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# Nephropathy and serum lipid profile in type 2 diabetes patients: A retrospective study in central India

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**Abstract**
**Background:** Microalbuminuria is an established marker of diabetic nephropathy. Microalbuminuria is thought to be the consequence of generalized endothelial damage along the vascular tree. 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. It begins insidiously and may precede the diagnosis of type 2 DM. 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. The prevalence of hypercholesterolemia (TC>200md/dl) alone, as reported in numerous studies across India, has varied from about 20% to 35%. However, what is more important is the pattern of dyslipidemia. When compared with the western populations, Indians and migrant Asian Indians tend to have higher triglyceride levels and lower HDL-C levels.
**Materials and Methods:** This was a comparative study conducted RKDF Medical College Hospital & Research Center, Bhopal, Madhya Pradesh, India among 120 cases. A pre-structural proforma will be used to collect baseline date detailed clinical history with clinical examination and relevant investigation will be done on participating individuals. 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) GFR was estimated from serum creatinine using the Modification of Diet in Renal Disease (MDRD) equation.
**Results:** A higher incidence and prevalence of renal failure particularly in nondiabetic renal patients is observed in men. According to Silbiger and Neugarten, the ratio between men and women that reaches renal insufficiency due to hypertensive nephropathy or glomerulonephritis is 1.6 men for each woman affected. There was correlation between lipid levels and duration of diabetes for all lipid fractions which were significant.
**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 Correlation coefficient between nephropathy and lipid profile was found to be significant.

**Keywords:** Diabetic nephropathy, microalbuminuria dyslipidemia, nephropathy, hypercholesterolemia, Hypertriglyceridemia, lipid profile

## 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. 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]. An elevated level of total cholesterol is the strongest risk factor for CAD [5].

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The mean level of total cholesterol in cord blood of newborns worldwide is 75 mg/dL, which rises to 120 mg/dL in two weeks and remains at that level until approximately 20 years of age, when it starts to gradually rise again [6]. Total cholesterol levels among Asian Indians are similar or lower than in Europids [7]. Long term prospective studies have shown an 8-fold higher CAD mortality with an increase in total cholesterol from <160 to >280 mg/dL among young Americans [8] The optimum level of total cholesterol appears to be <160 mg/dL, especially for Asian Indians, much lower than the 200 mg/dL considered desirable in the Western society. Contrary to common belief, very low levels of total cholesterol and LDL-C are not associated with increased risk of stroke or cancer [9, 10, 11]. The term dyslipidemia is used to denote the presence of any of the following abnormalities, occurring alone or in combination-increased concentration of TC or LDL-C or serum TG or a decreased concentration of HDL-C [12] although it is difficult to compare observations form different studies due to different cut-offs taken to define dyslipidemia. Different sampling procedures and different methodologies used for estimations of lipoproteins, dyslipidemia appears to be widely prevalent in India. The prevalence of hypercholesterolemia (TC>200md/dl) alone, as reported in numerous studies across India, has varied from about 20% to 35%. However, what is more important is the pattern of dyslipidemia. When compared with the western populations, Indians and migrant Asian Indians tend to have higher triglyceride levels and lower HDL-C levels. In contrast, mean serum cholesterol levels among Asian Indians have been shown to be similar to that of the general population in the US and lower than the levels in the UK.

The low HDL-C levels and hypertriglyceridemia are metabolically interlinked and their combination has been termed as "atherogenicdyslipidemia", which is also characterized by increased levels of small-dense LDL particles with relatively normal total LDL-C, and insulin resistance. Atherogenicdyslipidemia is particularly common in south Asians and has been shown to have a strong association with type 2 diabetes mellitus, metabolic syndrome and CVD [13]

Numerous studies have reported prevalence of different forms of lipid abnormalities among Indians. In Randomized sample of 13,414 adults in the age group 25-64 years living in urban Delhi, hypertriglyceridemia was found in 73%of the obese and 61% of the non-Obese individuals. In another more recent study from urban New Delhi, hypertriglyceridemia was observed 42.7% individuals.

