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Dyslipidemia among Patients with End Stage Renal Disease on Maintenance Hemodialysis

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Abstract: ***Dyslipidemia has been suggested to be one of the factors that contribute to the high incidence of cardiovascular disease in hemodialysis patients. Previous studies suggest that end-stage renal disease may contribute to dyslipidemia. The aim of the study: to assess the prevalence of dyslipidemia in patients on maintenance hemodialysis. Patients and Methods: A case-control study was conducted from February 2015 until August 2015 in Ibn-Sena teaching hospital on 100 participants (52 males and 48 females), 50 were patients with end-stage renal disease on regular hemodialysis and 50 were age and gender-matched apparently healthy subjects as the control. Questioner used to collect data, a thorough examination was done including height and weight and BMI. A blood sample from all participants in fasting state was sent for the renal function test, complete blood picture, serum albumin, electrolytes, TG, total cholesterol, LDL and HDL measured by the enzymatic method, plasma atherogenic index calculated as [log (TG/HDL)]. Results: Age of the participants ranged between 18 - 70 years and the mean age was (44.45 ± 13.6) years. In HD group, the mean cholesterol was (3.29 + 0.73) mmol/l, serum TG (2.38 ± 0.56) mmol/l, LDL (1.91 ± 0.66) mmol/l, HDL (0.88 ± 0.2) mmol/l, atherogenic index (0.434 ± 0.16), while in control group, the mean cholesterol was (4.17 ± 0.69) mmol/l, serum TG (1.6 ± 0.43) mmol/l, LDL (2.69 ± 0.63) mmol/l, HDL (1.066 ± 0.13) mmol/l, atherogenic index (0.177 ± 0.12). The lipid abnormalities in hemodialysis group were high plasma atherogenic index in 84%, hypertriglyceridemia 50%, hypercholesterolemia 8% and high LDL 6% and low HDL in 48%, while in control group, high plasma atherogenic index in 34%, hypertriglyceridemia in 26%, hypercholesterolemia 14% high LDL 7% and low HDL in 16%. Conclusions: patients with end-stage renal disease on hemodialysis have significant dyslipidemia compared to control group characterized by hypertriglyceridemia, low HDL and high atherogenic index of plasma.***

Keywords: dyslipidemia, end-stage renal disease, hemodialysis, atherogenic index of plasma**.**

1. INTRODUCTION

Lipids are transported in plasma through water-soluble molecules known as lipoproteins, besides their transport characteristics, different enzymes in the lipid metabolism also function as chemical reaction platforms converting transported lipids into one another. Lipoproteins have a core consisting of non-polar lipids such as triglyceride and cholesterol and a surrounding structure consisting of polar lipids such as apolipoprotein and phospholipids. [1].

The end-stage renal disease is associated with distinctive changes in lipoprotein metabolism and dyslipidemia [2], uremic dyslipidemia is presented as an abnormal apolipoprotein profile and alteration in the composition and concentrations of lipoprotein groups. [3].

The mechanism of lipid derangements in dialysis patients is multifactorial. The most important abnormalities are impaired catabolism of the major triglyceride containing lipoprotein fraction, disproportionate hepatic synthesis of triglyceride because of carbohydrate intolerance and stimulation of hepatic synthesis of free fatty acid released from tissue triglyceride stores by lipolytic hormones. A number of factors specific to hemodialysis patients may lead to hyperlipidemia, such as, acetate in the dialysate may be transformed into long chain fatty acids and cholesterol in the liver, the use of high concentration of glucose in the dialysate associated with an increase in the carbohydrate load and has been reported to increase serum triglyceride in dialysis patients, in patients on hemodialysis carnitine deficiency has been blamed to be a factor in the lipid abnormalities in these patients [4].

Aims of study: To assess lipid profile and atherogenic index of plasma in patients with end-stage renal disease on regular hemodialysis and to compare it with healthy people, and to correlate this lipid profile with age, gender, and BMI.

2. METHODS AND MATERIALS

Across-sectional case-control study, it was conducted in Ibn-Sena Teaching Hospital during the period from February 2015 until August 2015.

A total of 50 patients (mean age = 46.82 ± 12.6) with ESRD on regular hemodialysis (28 male and 22 Female; from the Department of Internal Medicine, Centre for Kidney Disease, Ibn-Sena Teaching Hospital were enrolled in the study.

