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Lipid Profiles of Hemodialysis Patients in the Jenin District of Palestine

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Abstract

Objectives: We aimed to 1) compare the lipid profiles in hemodialysis patients and healthy controls, 2) find out if there are any differences in lipid profiles between diabetic and non-diabetic patients on hemodialysis and 3) investigate the effects of age, sex, and duration of dialysis on the lipid profiles in hemodialysis patients. **Settings:** The study was conducted in the hemodialysis unit in Jenin district at The Martyr Dr. Khalil Sulaiman Hospital of Jenin city for one calendar year. **Patients and Methods:** Seventy one patients who were not receiving any lipid lowering therapy were included; of these 26 had diabetes. Age-matched 98 healthy persons served as controls. Total cholesterol, triglycerides, HDL-cholesterol, and LDL-cholesterol levels were determined and two atherogenic indices (i.e. TC/HDL-C and LDL-C/HDL-C ratios) were calculated for patients and controls. Independent sample T- test, Pearson's correlation factor, one way ANOVA, and LSD multiple comparison test was used to test the significance of the results. P values < 0.05 were considered as significant. **Results:** The results showed that hemodialysis patients have a significantly higher triglycerides and VLDL-C levels and lower HDL-C levels compared to controls. There were no statistically significant differences in total cholesterol or LDL-C levels, on the other hand, hemodialysis patients have a significantly higher TC/HDL-C and LDL-C/HDL-C ratios compared to controls. The lipid profile of diabetic hemodialysis patients is generally similar to the lipid profile of non-diabetics except that diabetic hemodialysis patients have a significantly lower HDL-C levels and a significantly higher TC/HDL-C and LDL-C/HDL-C ratios compared to non-diabetics reflecting the additional impact of diabetes on lipid profile. The lipid profile of hemodialysis patients seems to be independent of age, sex, or duration of dialysis. **Conclusions:** Hemodialysis patients, particularly those with diabetes, have an adverse lipid profile. This is likely contributing to the increased mortality rates. Further studies are needed to ascertain the cardiovascular abnormalities

and elucidate the causes of death among hemodialysis patients specifically in our population.

Key words: Diabetics, Hemodialysis patients, Jenin District, Lipid profile, Palestine.

Abbreviations: TC: total cholesterol; TG: triglycerides; HDL-C: high density lipoprotein cholesterol, VLDL-C: very low density lipoprotein cholesterol;

Introduction

Patients with chronic renal failure (CRF) commonly suffer from a secondary form of complex dyslipidemia. The most important abnormalities are elevated serum triglycerides (elevated VLDL-remnants/IDL), increased small LDL particles, and a low HDL cholesterol level. The highly atherogenic LDL subclass is called LDL-6 or small dense LDL. This LDL subclass accumulates preferentially in hypertriglyceridemic diabetic patients with nephropathy or in patients treated by hemodialysis. All these lipoprotein particles contain apolipoprotein B, thus the complex disorder can be summarized as an elevation of triglyceride-rich apolipoprotein B-containing complex lipoprotein particles. Growing body of evidence suggests that all of the components of this type of dyslipidemia are independently atherogenic. Another important issue is that these particles, especially the apolipoprotein B moiety, are predominantly prone to modification such as oxidation and glycosylation, which contributes to impaired clearance by the LDL receptor (1). In addition to the low HDL level, maturation of HDL is impaired and its composition is altered. Additionally, clearance of triglyceride-rich lipoproteins and their atherogenic remnants is impaired, their composition is altered in addition to the increase in their concentrations. Impaired maturation of HDL particles in CRF is primarily due to down-regulation of lecithin-cholesterol acyltransferase (LCAT) and, to a lesser extent, increased plasma cholesteryl ester transfer protein (CETP). Triglyceride enrichment of HDL in CRF patients is primarily due to hepatic lipase deficiency and elevated CETP activity (2). The CRF-induced hypertriglyceridemia, abnormal composition, and impaired clearance of triglyceride-rich lipoproteins and their remnants are primarily due to down-regulation of lipoprotein lipase, hepatic lipase, and the very-low density lipoprotein receptor, as well as, upregulation of hepatic acyl-CoA cholesterol acyltransferase (ACAT). In addition, impaired HDL metabolism contributes to the disturbances of triglyceride-rich lipoprotein metabolism. These abnormalities are compounded by down-regulation of apolipoproteins apoA-I, ApoA-II, and apoC-II in CRF (2). Diabetic nephropathy (DN) is a common cause of CRF. Patients with DN have abnormal lipoprotein metabolism that can be influenced by both the impairment of renal function and the metabolic control of diabetes (3). Numerous studies on dyslipidemia in CRF showed that the patients with diabetic nephropathy share the characteristic features of dyslipidemia of chronic renal failure as other patients with the accumulation of intact or partially delipidized apo B-containing lipoproteins enriched in apo C-peptides and apoE, which are present not only in VLDL and IDL but also in LDL density range. These alterations are more marked in DN than in non-diabetic CRF patients, reflecting the positive effects of diabetes and hyperglycemia on plasma triglyceride (3-5). The more obvious difference between patients with diabetic nephropathy and other patients of chronic renal failure, LDL triglyceride enrichment, was correlated negatively with hepatic lipase activity (5).