Studies from rural populations have shown lower prevalence of hypertriglyceridemia but the rates are still higher than the comparable data from the Caucasians. HDL-C levels are particularly low in Indians than in white Caucasians, as shown consistently in several comparative studies. In the afore-mentioned study from urban New Delhi, low HDL-C was found in 37% of the study population. In another study involving -2700 young office executives (men age 40 years) from New Delhi, low HDL-C was found in 39.5% Individuals. The prevalence of dyslipidemia, esp. Low HDLC, has been shown to be unusually high among patients undergoing coronary artery bypass surgery. In a cross sectional study on 1000 such consecutive patients, dyslipidemia was observed in 84.5% men and 93.9% women with high LDL-C levels in 23.3% patients, elevated TG in 37.0% and low HDL-C in 72.5% patients.

furthermore, it appears that average HDL-C concentrations in all Asian subgroups whether residing in India or elsewhere are lower than Caucasians. For example, according to Tai *et al.* -34% of the subjects with isolated low HDL-C levels in the multiethnic population in Singapore were Asian Indians. Finally, studies have also documented significantly higher prevalence of atherogenic small [14, 15]. Not only the prevalence of dyslipidemia is high among Indians, it has been increasing steadily over the past few decades. The serial Jaipur Heart Watch studies have demonstrated progressive increase in the mean levels of TC, LDL-C and non-HDL-C and a decline in the HDl-C levels.

The triglyceride levels, however, have not increased and in fact have shown a decline during the same period. Measurement of lipids is the first step towards management of dyslipidemia. The NECCP-ATP III guidelines recommend that a lipid profile should be obtained at least once every 5 years in adult's age 20 years or above.

However, considering the issues of applicability, accuracy and costs involved in India, the present consensus committee recommends performing lipid estimations as a routine in adults above 30 years of age. In patients younger than 30 years, the need to perform a lipid estimation should be individualized, based on the presence or absence of concomitant risk factors and evidence of pre-existing CVD.

This recommendation of higher age-threshold for initial lipid estimation is commensurate with that of the European Society of Cardiology/European atherosclerosis Society (recommend screening in adult men >40years of age, and in women>50 years of age). After initial lipid profile measurement, the timing and frequency of subsequent testing should be determined by the abnormalities detected in the initial assessment and can vary from once every five years to as frequent as every 6-12 seeks [16, 17].

## Materials and Methods
This was a comparative study conducted RKDF Medical College Hospital & Research Center, Bhopal, Madhya Pradesh, India among 120 cases. A pre-structural proforma will be used to collect baseline date detailed clinical history with clinical examination and relevant investigation will be done on participating individuals. 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) GFR was estimated from serum creatinine using the Modification of Diet in Renal Disease (MDRD) equation.

## Methods
Turbodyne HbA1c is a turbidimetric immunoassay for the direct determination of Hba1c in human blood without the need to estimate total haemoglobin.

## Principle
TM Turbodyne HbA1c is a turbidimetric immunoassay for direct determination of HbA1c and is based on the principle of agglutination reaction. The test specimen after treatment with Hemolysing solution is allowed to react with latex reagent (RI). Total Hb and HbA1c bind with same affinity to latex particles. The amount of binding is proportional to the relative concentration of both substance in blood. The reaction mixture is then allowed to react with mouse anti human Hba1c monoclonal antibody and goat anti-mouse

human lgG (R2) resulting in agglutination reaction that is measured at – 650nm. The increase in turbidity corresponds to the concentration of HbA1c in the test specimen. Specimen collection and preparation No special preparation of the patient is required prior to specimen collection by approved techniques. No special additives or preservatives other than anticoagulants are required. Collect venous blood in EDTA using aseptic techniques.

## Specimen preparation
1. Mix the specimen (sample or reconstituted calibrator or reconstituted control) thoroughly to obtain uniform distribution of erythrocytes. Avoid bubble formation.
2. Take 500ulTurbodyne HbA1cHemolysing solution in a test tube.

3. Add 10ul of homogenized specimen (sample/reconstituted calibrator/reconstituted control). Mix well and allow to stand for 15 minutes or until complete lysis is apparent. This hemolysed specimen is referred as Lysate.

