

Original Article



Dyslipidemia in End Stage Renal Disease: A Study on Dialysis Patients in Bangabandhu Sheikh Mujib Medical University Bangladesh

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Abstract

Background: Dyslipidemia contributes to the high cardiovascular risk in end stage renal disease (ESRD) or in dialysis patients; however, it remains an underestimated problem. **Objective:** To see the extent of dyslipidemia in patients of end stage renal disease i.e. chronic kidney disease (CKD) stage 5 who underwent hemodialysis or peritoneal dialysis procedure. **Materials and Methods:** This cross-sectional study was conducted from September 2016 to March 2018 Bangabandhu Sheikh Mujib Medical University (BSMMU) on 55 CKD (stage 5) patients where 31 in hemodialysis (HD) (group A) and 24 in continuous ambulatory peritoneal dialysis (CAPD) (group B). Serum lipid profile was estimated in both groups by using the standard laboratory technique. **Results:** Dialysis adequacy (Kt/V) was found 1.46 for HD patients (group A) and 1.81 for CAPD patients (group B). All serum lipids were higher in amount in CAPD patients than HD patients-total cholesterol (222.3±24.2 mg/dl vs. 198.9±28.4 mg/dl; $p<0.05$), triglycerides (179.6±24.7 mg/dl vs. 176.6±24.4 mg/dl; $p<0.05$), HDL cholesterol (40.8±3.90 mg/dl vs. 38.5±4.95 mg/dl; $p>0.05$) and LDL cholesterol (145.5±22.1 mg/dl vs. 123.2±26.5 mg/dl; $p<0.05$). Besides, dyslipidemia was more evident in CAPD patients than HD patients, as per raised serum total cholesterol (83.33% vs. 70.97%), raised triglycerides (95.83% vs. 83.87%), raised LDL (100% vs. 77.42%) and lowering of HDL cholesterol (87.5% vs. 80.65%) were found more in group B in comparison to group A. **Conclusion:** Dyslipidemic risk factors are highly evident in dialysis patients and the extent of dyslipidemia is observed more in CAPD than HD patients.

Key words: End stage renal disease, Chronic kidney disease, Dialysis, Dyslipidemia, Lipid profile.

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Introduction

The incidence and prevalence of chronic kidney disease (CKD) and end-stage renal disease (ESRD) are high and are increasing worldwide.¹ Dyslipidemia and its association with renal disease has been a known topic of research over more than 100 years.² However, dyslipidemic changes in chronic kidney disease, end stage renal disease and dialysis patients are still underestimated

concerns.³ The association between hyperlipidemia and accelerated cardiovascular disease is now well accepted, and many recent studies have focused on the nature and significance of lipid abnormalities in patients with renal disease.^{4,5} ESRD patients under dialysis are associated with specific qualitative and quantitative lipid abnormalities, resulting in specific dyslipidemia.⁵ Dyslipidemia is highly

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prevalent among CKD patients; it appears in the early stages of renal insufficiency and as CKD progresses, it becomes more intense, and in ESRD, may lead to fatality.^{6,7} Evidence showed that CKD patients are usually characterized by high triglycerides and low HDL levels, normal or slightly reduced cholesterol-LDL.⁸ Nevertheless, Cholesterol-LDL is not a reliable predictive cardiovascular risk factor in patients with advanced CKD.⁴ Moreover, in ESRD, low cholesterol levels have been related to high mortality risk, probably reflecting chronic inflammation and malnutrition, which is diametrically opposite to the well-established association of higher lipid levels with morbidity and mortality in the general population.⁹ Hence, controversies prevail among researchers in determining the role of dyslipidemia in the pathophysiology of atherosclerosis and its cardiovascular risks in patients with impaired renal function and demand more and more studies in different ethnicities. However, to our knowledge, no such study has been done in our country to date. Therefore, the present study was designed to see the extent of dyslipidemia in end stage renal disease (CKD stage 5) and compare the effect of hemodialysis and peritoneal dialysis on lipid profile in a tertiary level facility of the country.