The lipid abnormalities seen in CRF patients under hemodialysis especially in diabetic nephropathy patients enhance the risk for the development of atherosclerosis (3,5). In this study we aimed to firstly, compare the lipid profile of hemodialysis patients to the lipid profile of normal healthy controls, secondly, make a comparison in the lipid profile among diabetic hemodialysis patients, non-diabetic hemodialysis patients, and normal healthy controls and thirdly evaluate the effects age, sex, and duration of dialysis on the lipid profile of hemodialysis patients.

Patients and Methods

Settings

The study has been conducted at the laboratory and the kidney unit of The Martyr Dr. Khalil Sulaiman Hospital in Jenin city which is the only hemodialysis unit in Jenin District were all patients from Jenin District are treated. The study has been conducted in the period 1/8/2005 to 31/7/2006. Jenin District includes Jenin city and the surrounding villages with a population of about 280000 persons. The study concluded all hemodialysis patients from Jenin District who were not subjected to any lipid lowering therapy. 98 normal healthy persons from Jenin District served as controls. Patients and controls were matched for age and both patients and controls were not known to be alcoholic.

Study Population

The patients were 71 persons. The age of the patients ranged from 14 - 80 years with a mean age of (60 ± 17) years, 40

patients were males and 31 were females. The age of the controls range from 20-75 years. 58 of controls were males and 40 were females

Laboratory measurements

Venous blood samples (about 5 ml) were obtained from patients and controls after fasting for a minimum of 12 hours. Blood samples were taken from patients before the beginning of hemodialysis. Blood samples are allowed to clot for one hour at room temperature. After that the samples were centrifuged at 4000 rpm for 10 minutes to separate serum from blood cells. After separation from red celss, Sera were analysed for estimation of total cholesterol, triglycerides and serum HDL cholesterol, and for LDL cholesterol determination in patients having triglyceride concentration > 400 mg/dl using commercial kits (Randox Laboratories Ltd., London, UK). For the samples that had a triglyceride level less than 400 mg/dl, LDL-C concentration was calculated from total cholesterol, HDL-cholesterol, and triglyceride concentrations according to Friedewald formula (6). The atherogenic indices TC/HDL-C ratio and LDL-C/HDL-C ratio were also calculated for patients and controls. Biosystems photometer BTS-310 model spectrophotometer was used to estimate the lipid profiles.

Data analysis and statistics

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) version 10 (SPSS Inc., Chicago, IL, USA). Independent sample t-test was used to test the effect of gender on lipid profile. Pearson's correlation factor was used to test the effect of age and duration of dialysis on lipid profile. Independent sample t-test was also used to compare the lipid profile of hemodialysis patients to that of the healthy controls. One way ANOVA and LSD multiple comparison test were also used to compare the lipid profiles among diabetic hemodialysis, non-diabetic hemodialysis, and normal healthy controls. All tests were two sided and p values < 0.05 were taken as statistically significant.

