular monitoring for microalbuminuria and dyslipidemia so that complications can be detected much earlier and intervention can be applied at the right time.

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