Inclusion criteria: Patients with ESRD on regular hemodialysis. Age of patients between 18 and 70 years.

Exclusion criteria: Patients with diabetes mellitus, Patients with nephritic syndrome, acute kidney injury, renal transplant recipients, Pregnants and those receiving drugs known to alter lipid profile.

Fifty apparently healthy subjects, 24 male, 26 female and age (mean age = 34.16 ± 14.4, ranged between 18-70years) matched to HD group none of them were diabetic, alcoholic or using drugs that affect lipid profile.

A written consent was taken from each candidate to be enrolled in the study and confidentiality was taken into consideration.

The data were collected through direct interview using a special questionnaire, and clinical examination was done including height and weight to calculate BMI, The body weight was measured for the HD group after the dialysis session.

Laboratory methods:

Six ml of venous blood were taken from each candidate after 12 hours of the overnight fast. In hemodialysis group blood were taken before the dialysis session, 2 ml of blood were drawn into EDTA tube and send for a complete blood count, the rest 4 ml were put in gel tube and left to clot then centrifuged up to 3000 rpm to separate serum which was sent for measurement of albumin, electrolytes, fasting blood glucose, serum TG, total cholesterol, LDL and HDL by enzymatic method.

Reference range of serum albumin is (35 – 50 g/l) and for fasting blood glucose is (3.3-5.8 mmol/l) (11). For definition of an abnormal lipid values: s.Cholesterol. ≥ 5.2 mmol/l, LDL ≥ 3.3mmol/l, HDL ≤0.9mmol/l (12), s.TG ≥ 2.25mmol/l. (13)

Atherogenic index of plasma calculated as **[log (TG/HDL)]**, levels > 2.1 considered as high risk. (14)

Statistical analyses:

Statistical analyses were carried out using the Microsoft Excel 2007, Statistical analyses used: student t-test: to compare between means, linear regression analysis, chi-square for categorical variables. P value <0.05 significant, P value < 0.01 highly significant.

3. RESULTS

A total of 100 participants, 50 patients with end-stage renal disease on regular hemodialysis and the other 50 were apparently healthy subjects. Gender, age, and BMI distribution are shown in Table 1 and Table 2.

Table 1.: characteristics of the patients and control groups.

Group		Total Group	HD Group	Control	*P* value
Total No.		100	50	50	
Gender	Male No. %	52 52%	27 54%	25 50%	0.78
	Female No. %	48 48%	23 46%	25 50%	0.77
Age (years)	Mean ±SD	44.45 ±13.6	46.82 ±12.6	43.16 ±14.4	0.09
BMI (Kg/m^2)	Mean ±SD	24.37 ± 3.97	24.5 ± 4.52	24.23 ± 3.37	0.36*

Table 2.: Distribution of patients and control according to age groups.

Age (years) \ Groups	HD Group N (%)	Control N (%)
18 – 24	4 (8%)	6 (12%)
25 – 34	6 (12%)	9 (18%)
35 – 44	12 (24%)	14 (28%)
45 – 54	10 (20%)	8 (16%)
55 – 64	12 (24%)	11 (22%)
65 – 75	6 (12%)	2 (4%)
Total	50 (100%)	50 (100%)

Those with end-stage renal disease on maintenance hemodialysis have significantly lower HDL levels than the control (P-value = 0.008), higher TG levels than the control (P-value = 0.03) and higher plasma atherogenic index (P-value = 0.02) but they have lower Total cholesterol and LDL levels but it did not reach statistical significance as shown in Table 3 and Figure 1.

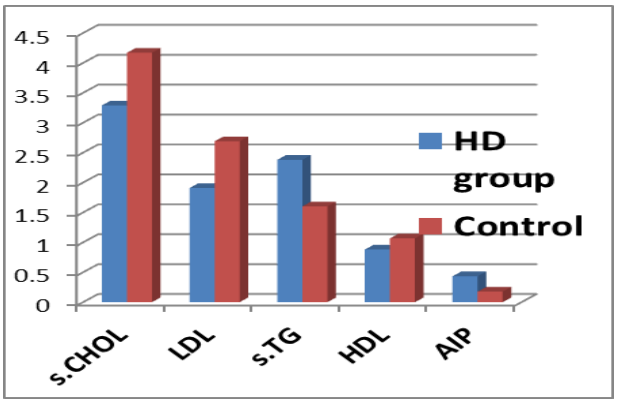

Figure 1. Comparison between lipids profiles in study groups.

