# A comparative study on levels of renal and lipid profile in type 2 diabetic and diabetic nephropathy patients - a case control study

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## ABSTRACT

**Introduction:** Diabetic nephropathy is a leading cause of end-stage renal failure worldwide. Its morphologic characteristics include glomerular hypertrophy, basement membrane thickening, mesangial expansion, tubular atrophy, interstitial fibrosis and arteriolar thickening. All of these are part of micro vascular complications of diabetes.

**Objective:** The present study is one such attempt to find the relation between renal and lipid profile in diabetic nephropathy in ethnic south Indian population.

**Materials and Methods:** In the present study, 60 cases presenting with diabetic Nephropathy and 60 age and sex matched controls with type 2 diabetes were included in the study.

**Results:** In the present study FBS, PPBS, Urea, Creatinine, Total cholesterol, Triglycerides; LDL levels are increased whereas, HDL levels are decreased in diabetic nephropathy when compared with type 2 diabetes mellitus patients.

**Conclusion:** The present study shows LDL mass without major compositional changes suggests that the elevation of LDL in incipient and established diabetic nephropathy is primarily due to the increased number of LDL particles.

**Keywords:** Diabetes; Nephropathy; Urea; Creatinine; Total cholesterol; Triglycerides; HDL.

## INTRODUCTION

Diabetes mellitus continues to be the leading cause of chronic kidney disease (CKD) and end-stage renal disease in the United States, Japan, and Europe, accounting for up to 45% of all cases in Western societies. Diabetic nephropathy (DN) is a clinical syndrome found in both type 1 diabetes and type 2 diabetes that is characterized by heavy proteinuria, renal failure, and arterial hypertension (1), with its hallmark being persistent albuminuria (> 300 mg/24 hours). Risk factors for DN include age, race, systemic hypertension, hyperglycaemia, male gender, race, smoking, genetic susceptibility, and dyslipidaemia. These variables have also been positively linked to the increase in cardiovascular events (2). In turn, abnormal renal function and albuminuria may independently predict cardiovascular risk. There is increasing evidence linking dyslipidaemia as an independent contributing factor in the development and progression of glomerular injury, although the underlying mechanisms are currently debated (3). Diabetic dyslipidaemia over two decades ago, the recent study shows suspected that the persistent filtration of lipids and lipoproteins promote progression of chronic renal injury. Many subsequent observational studies supported the role of elevated levels of serum lipids in the development of albuminuria and in the progression of glomerulosclerosis**.** The lipid profiles of individuals with DN have been characterized to have higher plasma concentrations of very low density lipoprotein cholesterol (VLDLC), low-density lipoprotein cholesterol (LDLC), intermediate-density lipoprotein cholesterol, and triglycerides but lower levels of HDLC (4) also noted are elevated plasma concentrations of Apo lipoprotein (apo) B, apo C-III, and apo (a). The aforementioned lipid profile has been termed “diabetic dyslipidaemia”; it is mostly seen in individuals with type 2 diabetes (5).

Moreover, this is further characterized by a preponderance of dense, small-diameter LDLC and HDLC particles along with excessive postprandial lipemia, which results from increased concentrations of VLDLC and chylomicron remnants. An increase in hepatic lipase activity and a reduced post heparin plasma lipoprotein lipase (LPL) ratio have also been documented. Interestingly, theafore mentioned lipid abnormalities in DN become more accentuated with worsening renal function and urinary albumin excretion (6). The lipid alterations stem from insulin resistance and a defective insulin action in the metabolism of lipoproteins (7).

Role of dyslipidaemia in renal injury pathogenesis of glomerular and tubulointerstitial injury in the human glomerulus, one often finds the formation of mesangial foam cells via the expression of scavenger receptors for modified, glycosylated and oxidized

LDLC. Accumulation of these substances in the mesangial matrix triggers the activation of monocytes into macrophages. It is believed that this pathophysiologic mechanism of renal injury is related to dyslipidaemia via three stages. First, exposure to oxidized lipoproteins stimulates the mesangial cell secretion of chemotactic agents and adhesion molecules further enhancing the recruitment of macrophages (8).

