# Evaluation of Association between Microalbuminuria and Serum Lipid Profile in Type 2 Diabetes Mellitus

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**Abstract:** *Nephropathy in type 2 diabetes mellitus (T2DM) develops due to chronic low grade inflammation and vascular endothelial dysfunction. Microalbuminuria (MAU) is thought be a result of generalized damage of the endothelium in T2DM. Insulin resistance results in high concentrations of serum lipids in diabetics due to increased mobilization of free fatty acids from fat depots. A chronic low-grade inflammatory condition has been proposed to underline increased risk for atherosclerotic disease, including renal dysfunction and cardiovascular disease suggesting a possible link between the high incidence of macrovascular complications and diabetes. Because MAU and serum lipid profile reflect closely related component of the same disease process, a strong relationship between these variables may be anticipated. We selected 50 patients of Type-2 diabetes mellitus and 50 normal healthy individuals to evaluate this association. The statistical analysis depicted a significant positive (r=0.36; p <0.01) correlation between microalbuminuria and total cholesterol, a highly-significant (p< 0.001) positive correlation (r=-0.48) between microalbuminuria and serum triglyceride and a significant (p> 0.033) negative correlation (r=-0.30) between microalbuminuria and serum HDL in type 2 diabetic patients. It can be argued that MAU may be related to insulin resistance in the prediction of cardiovascular events.*

## 1. Introduction

Microalbuminuria is an established marker of diabetic nephropathy. Microalbuminuria is thought to be the consequence of generalized endothelial damage along the vascular tree. [1] Microalbuminuria is defined as an excretion of albumin in the urine, amount ranging from 30 to 300 mg/day or 20 to 200 mg/L. [2] It begins insidiously and may precede the diagnosis of type 2 DM [1] It is at this stage that one can hope to reverse diabetic nephropathy or prevent its progression. Hyperglycaemia contributes largely to the development of endothelial dysfunction in diabetes and ultimately leads to albumin loss. [3] The abnormal high concentrations of serum lipids in diabetics is due, mainly to increase in the mobilization of free fatty acids from fat depots, since insulin inhibits the hormone sensitive lipase. [4]

The development of formula based calculation of estimated glomerular filtration rate (eGFR) has offered a very practical and easy approach for converting serum creatinine value into GFR result; taking into consideration patient's age, sex, ethnicity and weight (depending on equation type). In 2000 Levey *et al* subsequently published a 4-variables (4-v MDRD) equation that does not require albumin and urea with no impact on accuracy. [5] Both Increased urinary albumin excretion (albuminuria) and reduced GFR are risk factors for progressive kidney failure and cardiovascular disease. [6]

Because MAU and serum lipid profile seem to be closely related component of the same disease process, a strong relationship between these variables may be anticipated.

## 2. Materials and Methods

The present study was a case control prospective study undertaken in the Department of Biochemistry in collaboration with Department of Medicine, Sri Guru Ram Das Institute of Medical Sciences and Research, Amritsar. A total of 100 subjects willing to participate in the study with informed consent were included in the study. 50 patients of poorly controlled Type 2 Non Insulin Dependent Diabetes Mellitus (NIDDM) between 40-65 yrs of age, of either sex whose HbA1c was >7% and 50 healthy, age and sex matched controls from the same population but without any disease and without family history of DM.

**Exclusion criteria:** Patients suffering from type-1 DM, patients with acute complications of DM like Diabetic ketoacidosis, history of acute infections, other ailments like gross congestive heart failure, tuberculosis, gout, rheumatoid arthritis and skeletal muscle injury, serum creatinine > 1.5mg/dl, renal failure and those giving positive dip stick test for proteinuria were not included in the study.

The patients and controls were screened for fasting blood sugar (FBS), lipid profile, and microalbuminuria and the values were compared with that of normal healthy subjects. Microalbumin in urine was estimated by Nycocard Reader (Diabetes Care 1997) [7] GFR was estimated from serum creatinine using the Modification of Diet in Renal Disease (MDRD) equation.[8] Complete Lipid profile included the following estimations-a. Total Serum Cholesterol was be estimated by CHOD-PAP Method (Allain C.C. et al 1974) [9] b. Serum Triglyceride was be estimated by GPO-Trinder Method. (McGowan MW et al 1983)[10]c. Serum High Density Cholesterol (HDL-C) was be estimated by Phosphotungstic Acid Method (Gordon T. Et al 1977)[11]d. Low Density Lipoprotein-Cholesterol (LDL-C) and Very Low Density Lipoprotein-Cholesterol (VLDL-C) by Freidwald equation (Freidwald equation W.T.1974) Serum creatinine was estimated by jaffes kinetic method (Watchtel et al 1995) [12] and its calibrator has been standardized to ID-MS.

## 3. Result

There was no significant effect of age (p>0.05) and sex distribution (p > 0.05) in the study. Table 1 shows that FBS, HbA1c, total cholesterol, triglyceride and MAU levels were significantly high while HDL-C were significantly low in cases as compared to the controls. Whereas no significant difference was found in the values of creatinine and eGFR in cases when compared to controls.