Table 3: Comparison between the lipid profile of HD group and control.

Group / Lipid Profile	HD Group Mean ± SD	Control Mean ± SD	*P* value
S. Chol. mmol/l	**3.29 ± 0.73**	**4.17 ± 0.69**	**0.34**
S.TG mmol/l	**2.38 ±0.56**	**1.6 ±0.43**	**0.03**
LDL mmol/l	**1.91 ±0.66**	**2.69 ±0.63**	**0.35**
HDL mmol/l	**0.88 ±0.2**	**1.066 ±0.13**	**0.008**
AIP	**0.434 ±0.16**	**0.177 ±0.12**	**0.02**

Table 4 shows that (84%) of patients on regular hemodialysis have a high plasma atherogenic index, (50%) with hypertriglyceridemia, (48%) have low HDL level, (8%) have hypercholesterolemia, (6%) have high LDL.

Table 4: The frequency of lipid abnormalities in the study groups.

Group / Lipid Abnormalities	**HD group No. (%)**	**Control No. (%)**
S. Chol ≥ 5.2 mmol/l	**4 (8%)**	**7 (14%)**
S.TG ≥ 2.25 mmol/l	**25 (50%)**	**13 (26%)**
LDL ≥ 3.3 mmol/l	**3 (6%)**	**7 (14%)**
HDL ≤ 0.9 mmol/l	**24 (48%)**	**8 (16%)**
AIP ≥ 0.21	**42 (84%)**	**17 (34%)**

Table 3.5. Shows that patients with end-stage renal disease on maintenance hemodialysis have significantly lowered. albumin than control (P-value = 0.005).

There were no significant differences in the lipid profile between males and females, Table 3.6.

Table 3.7. Showed that participants with BMI ≥ 25 kg/m2 had significantly lower HDL and higher serum triglyceride and atherogenic index than those with BMI < 25, while total cholesterol and LDL was not significantly higher in those with BMI ≥ 25 kg/m2.

Table 5: Comparison of S. Albumin in study groups.

Group	S. Albumin (g/l) Mean ± SD	P value
HD group	36.38 ± 4.2	0.005
Control	41.96 ± 2.89	

Table 3.6.: Lipid profile according Gender

Lipid Profile mmol/l / Gender	S. Chol. (M±SD)	LDL (M±SD)	S.TG (M±SD)	HDL (M±SD)	AIP (M±SD)
Males No. = 52	3.74 ± 0.94	2.32 ± 0.81	2.03 ± 0.68	0.95 ± 0.2	0.31 ± 0.2
Females No. = 48	3.72 ± 0.72	2.28 ± 0.69	1.94 ± 0.85	0.99 ± 0.2	0.29 ± 0.18
P value	0.46	0.4	0.22	0.14	0.22

Table 7: Lipid profile according to BMI in all participants.

Lipid Profile mmol/l	BMI < 25 kg/m² No. = 64 Mean ± SD	BMI ≥ 25 kg/m² No. = 36 Mean ± SD	*P* value
S. Chol.	**3.66 ± 0.69**	**3.84± 1.02**	**0.16**
s.TG	**1.84 ± 0.52**	**2.22± 0.72**	**0.01**
LDL	**2.22 ± 0.65**	**2.43± 0.89**	**0.099**
HDL	**1.05 ± 0.15**	**0.84± 0.2**	**0.04**
Atherogenic Index of Plasma	**0.23 ± 0.14**	**0.41± 0.21**	**0.001**

There was a positive correlation between BMI and s. cholesterol in the HD group, Fig. 3.2 (r = +0.45, P = 0.001).

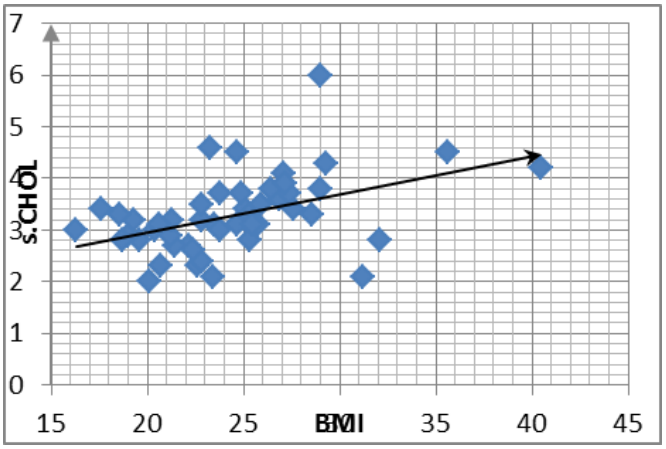

Figure 2: Correlation between S. Chol and BMI in HD group

There was an inverse correlation between BMI and HDL in HD group (r= -0.43 P-value = 0.001) Figure 3.

