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Original Research Article

Diabetic Dyslipidemia Insulin Resistance May Be One of the Causes of Microalbuminuria

Mahendra D. Bikkad, Suresh S. Ugle

Department of Biochemistry, MIMSR Medical College Latur, India.

Corresponding Author: Suresh S. Ugle

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ABSTRACT

Background and Objectives: The first clinical sign of renal dysfunction (nephropathy) in patients with diabetes generally is microalbuminuria (a sign of endothelial dysfunction that is not necessarily confined to the kidney). The present epidemic of diabetes is significantly increased by growing problems of lifestyle changes, faulty nutrition, obesity etc. The aim of our study was to know the occurrence of microalbuminuria in patients with type 2 diabetes mellitus and to study its relation with diabetic dyslipidemia and insulin resistance.
Methodology: The study was undertaken in MIMSR Medical College Latur. A total number of 50 type 2 diabetes mellitus patients and 50 healthy subjects satisfying the inclusion criteria were selected for study. The lipid profile, urinary microalbumin and creatinine, were determined and compared.
Results: In the control group 1 the mean values of total cholesterol were 173.92± 26.83 mg%, triglycerides 100.102±24.71 mg%, LDL-c were 106.67±27.82 mg%, HDL-c were 45.31±3.58 mg%, VLDL-c were 18.50±4.29 mg%, TG/HDL-c ratio were 2.05±0.46 mg%, urinary microalbumin were 7.20±31.95 mg/L and urinary creatinine were 3.64±4.5Mmol/L. In the group 2 the mean values of total cholesterol were 183.182±42.60 mg%, triglycerides 156.082±61.44mg%, LDL-c were 117.05±33.65mg%, HDL-c were 41.67±3.5mg%, VLDL-c were 31.64±11.63mg%, TG/HDL-c ratio were 3.81±1.3 mg%, urinary microalbumin were 78.60±41.89 mg/L urinary creatinine were 5.28±4.81Mmol/L. The serum triglycerides and TG/HDL-c ratio and urinary microalbumin in group 2 were significantly increased as compared to the group 1. The HDL-c in group 2 was significantly decreased as compared to the group 2.
Conclusion: The occurrence of microalbuminuria in type 2 diabetes patients in this study was significantly influenced by the dyslipidemia especially hypertriglyceridemia (TG/HDL-C ratio above three). The importance to lipid profile correction particularly to lower TG and increases HDL-C (to remove insulin resistance) has to be stressed, as it will help in better glycemic control and reduction to nephropathy.

Keywords: Type 2 diabetes, dyslipidemia, insulin resistance, microalbuminuria, and nephropathy.

INTRODUCTION

The major independent risk factors of the development of diabetes are the obesity, sedentary life, faulty nutrition. Diabetes Mellitus is a worldwide public health concern and important cause of morbidity and mortality. Abnormalities that characterized lipoprotein metabolism in non insulin dependent diabetes mellitus (NIDDM), fasting concentration of triglyceride rich lipoprotein especially very low density lipoprotein (VLDL) are higher and those of high density lipoprotein (HDL) commonly measured as HDL-c are lower than among people without diabetes. [(1,2)] Through lifelong vascular complication

diabetes leads excessive rates of myocardium infraction, stroke, renal failure, blindness and amputation. According to the WHO (2004) diabetes affects more than 170 million people worldwide; this number will rise to 370 million by 2030. About one third of type 2 diabetes will eventually have progressive deterioration of renal function. [(3)] Diabetic nephropathy is a public health concern of increasing proportions. It has become the most single cause of end stage renal disease all over the world. [(4)] Diabetic nephropathy is the consequence of diabetes mellitus (DM) and it is characterized by continuous albuminuria, elevated blood pressure, and decreased glomerular filtration rate (GFR) and high risk of CVD. The epidemiological studies have revealed that genetic susceptibility is an important factor in the development of diabetic nephropathy in patients with both type 1 and type 2 diabetes. Other contributing risk factors are glomerular hyper filtration, smoking, dyslipidemia, levels of proteinuria, and source of protein and fat in the diet. [(5,6)] Microalbuminuria is a marker of an increased risk of diabetic nephropathy in patients with type 1 as well as with type 2 diabetes. It is common in type two diabetes patients. Poor long term control of diabetes, hypertension, dyslipidemia and cigarette smoking facilitate the development of diabetic nephropathy. [(7)] Albumin, a protein having molecular weight of 50,000 is not easily filtered and is not excreted into urine. This makes albumin excretion into the urine a useful indicator of early glomerular disease. [(8)] Increase in urine albumin seen with diabetic nephropathy can be attributed to degradation of the glomerular basement membranes and hypertension both characteristics of diabetic nephropathy. [(9)] Use of the albumin-to-creatinine ratio in an untimed urinary sample is now recommended as the preferred screening strategy for all diabetic patients. [(10,11)]