## Results and Observations

**Table 1:** Sex with Nephropathy

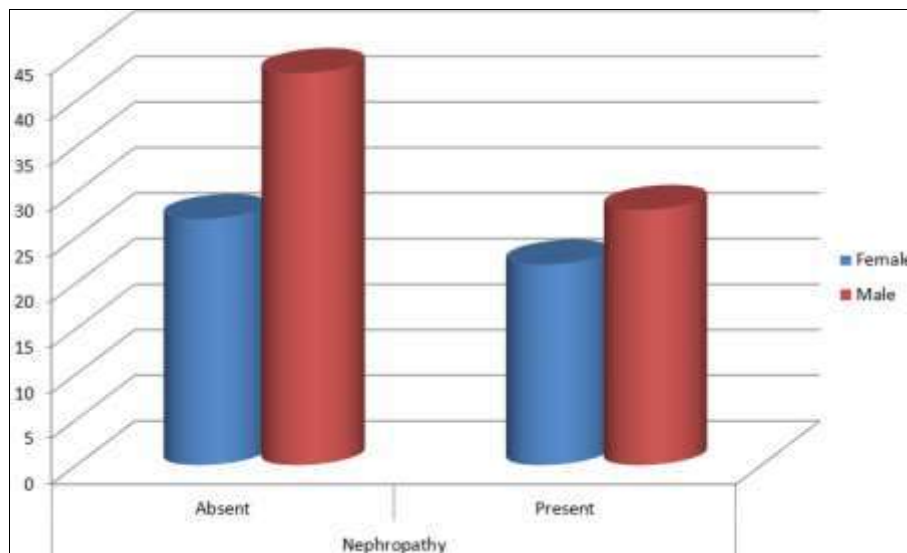| Gender | Nephropathy | | Total |
|--------|-------------|---------|-------|
| | Absent | Present | |
| Female | 27(55.10%) | 22(44.89%) | 49(100%) |
| Male | 43(60.56%) | 28(39.44%) | 71(100%) |
| Total | 70(58.33%) | 50(41.67%) | 120(100%) |



**Fig 1:** Gender impact of Nephropathy

A higher incidence and prevalence of renal failure particularly in non-diabetic renal patients is observed in men. According to Silbiger and Neugarten, the ratio between men and women that reaches renal insufficiency due to hypertensive nephropathy or glomerulonephritis is 1.6 men for each woman affected

**Table 2:** Age with Nephropathy

| Gender | Nephropathy | | Total |
|--------|-------------|---------|-------|
| | Absent | Present | |
| <+35 | 5 | 0 | 5 |
| 36-45 | 11 | 1 | 12 |
| 46-55 | 29 | 11 | 40 |
| 56-65 | 18 | 25 | 43 |
| 66+ | 7 | 13 | 20 |
| Total | 70 | 50 | 120 |

Mean + SD: 59.29 + 13.144

**Table 3:** Correlation coefficient between nephropathy and lipid

| Lipid Profile | Nephropathy |
|---------------|-------------|
| TC | 0.237** |
| LDL | 0.137** |
| TG | 0.38* |
| HDL | 0.081** |
| VLDL | 0.057** |

** Correlation is significant at $p<0.01$. * Correlation is significant at $p<0.05$.

**Table 4:** Association between nephropathy and lipid profile

| Lipid profile | Lipid profile with nephropathy | p-value |
|---------------|-------------------------------|---------|
| TC | 196.97 +48.18 | *$p<0.01$ |
| LDL | 122.75 +49.36 | *$p<0.01$ |
| TG | 160.93 + 56.21 | *$p<0.01$ |
| HDL | 39.64 +10.50 | *$p<0.01$ |
| VLDL | 32.21 + 11.32 | *$p<0.01$ |

* $p<0.01$ significant

## 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. It is known that cholesterol, triglycerides. A hospital based study done at RKDF Medical College Hospital & Research Center, Bhopal, Madhya Pradesh, India showed that the prevalence of dyslipedemia is high in diabetic population with high serum cholesterol>240 mg/dl was seen in 15%, serum triglycerides> 160 mg/dl in 42.41% increased LDL>130 mg/dl in 45.26% and HDL< 40 mg/dl 52.27% and Diabetic retinopathy and nephropathy were found to have significant correlation with low HDL, and raised LDL respectively.
`A study done at AIIMs, New Delhi showed that the hyperlipidemia in diabetes in associated with faster decline

in GFR, progression of albuminuria and nephropathy and retinopathy.

A study conducted by Amin-U1-Haq *et al*. Khyber Medical College, Peshawar, showed that there was significant dyslipidemia in type 2 diabetes mellitus patients was 90.7% [18].