The monocyte infiltration results in glomerulo-sclerosis and tubular fibrosis. Secondly, the uptake of oxidizing LDLC by recruited macrophages stimulates the release of reactive oxygen species and the expression of prosclerotic and proliferative cytokines (transforming growth factor [TGF]-β1 and platelet-derived growth factor-AB). Finally, these cytokines stimulate the production of extracellular matrix proteins subsequently promoting mesangial expansion (9). In the tubule-interstitium, the renal injury due to hyperlipidaemia has been suggested to be a prognostic indicator because tubulointerstitial lesions may precede glomerular changes and correlate better with renal disease progression. In studies of hyperlipidaemic, the tubular injury was ascribed to interstitial macrophage infiltration and an increase in TGF-β1 gene expression. It is believed that this is mediated via cytokine reactions and reactive oxygen species (10). These phenomena are similar to those in vivo studies where the tubular uptake and metabolism of filtered lipoproteins resulted in the expression of cytokines and subsequent local inflammation. The Present study is to find the relation between renal and lipid profile in diabetic nephropathy in South Indian population.

## MATERIALS AND METHODS

The present study was conducted in the Department of Biochemistry in collaboration with Department of Nephrology in Saveetha medical College, Thandalam, Chennai. The study was conducted on patients with type-2 diabetes mellitus and diabetic Nephropathy admitted in the nephrology unit in Saveetha Hospital and Medical College. This study was approved by Institutional Human ethics Committee. Study population consisted of 60 patients with diabetic nephropathy (Age range 40-75 yrs )and control group consisted of 60 patients with type-2 diabetes mellitus who are on medical treatment without any complications.

**Inclusion criteria:** Cases were taken who are diagnosed patients of diabetic Nephropathy attending the department of nephrology of saveetha medical college (defined as patients having arterial hypertension less than 200/160, eGFR > 45 and <90 mL/min/1.73 m2 and/or urinary albumin: creatinine ratio >3 mg/mmol (11). Controls: Known diabetes mellitus patients who are on medical treatment without any complications as controls and Age Group of 40-70yrs for both cases & controls.

**Exclusion criteria**

Patients will be excluded if they have any of the following: a history of cardiovascular disease, defined as having a clinical record of ischemic heart disease (angina, myocardial infarction, coronary artery revascularization and or heart failure), peripheral vascular disease (intermittent claudication or peripheral artery revascularization) or cerebrovascular disease (transient ischemic episodes or stroke). A history of malignancy or any other life threatening illness, current pregnancy, systolic blood pressure >200 mmHg, diastolic blood pressure >160 mmHg, hemoglobin A1c > 10 %, Significant renal impairment (eGFR< 45 mL/min 1.73 m2) and nephrotic range urine protein excretion (total protein excretion rate >3 g/day or albumin to creatinine ratio >300 mg/ mmol) and patients with age <40 and >70 are excluded. Sample collection and storage 5ml of venous whole Blood were collected from both type-2 diabetes mellitus and diabetic Nephropathy.

**Biochemical analysis**

Fasting Blood Sugar (FBS), Urea, Creatinine, Total Cholesterol, Triglycerides, High Density Lipoprotein (HDL), Low Density Lipoprotein (LDL) were estimated in VITROS 240. Statistical analysis were done using student 't'-test and p-value significance. P-value <0.01 were considered as significant.

## RESULTS

In the present study, a total number of 120 subjects comprising of 60 type-2 diabetes mellitus patients (control) and 60 diabetic nephropathy cases were included. Here, we have grouped 120 subjects into four groups based on gender. In the present study, we identified that association between renal and lipid profile in diabetic nephropathy. In the present study, there was significant increase in the Total cholesterol, triglycerides, LDL, Urea, Creatinine and decrease of HDL in the diabetic nephropathy patients when compared with diabetic patients (Table 1).

