Study of lipid profile in diabetic and non-diabetic chronic kidney disease patients on haemodialysis: a prospective comparative study from a sub Himalayan region in North India

Laxmi Nand1*, Rakesh Kumar2, Kamal Kumar2

1Department of Medicine, Indira Gandhi Medical College and Hospital, Shimla, Himachal Pradesh
2Department of Medicine, Regional Hospital Solan, Himachal Pradesh, India

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*Correspondence:
Dr. Laxmi Nand,
E-mail: laxminand66@gmail.com

ABSTRACT

Background: Diabetes mellitus (DM) is a major cause of chronic kidney disease (CKD) leading to diabetic kidney disease (DKD). Several studies have observed lipid profile abnormalities in non-diabetic CKD patients with and without haemodialysis. Our study aims to reveal lipid profile abnormalities both in DKD and non-diabetic CKD patients on haemodialysis.

Methods: A prospective comparative study included 50 DKD and 50 non-diabetic CKD patients on haemodialysis and 50 controls after fulfilling the inclusion and exclusion criteria. The demographic and biochemical, including lipid profile parameters data of all subjects was collected and statistically analysed. p<0.05 was considered as statically significant.

Results: A total of 100 study patients, 50 DKD and 50 non-diabetic CKD patients, both on haemodialysis revealed significant dyslipidaemia when compared to controls. Total cholesterol in DKD patients on haemodialysis when compared to controls (177.5±80.5 versus 146.5±31.8 mg/dl) was significantly elevated (p=0.01). Low density lipoprotein (LDL) in DKD patients when compared to controls (94.1±43.3 versus 76.3±26.3 mg/dl) was also significantly elevated (p=0.01). Triglyceride levels in both DKD and non-diabetic CKD patients on haemodialysis in comparison to controls (213.8±182.1 and 169.2±132.3 versus 109.2±28.9 mg/dl respectively) were significantly elevated (p=0.0002 and p=0.003 respectively). Similarly, very low-density lipoprotein (VLDL) levels in both DKD and non-diabetic CKD patients were also significantly elevated when compared to controls (p=0.002 and p=0.003 respectively) whereas high density lipoprotein (HDL) was significantly reduced.

Conclusion: Both DKD and non-diabetic CKD patients on haemodialysis revealed significant dyslipidaemia, a major cause of increased risk for cardiovascular diseases necessitating early treatment with statins.

Keywords: Chronic kidney disease, Dyslipidaemia, Haemodialysis, Lipid profile, Cardiovascular diseases
a level of eGFR <15 ml/min. Different types of etiological profiles involved in pathogenesis lead to development of uremic state in CKD. Diabetic kidney disease (DKD) develops in approximately 40% of diabetic patients and is a leading cause of CKD worldwide. DKD also termed as CKD due to diabetes, both type 1 and 2 is defined as persistently elevated albuminuria of >300 mg/24 hours (or >200 µg/min) or an urinary albumin to creatinine ratio (ACR) of >300 mg/gm with concurrent presence of diabetic retinopathy and absence of signs of other form of renal disease. National cholesterol education programme (NCEP) defines dyslipidemia as hypercholesterolemia ≥200 mg/dl of serum total cholesterol (TC), hypertriglyceridemia ≥150 mg/dl of serum triglyceride (TG), reduced high density lipoprotein cholesterol (HDL-C) <40 mg/dl for men and <50 mg/dl for women, elevated low density lipoprotein cholesterol (LDL-C) ≥130 mg/dl and high TC to HDL-C ratio of ≥4.5. Normal plasma lipids and lipoprotein metabolism is critical for cellular cholesterol homeostasis and protection against atherosclerosis, renal disease and other complication. ESRD results in dysregulation of several key enzymes and receptors involved in metabolism of lipoproteins particularly HDL-C and TG rich lipoproteins in CKD and DKD patients. The major changes include decrease in lecithin cholesterol acyl-transferase (LCAT), lipoprotein lipase (LPL), hepatic lipase, acyl-CoA diacylglycerol acyl-transferase (DGAT) and LDL receptor-related protein (LRP), and increase in cholesterol ester transfer protein (CETP) and acyl-CoA cholesterol acyl-transferase (ACAT). Studies have reported significant dyslipidemias in non-diabetic CKD patients on hemodialysis. Rifai et al reported elevated TG, LDL-C, TC to HDL-C ratio and reduced HDL-C in CKD patients on hemodialysis in comparison to controls. Mekki et al found that intermittent and long term dialysis fail to correct dyslipidemia generated by CRF. A study from India observed hypertriglyceridemia, elevated VLDL-C and lipoprotein-a and decreased HDL-C levels. There is increased lipid peroxidation and oxidative stress due to increased reactive oxygen species (ROS) and decreased superoxide dismutase (SOD) in CKD patients on hemodialysis. Ashish et al found significantly higher dyslipidemia in peritoneal dialysis (PD) than hemodialysis. Herzog et al found poor survival in acute myocardial infarction(MI) and Karnik et al observed cardiac arrest and sudden cardiac death in CKD patients on hemodialysis. Ganta et al reported that dyslipidemia in CKD accelerates the progression of cardiovascular disease and increased mortality. Both traditional and nontraditional risk factors and hypertriglyceridemia as an independent risk factor predict coronary heart disease in CKD. To reduce cardiovascular mortality due to dyslipidemia in CKD patients, early management with statins has been recommended by several studies. Rhe et al recommended to follow guidelines and risk assessment before start of treatment of dyslipidemia. Several studies have observed significant dyslipidemias as a major risk factor for CVD in non-diabetic CKD patients on hemodialysis and on conservative therapy. Our study aims to observe dyslipidemia both in DKD and non-diabetic CKD patients on hemodialysis with higher incidence and prevalence, especially in DKD.