Materials and Methods

This cross-sectional study was conducted in the Department of Nephrology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh, from September 2016 to March 2018. The study population was all the patients admitted in the BSMMU hospital with CKD stage 5 and either under hemodialysis or under continuous ambulatory peritoneal dialysis (CAPD) at least for 3 months during that study period. However, we adopted convenient purposive sampling method and study participants were selected based on the following inclusion and exclusion criteria:

Inclusion criteria

- 1) Age 18 years or above;
- 2) CKD stage 5 patients (as defined by the K/DOQI clinical practice guidelines for chronic kidney disease)¹⁰ having either HD or CAPD for at least 3 months; and
- 3) Patients on adequate dialysis, as estimated by Kt/V >1.2 for HD patients¹¹ and weekly Kt/V >1.7 for CAPD patients.¹²

Exclusion criteria

- 1) Patients receiving statin therapy;
- 2) Patients having chronic liver diseases;
- 3) Patients declined to participate in the study.

Finally, a total of 55 patients were included in the study - 31 in hemodialysis (HD) (group A) and 24 in continuous ambulatory peritoneal dialysis (CAPD) (group B).

Assessment of dialysis adequacy

Assessment of dialysis adequacy was done in terms of Kt/V. In hemodialysis (HD), probable study patient was asked to come in fasting state in the morning. They were on low flux dialysis with bicarbonate dialysate 4 hours twice weekly dialysis with

unfractionated heparin as anti-coagulant. Pre-dialysis and post-dialysis blood samples were taken for assessing urea. Post dialysis weight with ultrafiltrate amount also noted in that session. They were assessed for measuring dialysis adequacy using standard formula (Kt/V) for HD patients¹³ and finally, 31 patients were enrolled for the study group A (HD) having required Kt/V >1.2.

$$Kt/V = -\ln[U_{\text{post}}/U_{\text{pre}} - 0.008t] + [4?3.5U_{\text{post}}/U_{\text{pre}}] \times (W_{\text{post}} - W_{\text{pre}}) / W_{\text{post}}$$

where U_{post} = pos-dialysis urea in mg/dl; U_{pre} = pre-dialysis urea in mg/dl; t = time of dialysis session in hour; W_{post} = post-dialysis weight in kilograms; W_{pre} = pre-dialysis weight in kilograms; $(W_{\text{post}} - W_{\text{pre}})$ is the UF volume i.e. ultrafiltrate in kilograms.

In continuous ambulatory peritoneal dialysis (CAPD), patients were on 3 exchanges over 24 hours with 2 litres of 1.5% glucose fluid and asked to bring all the 3 dialysate bags used in last 24 hours in a pre-fixed date and aliquots were taken from each bag. According to the multiple-aliquot method (as described by Lyon et al.)¹⁴, net weight of fluid was determined in each bag. A small aliquot (10 ml) from each bag was collected for urea determination. Urea level was measured from each bag and fluid volume per bag was noted. Mean dialysate urea level was determined for each patient. Patients were also asked to bring last 24-hour urine collection. Total urine volume and urinary urea level were measured. At the same day, blood sample was collected (between the gap of the fluid exchange) for measuring urea level. Patients' weight was also measured. After collecting all data peritoneal and renal Kt/V were measured according standard formula.¹⁵

$$\text{Peritoneal Kt/V} = [D_{\text{urea}}/P_{\text{urea}} \times \text{Dialysate Volume}] \div V_{\text{durea}} \times 7 \text{ days}$$

$$\text{Renal Kt/V} = [U_{\text{urea}}/P_{\text{urea}} \times \text{Urine Volume}] \div V_{\text{durea}} \times 7 \text{ days}$$

where D_{urea} = Dialysate urea in mg/dl; P_{urea} = Plasma urea in mg/dl; U_{urea} = urine urea in mg/dl; V_{d} = volume of distribution = (Total body weight \times 0.6).