**Table 1:** Comparision of fasting blood sugar (FBS), post prandial blood sugar (PPBS), urea, creatinine, total cholesterol, triglycerides, HDl, LDL, VLDLin type 2 diabetes mellitus (T2DM-Controls) and diabetic nephropathy (DN- Cases)

| S. no | Parameter | Groups | Mean ± se | P value |
|---|---|---|---|---|
| 1 | FBS (mg/dL) | T2DM – Male | 123.82 ± 5.46 | <0.001 |
| | | DN- Male | 163.30 ± 2.50 | |

| | | | | |
|---|---|---|---|---|
| | | T2DM -Female | 119.00 ± 3.70 | <0.001 |
| | | DN- Female | 154.64 ± 7.62 | |
| 2 | PPBS (mg/dL) | T2DM – Male | 201.00 ± 7.32 | <0.001 |
| | | DN- Male | 235.09 ± 5.88 | |
| | | T2DM – Female | 198.94 ± 4.40 | <0.001 |
| | | DN- Female | 247.23 ± 11.42 | |
| 3 | UREA (mg/dL) | T2DM – Male | 28.78 ± 1.39 | <0.001 |
| | | DN- Male | 60.53 ± 1.60 | |
| | | T2DM – Female | 30.54 ± 1.05 | <0.001 |
| | | DN- Female | 58.76 ± 2.47 | |
| 4 | CREATININE (mg/dL) | T2DM – Male | 0.88 ± 0.04 | <0.001 |
| | | DN- Male | 3.73 ± 0.31 | |
| | | T2DM – Female | 0.90 ± 0.03 | <0.001 |
| | | DN- Female | 3.85 ± 0.54 | |
| 5 | TC (mg/dL) | T2DM – Male | 205.52 ± 1.29 | <0.001 |
| | | DN- Male | 228.56 ± 2.87 | |
| | | T2DM – Female | 207.05 ± 1.16 | <0.001 |
| | | DN- Female | 228.47 ± 4.57 | |
| 6 | TGL (mg/dL) | T2DM – Male | 172.96 ± 3.49 | <0.001 |
| | | DN- Male | 189.51 ± 2.67 | |
| | | T2DM – Female | 174.81 ± 2.30 | <0.001 |
| | | DN- Female | 189.47 ± 3.97 | |
| 7 | HDL (mg/dL) | T2DM – Male | 41.26 ± 0.80 | <0.001 |
| | | DN- Male | 30.86 ± 0.38 | |
| | | T2DM – Female | 40.84 ± 0.53 | <0.001 |
| | | DN- Female | 30.65 ± 0.69 | |
| 8 | LDL (mg/dL) | T2DM – Male | 134.69 ± 1.34 | <0.001 |
| | | DN- Male | 143.00 ± 1.13 | |
| | | T2DM – Female | 135.51 ± 0.94 | <0.001 |
| | | DN- Female | 143.94 ± 2.82 | |
| 9 | VLDL (mg/dL) | T2DM – Male | 34.59 ± 0.70 | <0.001 |
| | | DN- Male | 37.90 ± 0.53 | |
| | | T2DM – Female | 34.96 ± 0.46 | <0.001 |
| | | DN- Female | 37.89 ± 0.79 | |

## DISCUSSION

Table 1 shows the mean value of Fasting Blood Sugar of male in type-2 diabetes mellitus and diabetic nephropathy are 123.82 and 163.30 respectively. Its P value is < 0.001. It is found to be statistically significant (12).

Similarly, the mean value of Fasting Blood Sugar of female in type-2 diabetes mellitus and diabetic nephropathy are 119.00 and 154.64 respectively. Its P value is < 0.001. It is found to be statistically significant. Increased values of Fasting Blood Sugar in diabetic nephropathy in both male and female is observed. The mean value of Postprandial blood sugar of male in type-2 diabetes mellitus and diabetic nephropathy are 201.00 and 235.09 respectively. Its P value is <0.001. It is found to be statistically significant. Similarly, the mean value of Postprandial Blood Sugar of female in type-2 diabetes mellitus and diabetic nephropathy are 198.94 and 247.23 respectively. Its P value is < 0.001. It is found to be statistically significant. Increased values of post-prandial blood sugar in diabetic nephropathy in both male and female is observed.