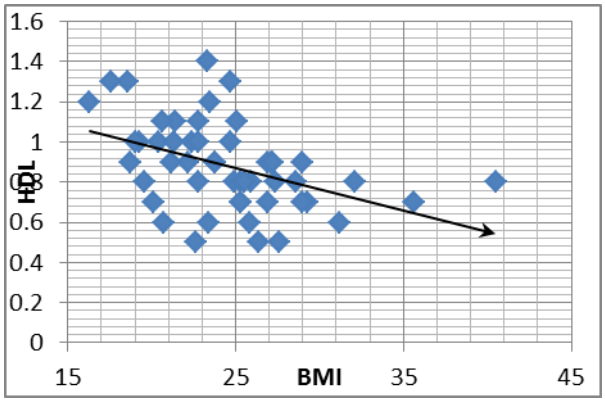

Figure 3: Correlation between HDL and BMI in HD group.

There was no significant correlation between BMI and S. triglyceride in HD group (r=+0.01 P-value = 0.92), Figure 4.

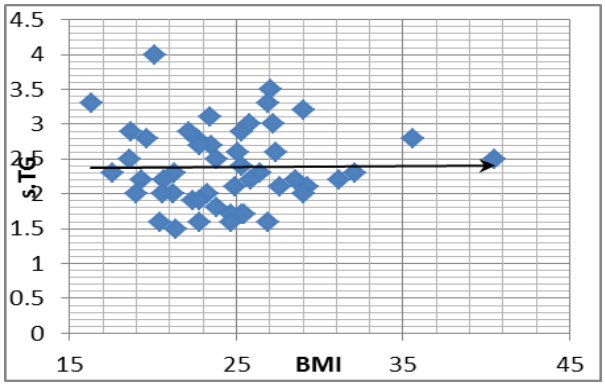

Figure 4: Correlation between S.TG and BMI in HD group.

Figure 5 showed no significant correlation between lipid profile and age in the study population.

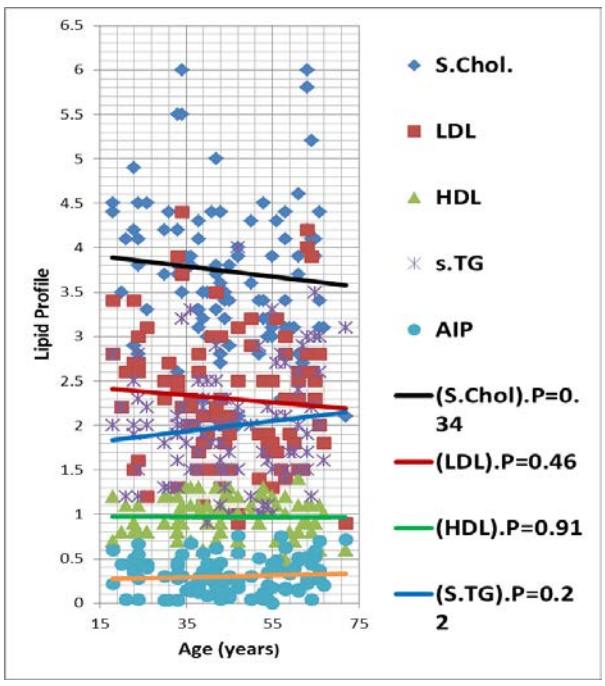

Figure 5: Correlation between age and lipid profile in the study population.

4. DISCUSSION

The end-stage renal disease leads to intense lipid disorders in a form of dysregulation of high-density lipoprotein (HDL) and triglyceride-rich lipoprotein metabolism, as a result of impairment in the maturation of HDL and alteration in its composition. In addition, clearance of triglyceride-rich lipoproteins and their atherogenic remnants is impaired and their plasma concentrations are elevated [5].