Then total Kt/V was calculated by summation of peritoneal and renal Kt/V for CAPD patients. Finally, 24 patients with total Kt/V >1.7 were included in our study.

Assessment of dyslipidemia

Fasting lipid profile was done from 12-hour fasting blood samples. Centrifuged serum of the two group of patients were stored in -20°C in the Biochemistry Laboratory of BSMMU Hospital. Total cholesterol was measured by enzymatic methods by using cholesterol esterase and cholesterol oxidase. Triglycerides were measured with glucose oxidase method by using glycerol phosphate oxidase and glucose. High density lipoprotein (HDL) cholesterol was measured by the direct method using elimination/catalase, while low density lipoprotein (LDL) cholesterol was calculated using the 'Friedewald formula'. Dyslipidemia was determined if any

patient had "total cholesterol >190 mg/dl, triglycerides >150 mg/dl, LDL-cholesterol >115 mg/dl, HDL-cholesterol <45 mg/dl".¹⁶ Standard laboratory techniques were followed using Mindray BS-230 Automated Clinical Chemistry Analyzer; Made in Shenzhen, China.

All data were recorded systematically in data table. Quantitative data were expressed as mean and standard deviation and qualitative data were expressed as frequency and percentage. Statistical analyses were performed using SPSS (Statistical Packages for Social Sciences) Association between variables were done by unpaired Student 't' test and by Mann-Whitney test. P value <0.05 was considered as statistically significant.

The study was approved by the Institutional Review Board (IRB) of BSMMU, Dhaka, Bangladesh.

Results

In the present study, 31 patients were under hemodialysis (HD) (group A), while 24 patients were under continuous ambulatory peritoneal dialysis (CAPD) (group B). In group A, most of the patients were from 31-50 age group (45.1%), while in group B, majority were from >50 age group (54.16%). Patients' gender shows male predominance in both groups, which was more marked i.e. 54.83% and 70.83% in group A and B respectively. Most of the patients were from urban areas i.e. 87.1% and 70.8% group A and B respectively (Table I). The difference in duration of CKD in between groups was not significantly significant (p>0.05); however, the duration of dialysis was quite different between the CAPD and HD patients and was significant (p<0.01). Dialysis adequacy in the form of Kt/V was found 1.46 for HD patients and 1.81 for CAPD patients (Table II). Lipid profiles showed that all serum lipids were higher in amount in CAPD patients than HD patients - total cholesterol (222.3±24.2 mg/dl vs. 198.9±28.4 mg/dl; p<0.05), triglycerides (179.6±24.7 mg/dl vs. 176.6±24.4 mg/dl; p<0.05), HDL cholesterol (40.8±3.90 mg/dl vs. 38.5±4.95 mg/dl; p>0.05) and LDL cholesterol (145.5±22.1 mg/dl vs. 123.2±26.5 mg/dl; p<0.05) (Table III). Dyslipidemia was more evident in CAPD patients than HD patients, as per raised serum total cholesterol (83.33% vs. 70.97%), raised triglycerides (95.83% vs. 83.87%), raised LDL (100% vs. 77.42%) and lowering of HDL cholesterol (87.5% vs. 80.65%) were found more in group B in comparison to group A (Table IV).

Table I: Demographic characteristics of study subjects (n=55)

	Group A (CKD 5 with HD) (n=31)		Group B (CKD 5 with CAPD) (n=24)	
	Frequency	Percentage	Frequency	Percentage
Age (years)				
18-30	4	12.9	3	12.5
31-50	14	45.1	8	33.33
> 50	13	41.9	13	54.16
Sex				
Male	17	54.83	17	70.83
Female	14	45.17	7	29.16
Residence				
Rural	4	12.9	7	29.1
Urban	27	87.1	17	70.8

Table II: Duration of dialysis and chronic kidney disease (CKD) and dialysis adequacy (n=55)