METHODS

The study was conducted from June 2019 to May 2020 over a period of one year in a regional hospital catering CKD patient with high incidence and prevalence in sub Himalayan region of North India. A total of 100 study patients included 50 diabetic and 50 non-diabetic CKD patients on hemodialysis and were compared to 50 healthy individuals (controls).

Inclusion criteria

The inclusion criteria for the study was as follows: patients aged 18 years and above of both sexes; patients fulfilling the criteria of having diabetes mellitus both type 1 and type 2, albuminuria of >300 mg/ 24 hours or 200 µg/min or ACR of >300 mg/gm with concurrent presence of diabetic retinopathy with absence of signs of other form of renal disease and/or radiologically enlarged kidneys, allocated to diabetic CKD patients; patients of CKD without evidence of diabetes, allocated to non-diabetic CKD patients; both diabetic and non-diabetic CKD patients of ESRD with glomerular filtration rate (eGFR of <15 ml/min) on hemodialysis for a duration of more than 6 months and; age and sex matched to study group, the healthy individuals having normal renal function, allocated to controls, were included in the study.

Exclusion criteria

The exclusion criteria for the study was as follows: patients aged <18 years; patients taking statins, seriously ill patients and; non-consenting patients and controls were excluded from the study.

Approval from Institutional Ethical Committee was obtained. All eligible study patients and controls were thoroughly investigated and lipid profile including TC, TG, HDL-C, LDL-C and VLDL-C were done by enzymatic method using Merilyzer auto quat 100 machine. NCEP guidelines were used for definition of dyslipidemia as having TC levels ≥200 mg/dl, TG levels ≥150 mg/dl LDL-C <40 mg/dl for men and <50 mg/dl for women and HDL-C ≥130 mg/dl.

Statistical analysis

The data was entered in excel sheet and analyzed statistically using Epi-info version 7. Chi square (χ²) test for comparison of categorical variables and student ‘t’ test for comparison of means were used. For all comparison, of p<0.05 was considered as statistically significant.

RESULTS

A total of 100 study patients, 50 DKD and 50 non-diabetic CKD patients revealed mean age of 59.4±10.0 and 45.4±13.4 years with male to female ratio of 2.3:1 and
1.9:1 respectively as compared to 50 controls revealing mean age of 54.80±13.3 years with male to female ratio of 1:1:1. Both DKD and non-diabetic CKD patients on hemodialysis had ESRD (eGFR<15 ml/min) revealing significantly increased blood urea nitrogen (BUN) and serum creatine in comparison to controls (Table 1).