A study conducted at Baylor college of Medicine, Houston, USA showed that Diabetic dyslipidemia is characterized by a constellation of lipid derangements-hypertriglyceridemia, a low concentration of high-density lipoprotein cholesterol. A study conducted in university of Verona showed that the TG/HDL-C ratio was positively associated with an increased risk of incident retinopathy and/or CKD independently of age, sex, body mass index, diabetes duration, Hba1c, hypertension, smoking history, low-density lipoprotein cholesterol, albuminuria. These findings suggest that TH/HDL-C ratio was associated with an increased incidence of micro vascular complications in individuals with type 2 diabetes mellitus without prior cardiovascular disease, independently of several potential confounders [19]. Intensive dietary therapy in 57 newly diagnosed Type 2 (non-insulin-dependent) diabetic patients led to an increase, compared with pre-treatment levels, in serum high density lipoprotein (HDL) cholesterol and the HDL/total cholesterol ratio after 3 and 6 months (0.05 less than p less than 0.1). The increase in HDL cholesterol was related to the degree of weight loss achieved. In 28 patients whose weight decreased by greater than or equal to 10% average body weight during the 6 months, HDL, cholesterol rose from 1.22 +/- 0.06 to 1.36+- 0.06 mmol/1 (p less than 0.001), whereas patients who lost less weight showed no significant increase in HDL cholesterol. The increase in mean serum HDL-cholesterol levels in female patients was associated with a mean weight reduction of 12.1% average body weight. Patients who were obese at diagnosis lost more weight during the study than non-obese patients (mean 13.2 versus 5.6% average body weight), and showed a significant increase in serum HDL cholesterol levels. We conclude that intensive dietary therapy may lead to a less atherogenic lipid profile in Type 2 diabetes, particularly in patients who achieve a major weight reduction [20]. The United Kingdom Prospective Diabetes Study (UKPDS) studied the course of > 5000 individuals with type 2 DM for >10 years. This study used multiple treatment regimens and monitored the effect of intensive glycemic control and risk factor treatment on the development of diabetic complications. Newly diagnosed individuals with type 2 DM were randomized to (1) intensive management using various combinations of insulin, a sulfonylurea, or metformin or (2) conventional therapy using dietary modification and pharmacotherapy with the goal of symptom prevention. In addition, individuals were randomly assigned to different antihypertensive regimens. Individuals in the intensive treatment arm achieved an HbA1c of 7%, compared to a 7.9% HbA1c in the standard treatment group, the UKPDS demonstrated that each percentage point reduction in HbA1c was associated with a 35% reduction in micro vascular complications. As in the DCCT, there was a continuous relationship between glycemic control and development of complications. Improved glycemic control also reduced the cardiovascular event rate in the follow-up period of > 10 years [21].

Reductions in the risks of retinopathy and nephropathy were also seen in a small trial of lean Japanese individuals with type 2 DM randomized to either intensive glycemic control or standard therapy with insulin (Kaumamoto study). These results demonstrate the effectiveness of improved glycemic control in individuals of different ethnicity and, presumably, a different etiology of DM (i.e., phenotypically different from those in the DCCt and UKPDS). The action to Control Cardiovascular Risk in Diabetes (ACCORD) and Action in Diabetes and Vascular Disease: Preterax and Diamicron MR controlled Evaluation (ADVANCE) trials also found that improved glycemic control reduced micro vascular complications [22]. Individuals with DM may have several forms of dyslipidemia. Because of the additive cardiovascular risk of hyperglycemia and hyperlipidemia, lipid abnormalities should be assessed aggressively and treated as part of comprehensive diabetes care. The most common pattern of dyslipidemia is hypertriglyceridemia and reduced high density lipoprotein (HDL) cholesterol levels. DM itself does not increase levels of low-density lipoprotein (LDL), but the small dense LDL particles found in type 2DM are more atherogenic because they are more easily glycated and susceptible to oxidation. Almost all treatment studies of diabetic dyslipidemia have been performed in individuals with type 2 DM because of the greater frequency of dyslipidemia in this form of diabetes [23]. A higher incidence and prevalence of renal failure particularly in non-diabetic renal patients is observed in men. According to Silbiger and Neugarten, the ratio between men and women that reaches renal insufficiency due to hypertensive nephropathy or glomerulonephritis is 1.6 men for each woman affected [24] Figure,1. There is a statistically significant large effect in FBS, PPBS, HbA1c, TAG, VLDL, HDL, and lipoprotein (a) levels of cases compared with controls, whereas LDL and cholesterol levels are no significant. Increased cholesterol /HDL, ratio is well known risk factors of coronary artery disease. HDL, LDL, cholesterol, and TAG levels were well associated with HbA1c, whereas lipoprotein (a) levels are not associated with HbA1c.

## 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 Correlation coefficient between nephropathy and lipid profile was found to be significant. There was correlation between lipid levels and duration of diabetes for all lipid fractions which were significant. All lipid fractions showed a progressive increase in severity of diabetes. The difference was statically significant. Degree of control diabetes was inadequate as more than 50% had high HbA1c.This probably is the main reason for significant dyslipidemia and as well as complication.

## Conflict of Interest
Not available

## Financial Support
Not available

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