Patients with the end-stage renal disease on regular hemodialysis were found to have significantly higher triglyceride and lower HDL levels than control, whereas total cholesterol and LDL levels were lower than control (not statistically significant). These findings are consistent with the description of uremic dyslipidemia in most studies Lokesh R. et al [6], Hariom S. et al [7], Sara S. et al [8], Luca V. et al [9] and Şükrü U. et al [10], and Which show high serum triglyceride and low HDL with normal or near normal total cholesterol and LDL as a result of changes in lipid catabolism and to some extent lipogenesis. Decreased lipolysis is primarily the result of the diminished activity of lipoprotein lipase and hepatic lipase which leads to decreased catabolism of lipoproteins and chylomicrons [11].

Other studies like Nzere N. et al. [12] which shows elevated total cholesterol, serum triglyceride and LDL with low serum HDL in patients with end-stage renal disease on regular hemodialysis and Somia M. et al. [13] which shows elevated total cholesterol and serum triglyceride, which may be due to exclusion of diabetic patients in our study.

Regular usage of Erythropoietin supplement which may increase plasma lipoprotein lipase that leads to decrease Plasma concentrations of total cholesterol, triglycerides, and low-density lipoprotein cholesterol after treatment of anemia [14, 15] and effects of conventional heparin on lipid profile in hemodialysis patients [16].

Regarding plasma atherogenic index calculated as [log(TG/HDL)], there are significantly higher levels in hemodialysis in comparison with control group Possibly, the HDL related protein destructs the oxidized LDL, which may explain HDLs protective ability against heart disease. On the other hand oxidized atherogenic lipoprotein is taken up by immune system cells, which becomes gathered in foam cells which become trapped in the wall of the blood vessels and leads to the formation of atherosclerosis plaques that causes arterial narrowing and lead to heart diseases which is consistent with study done in Baghdad in 2012 [17].

In this study, (34%) of patients on regular hemodialysis have triglyceride more than 2.5 mmol/land (50%) > 2.25 mmol/ l, (48%) have low HDL level, (8%) have hypercholesterolemia, (6%) have high LDL. In comparison with Tetsuo S. [18] the prevalence of patients with hypertriglyceridemia was 20%, decreased levels of HDL found in 35.6%, elevated LDL levels found in 15.5%, in this study they include 45,390 patients treated with three times weekly hemodialysis, age ranged between 20 and 90 years, so different sample size and the hours of HD (usually 6hours/week for our patients) may be the cause for these differences.

In a study by Hiroaki O. et al [19], the prevalence of elevated total cholesterol was 38.7% and elevated serum

triglyceride (> 2.25 mmol/l) was found in 49.2%, the prevalence of high LDL was 30.5% and low HDL < 1.3 mmol/l was found in 87.6%, they didn't exclude diabetic patients from their study which may explain this higher prevalence of both total cholesterol and LDL, regarding high prevalence of low HDL may be due to including every patient his HDL level < 1.3 mmol/l in their study.

In this study serum albumin in patients with end-stage renal disease on regular hemodialysis is significantly lower than in control group which is consistent with Allon N. et al [20] that may be due to inflammation from concurrent illnesses and chronic metabolic acidosis.

Lipid profile differences between males and females were not significant, which was comparable in Hariom S. et al [7] while in buthainah A. et al [21] S. Chol and Serum TG was higher in the female group that may be due to narrow age range in their study which was 19 – 20 years.

We found that participants with BMI ≥ 25 kg/m2 had significantly higher serum triglyceride and plasma atherogenic index with significantly lower HDL, while total cholesterol and LDL were not significantly higher in those with BMI ≥ 25 kg/m2, which is in accordance with Shamai L et al. [22] and Aziz J et al. [33].

Somesh R. et al. [34] study showed no relation between BMI and total cholesterol, HDL and s.TG, which may be due to their sample that contains only healthy males, while in our study there are 50 patients with ESRD on HD and 48 females.

There was no significant correlation between lipid profile and age in our study, in comparison with Tariq A. et al. [25)], that showed the same results except for S.Chol. and LDL, which may be due to exclusion of obese subjects in their study and their age ranged from 55 to 84 years.

5. CONCLUSION

In conclusion, High atherogenic index of plasma, low HDL and hypertriglyceridemia are the commonest abnormalities found in patients on maintenance hemodialysis. There is a significant difference in lipid profile between those who are overweight and obese and those who are normal and underweight characterized by higher AIP and S.TG with lower HDL in the overweight and obese group. No significant correlation was found between age, gender and lipid profile.

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