**Table 1:** Comparison of various parameters estimated in patients and controls

| | Cases (Mean±SD) | Controls (Mean±SD) | p value |
|---|---|---|---|
| Fasting blood sugar (mg/dl) | 194.38 ± 53.60 | 100.30 ± 12.46 | < 0.001* |
| HbA1c (% ) | 8.758 ± 1.83 | 5.148 ± 0.51 | < 0.001* |
| Total cholesterol (mg/dl) | 223.20 ± 45.41 | 174.46 ± 33.90 | < 0.001* |
| Triglycerides(mg/dl) | 224.70 ± 76.77 | 161.14 ± 32.42 | < 0.001* |
| HDL-C(mg/dl) | 40.48 ± 8.18 | 55.00 ± 12.04 | < 0.001* |
| Albumin in urine (mg/L) | 35.36 ± 15.36 | 18.28 ± 1.47 | <0.001* |
| Serum creatinine (mg/dl) | 1.09 ± 0.257 | 1.05 ± 0.318 | 0.502*** |
| eGFR (ml/mim/1.73 m$^2$) | 68.28 ± 24.83 | 68.54 ± 31.87 | 0.201*** |

 *P<.001 =highly significant
**p<0.05-significant
***p>0.05- non significant

Table 2 shows that FBS, HbA1c and triglycerides had a highly significant correlation with MAU in type 2 diabetics. Total cholesterol and HDL-C had a significant correlation with MAU in type 2 diabetic patients.

**Table 2:** Correlation of MAU in type 2 Diabetes Mellitus with FBS, HbA1c and lipid profile

| | MAU (mg/L) | |
|---|---|---|
| | R | P |
| Fasting blood sugar (mg/dl) | 0.47 | <0.001* |
| HbA1c (% ) | 0.60 | <0.001* |
| Total cholesterol (mg/dl) | 0.36 | 0.01** |
| Triglycerides(mg/dl) | 0.48 | <0.001* |
| HDL-C(mg/dl) | -0.30 | 0.033** |

*P<.001 =highly significant
**p<0.05-significant
***p>0.05- non significant

## 4. Discussion

In our study Plasma Lipid profile showed significant increase (p< 0.001) in Total cholesterol (TC), Triglycerides (TG), Low Density Lipoprotein (LDL) and Very Low Density Lipoprotein (VLDL) in diabetics when compared to controls. In contrast there was significant decrease (p< 0.001) in HDL-C in diabetics. (Tables 1)  It is known that cholesterol, triglycerides, LDL and VLDL are elevated in diabetic patients. The abnormal high concentrations of serum lipids in diabetics is due, mainly to increase in the mobilization of free fatty acids from fat depots, since insulin inhibits the hormone sensitive lipase. Excess fatty acids in serum of diabetics are converted into phospholipids and cholesterol in liver. These two substances along with excess triglycerides formed at the same time in liver may be discharged into blood in the form of lipoproteins. [4]   These

results were supported by studies of M. M. Yassin et al (2010) [13] and Dayanand C D et al (2010) [13]

In our study, it was observed that the difference between the mean ± SD values for microalbumin in urine in normal individuals (18.28 ± 1.47 mg/L) and patients (35.36 ± 15.36 mg/L) was highly significant (p< 0.001) with patient group having significantly higher levels than the normal individuals. (Table 1) This increase can be interpreted as an early sign of nephropathic changes in the diabetic patients, which could possibly be attributed to the degradation of the glomerular basement membrane and in particular, damage to the surface layer on the endothelium, the glycocalyx. As a result, there is an increased filtration of albumin through the damaged glomerular filtration barrier and hence an increased albumin loss in the urine. [3] In conclusion, based on present findings one could argue that urinary microalbumin may possibly be used as a marker for early indication of diabetic nephropathy. These findings were supported by Maduka Ignatius C et al (2009) [14] and Krishnamurthy U et al 2011. [15]   D A Muttur et al 2010 [3] showed that urine microalbumin, expressed as albumin-to-creatinine ratio was statistically highly significant (p<0.003) among diabetic patients (2.5±3.8 mg/mmol) compared to non diabetic subjects (0.8±1.1 mg/mmol) and were found to be significantly correlated with risk factors linked to diabetes related vascular diseases.

In our study, no significant difference in the values of eGFR in cases and control was found (Table 1). This may be because the increase Microalbuminuria precedes a fall in glomerular filtration rate in patients developing diabetic chronic kidney disease (CKD). [16] [17]

In our study (TABLE 2) we found a significant positive correlation of microalbuminuria with total cholesterol and triglyceride while a significant negative correlation with HDL which was supported by the study of Martin B et al (1998) [18] which also showed the similar results. It can be argued that MAU may be related to insulin resistance in the prediction of cardiovascular events.

Chronic low-grade inflammation and endothelial dysfunction play a fundamental role from initiation and progression of atherothrombosis and the development of cardiovascular disease and microalbuminuria in diabetic patients, as well as in non diabetic individuals, is associated with both of them. Therefore, it may be possible that endothelial dysfunction and chronic low-grade inflammation underlie the association between microalbuminuria and cardiovascular disease in type 2 diabetes. [3]

Studies in the Western literature have documented the linear relationship of degree of microalbuminuria with the body mass index (BMI), blood pressure and duration of diabetes. [19]

Once microalbuminuria is diagnosed in a patient with diabetes, it is time to stress to the patient the need to manage multiple risk factors for cardiovascular disease. The target blood pressure should be below 130/80 mm Hg, the target low-density lipoprotein cholesterol level should be below 2.5 mmol/L, and smoking cessation should be mandatory. [20]

# 5. Conclusion

In type 2 diabetic patients, microalbuminuria is significantly associated with elevated serum total cholesterol, triglyceride and decreased levels of HDL. Thus, microalbuminuria is an indication for screening for possible vascular disease and aggressive intervention to reduce all cardiovascular risk factors (e.g. lowering of LDL cholesterol, antihypertensive therapy, cessation of smoking, institution of exercise etc). This study may also highlight the importance of proper glycemic control in arresting the progression of inflammation.

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