Results

The results of lipid profiles of hemodialysis patients and controls are shown in table 1. Patients on hemodialysis have a significantly higher serum triglycerides and VLDL-C levels and lower HDL-C levels compared to healthy controls. There were no statistically significant differences in total cholesterol or LDL-C levels but patients had significantly higher TC/HDL-C and LDL-C/HDL-C ratios than controls. The mean lipid profile readings in diabetic hemodialysis patients, non-diabetic hemodialysis patients

Table 1. Independent sample T-test testing the significance of difference in lipid profile between hemodialysis patients and controls.

Test	Group	No.	Mean	SD	DF	T-value	P-value
Total Cholesterol	dialysis patients	71	160	41.6	167	-0.490	0.625
	controls	98	162	27.3			
Triglycerides	dialysis patients	71	132	84.9	167	2.645	0.009
	controls	98	107	38.6			
LDL Cholesterol	dialysis patients	71	98	35.3	167	0.234	0.816
	controls	98	97	23.4			
HDL Cholesterol	dialysis patients	71	35	13.0	167	-4.875	0.000
	controls	98	43	9.4			
VLDL Cholesterol	dialysis patients	71	26.2	15.9	167	2.633	0.009
	controls	98	21.3	7.7			
TC/HDL-C Ratio	dialysis patients	71	5.3	2.9	167	4.698	0.000
	controls	98	3.7	0.9			
LDL-C/ HDL-C Ratio	dialysis patients	71	3.4	2.2	167	4.326	0.000
	controls	98	2.3	0.7			

Table 2. Mean lipid profile readings in diabetic patients, non-diabetic patients and controls.

Test	Group	Number	Mean	Standard deviation
Total Cholesterol	A	26	160	49.33
	B	45	159	37.04
	C	98	162	27.34
Triglycerides	A	26	138	98.98
	B	45	129	76.68
	C	98	107	38.56
LDL Cholesterol	A	26	104	42.24
	B	45	95	30.69
	C	98	97	23.40
HDL Cholesterol	A	26	30	10.70
	B	45	38	13.37
	C	98	43	9.43
VLDL Cholesterol	A	26	27	17.18
	B	45	26	15.33
	C	98	21	7.71
TC/HDL-C Ratio	A	26	6.2	3.45
	B	45	4.8	2.51
	C	98	3.0	0.87
LDL-C/HDL-C Ratio	A	26	4.1	2.71
	B	45	3.0	1.72
	C	98	2.3	0.73

A: Diabetic hemodialysis patients; B: Non-diabetic hemodialysis patients; C: Healthy controls.
All lipids levels are in mg/dl.

and normal healthy controls are given in table 2. One way ANOVA test was used to test if there was any statistically significant differences at ($\alpha = 0.05$) level in lipid profile among diabetic dialysis patients, non-diabetic dialysis patients or normal healthy controls. The ANOVA results are shown in table 3. These show statistically significant differences in TG, HDL-C, VLDL-C, TC/HDL-C and LDL-C/HDL-C levels but not in the TC or LDL-C levels.

To further examine the exact causes of the differences in lipid parameters among these three groups, an LSD *Post Hoc* multiple comparison test was done (Table 4). There is no statistically significant difference in triglycerides and VLDL-C levels between diabetic and non-diabetic hemodialysis patients but there is a statistically significant difference in triglycerides and VLDL-C levels between both hemodialysis groups (diabetic and non-diabetic) and normal healthy controls. There is a statistically significant difference in HDL-C level between diabetic and non-diabetic hemodialysis patients i.e. diabetic hemodialysis patients have a significantly lower HDL-C concentrations compared to non-diabetics. Diabetic hemodialysis patients have a significantly lower HDL-C concentrations compared to normal healthy controls. Non-diabetic hemodialysis patients have a significantly lower HDL-C concentrations compared to normal healthy controls. Diabetic hemodialysis patients have a significantly higher TC/HDL-C and LDL-C/HDL-C ratios compared to non -diabetics. Diabetic hemodialysis patients have a significantly higher TC/HDL-C and LDL-C/HDL-C ratios compared to normal healthy controls. Non-diabetic hemodialysis patients have a significantly higher TC/HDL-C and (LDL-C/HDL-C)

Table 3. One way ANOVA for testing the significant of difference in lipid profile among diabetic dialysis patients, non-diabetic dialysis patients and normal controls.