The effect of volume can be avoided entirely by calculation of the albumin-to-creatinine ratio in an untimed urine specimen. A ratio above 30 mg/g (or 0.03 mg/mg) suggests that albumin excretion is above 30mg per day and therefore that microalbuminuria is probably present. [(12)] Microalbumin has been reported in several studies to predict development of diabetic nephropathy and its mortality risk in diabetic patients. Early detection and aggressive intervention should be given to retard the progression of diabetic nephropathy to end stage renal failure. [(13)]

MATERIALS AND METHODS

We studied 50 healthy and 50 diabetic patients matched for age and body mass index. Subjects were selected from medical, paramedical staff and general public who were around 40 to 60 year of age. All subjects were belonged to the Latur district of Marathwada region. Patient belonging to group II were selected after attending medicine OPD of MIMSR Medical College, Latur and diagnosed as diabetic. The healthy subjects were nonsmokers, non obese, nonalcoholic and free from any disease and not taking any drugs that alter lipid and carbohydrates metabolism. All patients belonging to group II had NIDDM. A criterion of diagnosis of diabetic is: fasting blood sugar levels not less than 140.0 mg % and HbA1C above 7. All subjects after taking informed consent was interrogated and detailed examination was done. First morning urine samples were collected and blood samples drawn after an overnight fast. After serum separation the analysis was done on the same day. We estimated serum triglycerides by enzymatic method (Auto pack Siemens kit) and total cholesterol by enzymatic methods (Auto pack Siemens kit) HDL-c measured by phosphotungstate method (Auto pack Siemens kit). LDL-c and VLDL- c values were calculated by Friedwald's equation. [(14)] Urinary microalbumin and creatinine were determined on urine analyzer (Siemens Clinitek microalbumin 2).

RESULTS

In the control group 1 the mean values of total cholesterol were 173.92±

26.83 mg%, triglycerides 100.102±24.71 mg%, LDL-c were 106.67±27.82 mg%, HDL-c were 45.31±3.58 mg%, VLDL-c were 18.50±4.29 mg%, TG/HDL-c ratio were 2.05±0.46 mg%, urinary microalbumin were 27.20±31.95 mg/L and urinary creatinine were 3.64±4.5 Mmol/L. In the group 2 the mean values of total cholesterol were 183.182±42.60 mg%, triglycerides 156.082±61.44 mg%, LDL-c were 117.05±33.65 mg%, HDL-c were 41.67±3.5 mg%, VLDL-c were 31.64±11.63 mg%, TG/HDL-c ratio were 3.81±1.3 mg%, urinary microalbumin were 78.60±41.49 mg/L and urinary creatinine were 5.28±4.81 Mmol/L. The serum triglycerides and TG/HDL-c ratio and urinary microalbumin in group 2 were significantly increased as compared to the group 1. The HDL-c in group 2 was significantly decreased as compared to the group 2.

Table 1: Total cholesterol, triglycerides, urinary microalbumin and other biochemical parameters in group 1 (healthy subjects) and group 2 (diabetic patients).

Variable	Group 1	Group 2
Total cholesterol (mg%)	173.92± 26.83 •	183.182±42.60 •
Triglycerides (mg%)	100.102±24.71*	156.082±61.44*
HDL- cholesterol (mg%)	45.31±3.58*	41.67±3.5*
LDL- cholesterol (mg%)	106.67±27.82^{o}	117.05±33.65^{o}
VLDL- cholesterol (mg%)	18.50±4.29*	31.64±11.63*
TG/HDL- cholesterol (mg%)	2.05±0.46*	3.81±1.3*
Urinary microalbumin (mg/L)	27.20±31.95*	78.60±41.89*
Urinary creatinine (Mmol/L)	3.64±4.5 ^{o}	5.28±4.81^{o}

Comparison between group 1 and group 2, P^{*} is less than 0.0001 extremely statistically significant, $P^{\bullet}$ is less than 0.45not significant and P^{o} is 0.084, less significant.