	Group A (CKD 5 with HD) (n=31)		Group B (CKD 5 with CAPD) (n=24)		P value
	Median	Range	Median	Range	
Duration of Dialysis (months)	10.0	3-24	9.0	3-12	0.009
Duration of CKD (months)	24.0	8-60	18.0	10-60	0.333
Dialysis Adequacy (Kt/V)	1.46	1.2-1.86	1.81	1.71-2.00	-

Table III: Lipid profiles of study subjects (n=55)

	Group A (CKD 5 with HD) (n=31)		Group B (CKD 5 with CAPD) (n=24)		P value
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
Total Cholesterol (mg/dl)	198.9±28.4	222.3±24.2			0.002
Triglyceride (mg/dl)	176.6±24.4	179.6±24.7			0.658
HDL Cholesterol (mg/dl)	38.5±4.95	40.8±3.90			0.065
LDL Cholesterol (mg/dl)	123.2±26.5	145.5±22.1			0.002

P value reached from unpaired Student t-test.

Table IV: Dyslipidemia among study subjects (n=55)

Dyslipidemic Factor	Group A (CKD 5 with HD) (n=31)		Group B (CKD 5 with CAPD) (n=24)	
	Frequency	Percentage	Frequency	Percentage
Total Cholesterol >190 mg/dl	22	70.97	20	83.33
Triglyceride >150 mg/dl	26	83.87	23	95.83
LDL >115 mg/dl	24	77.42	24	100.00
HDL <45 mg/dl	25	80.65	21	87.50

Discussion

Our results showed elevated total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C) and lower concentration of high-density lipoprotein cholesterol (HDL-C) in ESRD patients, which was much more evident in CAPD patients in comparison to HD patients. Our findings are supported by the evidence as described by Siamopoulou et al., Jeong et al., Attman et al., Kronenberg et al., Borazan, Ustün and Yilmaz, Weiner and Sarnak, Yilmaz et al., Tsimihodimos, Dounousi and Siamopoulos and Lacquaniti et al.¹⁷⁻²⁴

Dyslipidemia is common among patients with end-stage renal disease, whether treated by hemodialysis (HD) or peritoneal dialysis (PD).^{3,8} The mechanism for increased concentration of triglyceride as due to delayed catabolism in ESRD patients. The reduced catabolic rate is likely due to diminished lipoprotein lipase activity as a consequence of the down-regulation of the enzyme gene and the presence of lipase inhibitors in CKD patients.^{5,8,23} In comparison to HD patients, hypertiglyceridemia is more prevalent in CAPD patients, the pathophysiological mechanism is not clear though. However, it has been suggested that the significant absorption of glucose from the dialysis fluid may play a significant role as it can lead to an increase in insulin levels and may enhance the hepatic synthesis and secretion of VLDL.²⁵ Although no direct correlation has been observed between peritoneal glucose absorption and serum lipid levels in peritoneal dialysis patients, recent studies indicate that the reduction of glucose load with the use of less absorbed icodextrin-containing dialysis solution instead of glucose for the overnight dwell, sufficiently improves the lipid profile of those patients.²⁶ CAPD patients exhibit a more atherogenic lipid profile that is especially characterized by higher total cholesterol and LDL cholesterol values, which was also evident in our study.^{3,5} The following factors associated with the PD treatment may explain those alterations in lipoprotein metabolism. CAPD patients lose substantial amounts of plasma proteins into the peritoneal dialysate, which stimulates synthesis of albumin and other liver-derived proteins, including cholesterol-enriched lipoproteins.^{8,24} However, it may mentioned that substantial amounts of apolipoproteins and intact lipoproteins are also lost via the peritoneal cavity during CAPD.²⁵

Conclusion

CAPD patients had higher serum triglycerides and HDL cholesterols than HD group which were not statistically significant. However, CAPD patients also revealed higher total cholesterol and LDL Cholesterol level than HD group, which were statistically significant. In our study, dyslipidemic risk factors are highly evident in dialysis patients, and the extent of dyslipidemia is observed more in CAPD than HD patients.

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