Table 1: Demographic and diagnostic parameters of diabetic and non-diabetic CKD patients on haemodialysis and controls.

| Parameters                  | Diabetic CKD (n=50) | Non diabetic CKD (n=50) | Control (n=50) | p value |
|-----------------------------|---------------------|-------------------------|----------------|---------|
| Age (years)                 | Male                | 59.7±10.7               | 44.3±13.6      | 55.5±14.2 | 0.21  | 0.003** |
|                             | Female              | 58.5±8.3                | 47.7±12.6      | 53.9±12.0 | 0.18  | 0.13   |
|                             | Total               | 59.4±10.0               | 45.4±13.4      | 54.80±13.3| 0.06  | 0.0008**|
| Sex N (%)                   | Male                | 35 (70%)                | 33 (66%)       | 27 (54%)  | 0.15  | 0.16   |
|                             | Female              | 15 (30%)                | 17 (34%)       | 23 (46%)  | 0.15  | 0.16   |
| Blood urea nitrogen (mg/dl) |                     | 83.46±36.3              | 76.4±37.6      | 20.8±4.3  | 0.002* | 0.01*  |
| Serum creatine (mg/dl)      |                     | 8.7±3.1                 | 11.5±10.6      | 0.7±0.09  | <0.001*| <0.001*|
| Fasting blood sugar (mg/dl) |                     | 146.26±23.74            | 99±16.29       | 93.76±13.36| 0.0001*| 0.08   |
| HBA1C (%)                   |                     | 7.28±1.2                | 5.47±0.52      | 5.48±0.85 | 2.3   | 1.8    |
| Albumin creatinine ratio (mg/gm) | 2469.3±1809.8        | 139.2±94.3              | -              | 0.00001†  |
| Diabetic retinopathy        | +                   | -                       | -              | -        |
| Duration of diabetes (years)|                     | 10.24±4.97              | -              | -        |

p<0.05; *significant (diabetic CKD versus controls), **significant (non-diabetic CKD vs controls) and †significant (diabetic CKD versus non-diabetic CKD). CKD; chronic kidney disease.

Table 2: Serum lipid profile (TC, TG, HDL, LDL, VLDL) in diabetic and non-diabetic CKD patients on hemodialysis and controls.

| Group            | TC (mg/dl) | TG (mg/dl) | HDL (mg/dl) | LDL (mg/dl) | VLDL (mg/dl) |
|------------------|------------|------------|-------------|-------------|--------------|
| Diabetic CKD (n=50) | 177.5±80.5 | 213.8±182.1 | 38.7±14.0   | 94.1±43.3   | 42.6±36.5    |
| Non-diabetic CKD (n=50) | 158.3±72.5 | 169.2±132.3 | 41.9±10.0   | 82.4±47.4   | 33.8±26.4    |
| Control (n=50)   | 146.5±31.8 | 109.2±28.9  | 48.3±5.6    | 76.3±26.3   | 21.8±5.7     |
| P value          | 0.01†      | 0.0002*     | 0.0003*     | 0.01†       | 0.002*       |
|                  | 0.3        | 0.003**     | 0.0001**    | 0.4         | 0.003**      |

p<0.05; *significant (diabetic CKD versus controls) and **significant (non-diabetic CKD versus controls). CKD; chronic kidney disease, TC; total cholesterol, TG; triglycerides, HDL; high density lipoproteins, LDL; low density lipoprotein, VLDL; very low-density lipoprotein.

Table 3: Comparison of serum lipid profile (TC, TG, HDL, LDL, VLDL) in diabetic and non-diabetic CKD patients on hemodialysis.

| Group            | TC (mg/dl) | TG (mg/dl) | HDL (mg/dl) | LDL (mg/dl) | VLDL (mg/dl) |
|------------------|------------|------------|-------------|-------------|--------------|
| Diabetic CKD (n=50) | 177.5±80.5 | 213.8±182.1 | 38.7±14.0   | 94.1±43.3   | 42.6±36.5    |
| Non-diabetic CKD (n=50) | 158.3±72.5 | 169.2±132.3 | 41.9±10.0   | 82.4±47.4   | 33.8±26.4    |
| p value          | 0.2        | 0.1        | 0.0001**    | 0.2         | 0.1          |

p<0.05; **significant (diabetic CKD versus non-diabetic CKD). CKD; chronic kidney disease, TC; total cholesterol, TG; triglycerides, HDL; high density lipoproteins, LDL; low density lipoprotein, VLDL; very low-density lipoprotein.