DISCUSSION

The catabolism of triglyceride-rich lipoproteins is initiated by lipoprotein lipase, an endothelial enzyme that hydrolyses the triglyceride moiety of chylomicrons and VLDL, and releases fatty acids for energy production in muscle and for storage in adipose tissue. The activity of this enzyme is generally lower in NIDDM patient than in non diabetic people of similar age and degree of adiposity: The difference is more striking for patient with both NIDDM and coronary artery disease (CAD). [(15)] Lipoprotein lipase activity is low in untreated or poorly controlled NIDDM and increase with improved glycemic control. [(16)] In NIDDM passage of triglyceride- rich lipoproteins through the lipolytic cascade is delayed for two reasons: there is a shortage of catalytic sites on lipoprotein lipase, and overproduction of triglyceride saturates the sites that are available. Both mechanisms promote hypertriglyceridemia. The two components of diabetic dyslipidemia, high concentrations of triglyceride-rich lipoproteins and low concentrations of HDL, are closely interwoven. Lowered plasma HDL-c and elevated plasma triglyceride levels are features of NIDDM dyslipidemia (TG/HDL-c ratio above 3) which is a reliable predictor of insulin resistance. Insulin resistance is the syndrome that favors atherosclerosis and thus CAD. Relying on LDL-c or total cholesterol alone can be misleading. It is also proved that people with obesity, metabolic syndrome or diabetic lipid disorders often have raised triglycerides, low HDL-c and normal or closed to normal LDL-c. The first clinical sign of renal dysfunction in patients with diabetes generally is microalbuminuria (sign of endothelial dysfunction that is not necessarily confined to the kidney). Microalbuminuria refers to the excretion of albumin in the urine at a rate that exceeds normal limits but is less than the detection level for traditional dipstick methods (American Diabetes Association, 2003). It is often present at the time of diagnosis, either due to insidious nature or asymptomatic during initial years of type 2 diabetes or its positive association with insulin resistance,

even in non diabetic people. [17] The degree of microalbuminuria determines the progression of diabetic nephropathy. Microalbuminuria is associated with excess cardiovascular mortality in both diabetic and non diabetic subjects. Patients with NIDDM and microalbuminuria are more insulin resistance than those without microalbuminuria. However, the relation between insulin resistance and microalbuminuria in patients with NIDDM could be due to hyperglycemia, hypertriglyceridemia (higher TG/HDL-c ratio) and hypertension associated with diabetes which can cause both insulin resistance and an increase in albumin excretion rate. Nephropathy in NIDDM may be due to multiple factors such as diabetes and associated dyslipidemia hyperglycemia, hypertension, insulin resistance, atherosclerosis which act together and begin damage to kidney. In our study triglycerides, VLDL-c and TG/HDL-c ratio mean values were observed positively related to urinary microalbumin. Kim et.al [18] reported that triglycerides as a key factor in the advancement of diabetic nephropathy. In a prospective study an increased TC/HDL ratio in type 2 diabetic patients was found independently associated with microalbuminuria. [19] Our results are correlated with these studies. Thus there is association between diabetes, diabetic dyslipidemia (hypertriglyceridemia), TG/HDL-c ratio, insulin resistance with microalbuminuria (Nephropathy). Hypertriglyceridemia and nephropathy in NIDDM may be due to disturbed lipoprotein metabolism and decreased removal of apolipoprotein.

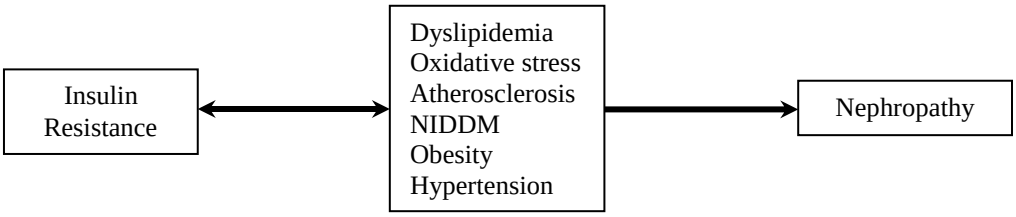

Fig 1: Biochemical and pathological consequences of insulin resistance.