Table 1 shows the mean value of Urea of male in type-2 diabetes mellitus and diabetic nephropathy are 28.78 and 60.53 respectively. Its P value is < 0.001. It is found to be statistically significant. Similarly, the mean value of Urea of female in type-2 diabetes mellitus and diabetic nephropathy are 30.541 and 58.76 respectively. Its P value is <0.001. It is found to be statistically significant. Increased values of Urea in diabetic nephropathy in both male and female is observed (13).

Table 1 shows the mean value of Creatinine of male in type-2 diabetes mellitus and diabetic nephropathy are 0.883 and 3.733 respectively. Its P value is <0.001. It is found to be statistically significant (14).

Similarly, the mean value of Creatinine of female in type-2 diabetes mellitus and diabetic nephropathy are 0.900 and 3.859 respectively. Its P value is <0.001. It is found to be statistically significant. Increased

values of Creatinine in diabetic nephropathy in both male and female is observed.

Table no 1 shows the mean value of total Cholesterol of male in type-2 diabetes mellitus and diabetic nephropathy are 205.52 and 228.55 respectively. Its P value is < 0.001. It is found to be statistically significant. Similarly, the mean value of total Cholesterol of female in type-2 diabetes mellitus and diabetic nephropathy are 207.05 and 228.47 respectively. Its P value is < 0.001. It is found to be statistically significant. Increased values of total Cholesterol in diabetic nephropathy in both male and female is observed (15).

Table no 1 shows the mean value of triglycerides of male in type-2 diabetes mellitus and diabetic nephropathy are 172.95 and 189.51 respectively. Its P value is < 0.001. It is found to be statistically significant. Similarly, the mean value of triglycerides of female in type-2 diabetes mellitus and diabetic nephropathy are 174.81 and 189.47 respectively. Its P value is < 0.001. It is found to be statistically significant. Increased values of triglycerides in diabetic nephropathy in both male and female is observed (15).

Table no 1 shows the mean value of HDL of male in type-2 diabetes mellitus and diabetic nephropathy are 41.261 and 30.860 respectively. Its P value is < 0.001. It is found to be statistically significant. Similarly, the mean value of HDL of female in type-2 diabetes mellitus and diabetic nephropathy are 40.838 and 30.647 respectively. Its P value is < 0.001. It is found to be statistically significant. Decreased values of HDL in diabetic nephropathy in both male and female is observed (16).

Table no 1 shows the mean value of LDL of male in type-2 diabetes mellitus and diabetic nephropathy are 134.696 and 143.00 respectively. Its P value is < 0.001. It is found to be statistically significant. Similarly, the mean value of LDL of female in type-2 diabetes mellitus and diabetic nephropathy are 135.514 and 143.941 respectively. Its P value is < 0.001. It is found to be statistically significant. Increased values of LDL in diabetic nephropathy in both male and female is observed (17).

VLDL of male in type-2 diabetes mellitus and diabetic nephropathy are 34.591 and 37.902 respectively. Its P value is < 0.001. It is found to be statistically significant. Similarly, the mean value of VLDL of female in type-2 diabetes mellitus and diabetic nephropathy are 34.962 and 37.894 respectively. Its P value is < 0.001. It is found to be statistically significant. Increased values of VLDL in diabetic nephropathy in both male and female is observed.

## CONCLUSION

The present study shows LDL mass without major compositional changes suggests that the elevation of LDL in incipient and established diabetic nephropathy is primarily due to the increased number of LDL particles. The net result consists of enhanced lipolysis with a subsequent increase in free fatty acids and VLDLC synthesis, a defect in LPL activity leading to the increased life span of chylomicrons and VLDLC in circulation, an increased transfer of cholesterol esters resulting in triglyceride-rich LDLC, and finally the elevation of plasma triglycerides and the reduced ratio of LPL to hepatic lipase causing the accelerated breakdown of HDLC.

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## CONFLICT OF INTEREST

The authors declare that there is no conflict of interest in this study.

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