DKD patients with 10.24±4.97 years of mean duration of having diabetes in comparison to non-DKD patients revealed significantly increased ACR (p<0.001) with concurrent non-proliferative diabetic retinopathy (NPDR) which fully met out the diagnostic criteria of DKD (Table 1 and Figure 1).
controls (p=0.4). HDL-C in both DKD and non-diabetic CKD patients in comparison to controls (38.7±14.0 and 41.9±10.0 versus 48.3±5.6 mg/dl respectively) was significantly decreased (p<0.001). TG levels in both DKD and non-diabetic CKD patients in comparison to controls (213.8±182.1 and 169.2±132.3 versus 109.2±28.9 mg/dl respectively) were significantly elevated (p=0.0002 and 0.003 respectively). Similarly, VLDL-C levels in both DKD and non-diabetic CKD patients in comparison to controls were also significantly elevated (p=0.002 and 0.003 respectively). Comparative results of lipid profile abnormalities in study patients in comparison to controls are revealed by p value for significance (Table 2) and also depicted graphically (Figure 2).

**DISCUSSION**

One-year study was conducted in regional hospital catering patients of DKD and non-diabetic CKD with increased incidence and prevalence in periphery. This comparative study included 50 DKD and 50 non-diabetic CKD patients on hemodialysis with mean age of 59.4±10.0 and 45.4±13.4 years with male to female ratio of 2:3:1 and 1:9:1 respectively in comparison to 50 controls with mean age of 54.8±13.3 years and male to female ratio of 1:1.1. In a similar comparative study by Raju et al, 45 CKD patients on hemodialysis, 50 non-hemodialysis CKD patients and 50 controls had mean age of 45.2±11.03, 45.9±10.50 and 40.94±10.0 2 years with male to female ratio of 1.2:1, 1.4:1 and 1.5:1 respectively. In the present study revealed increased incidence of DKD and non-diabetic CKD in males. BUN and serum creatine levels were significantly increased in comparison to controls (8.7±3.1 and 11.5±10.6 versus 0.7±0.09 mg/dl respectively), as the DKD and non-diabetic CKD patients had ESRD (stage 5) and were on hemodialysis. These observations are closely related to study by Kularia et al where CKD patients with and without dialysis and controls revealed BUN and serum creatine of 9.66±2.98, 7.67±2.45 and 0.76±0.34 mg/dl respectively. In the present study DKD patients revealed mean duration of 10.24±4.9 7 years of diabetes and high ACR in comparison to non-diabetic CKD patients (2469.3±1809.8 versus 139.2±49.3 mg/gm) with concurrent NPDR (Table 1). Wu et al reported more severe diabetic retinopathy and macular oedema. In the present study, TC and LDL-C levels were significantly elevated in DKD patients on hemodialysis (p<0.01) but not significantly elevated in non-diabetic CKD patients(p>0.05) when compared to controls, although the mean levels were in normal range in both DKD and non-diabetic CKD patients but insignificantly higher in DKD patients (p>0.05). TG (213.8±182.1 mg/dl) resulting in hypertriglyceridemia and VLDL-C levels were significantly elevated and HDL-C was significantly reduced in DKD patients in comparison to controls (p<0.001; Table 2). These observations of dyslipidemia in DKD patients on hemodialysis is similar to a study by Maurya et al where they observed increased levels of both TC and LDL-C along with increased levels of TG and VLDL-C with reduced HDL-C levels in CKD patients on hemodialysis. However Ashish et al found TC, LDL-C significantly higher and HDL-C significantly lower in CKD patients on PD than on hemodialysis. The present study revealed significantly increased TG and VLDL-C (p=0.003) and significantly reduced HDL-C levels compared to non-diabetic CKD patients (p>0.05; Table 3). Although mean lipid profile levels in DKD and non-diabetic CKD patients except for DKD patients revealing hypertriglyceridemia (213.8±182.1 versus 169.2±132.3 mg/dl), were in normal range but exhibited significant dyslipidemia when compared to controls (Table 2 and 3). However, HDL-C in DKD patients in comparison to non-diabetic CKD patients (38.7±14.0 versus 41.9±10.0 mg/dl) was significantly decreased (p<0.001).
CONCLUSION

Both DKD and non-diabetic CKD on haemodialysis revealed significant dyslipidaemia with a difference of DKD patients revealing significantly elevated TC and LDL-C levels as well in comparison to controls and significantly reduced HDL-C in comparison to non-diabetic CKD patients leading to significant difference of dyslipidaemia also between DKD and non-diabetic CKD patients, a major cause of increased risk for CVD attributable to necessitating early treatment with statins. However, a larger study recruiting DKD patients with and without haemodialysis and controls needs to be conducted for better comparative analysis of dyslipidaemia in DKD.

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