CONCLUSION

The occurrence of microalbuminuria in type 2 diabetes patients in this study was significantly influenced by the dyslipidemia especially hypertriglyceridemia (TG/HDL-c Ratio above three). The importance to lipid profile correction particularly to lower TG and increases HDL-c (to remove insulin resistance) has to be stressed, as it will help in better glycemia and blood pressure control and reduction to nephropathy.

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DECLARATIONS

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Conflict of interest: Are none to be declared.

Ethical approval: Approved by Ethical committee of MIMSR Medical College Latur.

REFERENCES

1. Taskinen M. R. Hyperlipidemia in diabetes. Bailliere Clin. Endocrinol Metab. 1990; 4; 743-75.
2. Howard B.V.; Lipoprotein metabolisim in diabetes mellitus. J.Lipid Res.1987; 28; 613-28.
3. Remuzzi J, Schieppati A and Ruggenentip. Nephropathy in patients with type 2 diabetes. The New England Journal of Medicine 2002, 346, 1145-51.
4. Molitch ME, DeFronzo RA, Franz MJ, Keane WF, Mogensen CE, Parving HH and Steffes MWThe American Diabetes Association: Nephropathy in diabetes (Position Statement). Diabetes Care (2004), 27(Suppl. 1) S79-S83.
5. Gross JL, Azevedo MJD, Silveiro SP, Canani LH, Caramori ML, Zelmanovitz T. Diabetic Nephropathy: Diagnosis,

Prevention, and Treatment. Diabetes Care 2005; 28: 1164-1176.
6. Chaturvedi N, Fuller JH, Taskinen MR. Differing associations of lipid and lipoprotein disturbances with the macro vascular and micro vascular complications of type 1 diabetes. Diabetes Care 2001; 24: 2071-2077.
7. Casper GS, Nicole L, Harry T, et al.: Amadori Albumin in Type 1 Diabetic Patients Correlation With Markers of Endothelial Function, Association with Diabetic Nephropathy, and Localization in Retinal Capillaries, Diabetes, December 1999;48(12):2446-2453.
8. American diabetes association, Nephropathy in Diabetes, diabetes care, january 2004; 27(1):S79-S83.
9. Ghazalli R: Diabetic Nephrolpathy in Clinical practice guidelines, July 2004: 1-38.
10. Mogensen CE, Vestbo E, Poulsen PL, et al.: Microalbuminuria and potential confounders. A review and some observations on variability of urinary albumin excretion. Diabetes Care 1995; 18:572-581.
11. K/DOQI Clinical Practice Guidelines and Clinical Practice recommendations for diabetes and chronic kidney disease. Am J Kidney Dis 2007; 49(2):S21-S95.
12. Nakamura Y, Myers BD: Charge selectivity of proteinuria in diabetic glomerulopathy. Diabetes 1988; 37:1202-1211.
13. Graziella B, Franco M: Progression to overt nephropathy in type -2 diabetes. The Casale Monferrato study. Diabetes Care 2003; 26:2150-2155.
14. Friedwald Levy R.I. and Fridickson D.S.(1972). Friedwald formula, clin, chem. 18,499, in a clinical laboratory method. John D Bauer, 9th ed. Page 555.
15. Miesenbock G, Patsch JR. Postprandial - hyperlipidemia; the search for the atherogenic lipoprotein. Curr Opin Lipidol 1992; 3; 196-201.
16. Grundy SM, Vega Gl, Two different views of the relationship of hypertriglyceridemia to coronary heart disease; implication for treatment. Arch Intern Med 1992; 152; 28-34.
17. Mykkanen L, Zaccaro DJ, Wagenknecht LE, Robbins DC, Gabriel M and Haffner SM. Microalbuminuria is associated with 97 insulin resistance in non diabetic subjects: The Insulin Resistance Atherosclerosis Study. Diabetes (1998)47 793-800.
18. Kim DM, Ahn CW, Park JS. An implication of hypertriglyceridemia in the progression of diabetic nephropathy in metabolically obese, normal weight patients with type 2 diabetes mellitus in Korea. Diabetes Res Clin Pract 2004; 66: 169-172.
19. Retnakaran R, Cull CA, Thorne KI. Risk factors for renal dysfunction in type 2 diabetes: UK Prospective Diabetes Study 74. Diabetes 2006; 55: 1832-1839.

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