Dependent Variables	Independent Variables	Sum of Squares	Df	Mean	F	P-value
Total Cholesterol	Between groups	309	2	154	0.132	0.876
	Within groups	193720	166	1167		
	Total	194030	168			
Triglycerides	Between groups	28556	2	14278	3.658	0.028
	Within groups	647900	166	3903		
	Total	676456	168			
LDL Cholesterol	Between groups	1182	2	591	0.705	0.496
	Within groups	139201	166	839		
	Total	140383	168			
HDL Cholesterol	Between groups	3984	2	1992	17.091	0.000
	Within groups	19349	166	117		
	Total	23333	168			
VLDL Cholesterol	Between groups	996.140	2	498	3.519	0.032
	Within groups	23492.977	166	142		
	Total	24489.118	168			
TC/HDL-C Ratio	Between groups	120.528	2	60	15.441	0.000
	Within groups	647.856	166	4.0		
	Total	768.384	168			
LDL-C/HDL-C Ratio	Between groups	64.768	2	32	14.691	0.000
	Within groups	365.911	166	2		
	Total	430.680	168			

ratios compared to normal healthy controls. No significant differences in lipid profile were evident between males and females in case of diabetic hemodialysis patients, non-diabetic hemodialysis patients, or all hemodialysis patients respectively (Table 5).

There was no significant correlation between age and lipid profile in diabetic hemodialysis patients, non-diabetic hemodialysis patients, or all hemodialysis patients (Table 6). Similarly, there was no significant correlation between duration of dialysis and lipid profile in diabetic hemodialysis patients, non-diabetic hemodialysis patients, or all hemodialysis patients (Table 7).

Discussion

Some of our findings are concordant with previous similar reports but at variance with others. Our hemodialysis patients have a statistically significant higher triglycerides and VLDL-C levels and low HDL-C levels compared to normal healthy controls. There were no statistically significant differences in total cholesterol or LDL-C levels. These results are in agreement with many previous studies (7-15) but the results are at variance with one study in which total cholesterol and LDL-C levels were significantly lower in the dialysis patients than in normal controls (16). Additionally, our results also disagree with some other studies which found that hemodialysis patients have a statistically significant higher levels of total cholesterol and LDL-C compared to normal healthy controls (17,18). Our results showed significantly lower HDL-C levels in hemodialysis patients compared to normal controls consistent with many previous reports (7-15) but these results is not in line with previous study which found that there was no statistically significant difference in HDL-C levels between hemodialysis patients and normal healthy controls (17).The results of this study also showed that the

Table 4. LSD Post Hoc multiple comparison test comparing lipid profiles of diabetic hemodialysis patients, non-diabetic hemodialysis patients and normal healthy controls.

Test	(I) test	(J) test	Mean difference (I-J)	Std. error	P- value (Sig.)
T.G	A	B	9.1086	15.38991	0.555
	A	C	31.4710	13.78196	0.024
	B	C	22.3624	11.24990	0.048
HDL-C	A	B	-8.0871	2.65957	0.003
	A	C	-13.5279	2.38170	0.000
	B	C	-5.4408	1.94413	0.006
VLDL-C	A	B	1.0957	2.93056	0.709
	A	C	5.5642	2.62438	0.035
	B	C	4.4685	2.14222	0.039
TC/HDL-C ratio	A	B	1.3675	0.48666	0.006
	A	C	2.3428	0.43581	0.000
	B	C	0.9754	0.35574	0.007
LDL-C/HDL-C Ratio	A	B	1.1388	0.36574	0.002
	A	C	1.7485	0.32753	0.000
	B	C	0.6096	0.26735	0.024

Table 5. Independent T-test for testing the relation between gender and lipid profile in diabetics on hemodialysis, Non-diabetics on hemodialysis and all patients on hemodialysis.

Parameters	Diabetic Patients on Hemodialysis					Non-diabetic Patients on Hemodialysis.					All Patients on Hemodialysis.				
Tests	Sex	No	Mean	SD	P-Value	Sex	No	Mean	SD	P-value	Sex	No	Mean	SD	P-value
TC	M	14	162	62	0.881	M	26	158	35	0.819	M	40	159.23	45.26	0.954
	F	12	159	32		F	19	161	41		F	31	159.81	37.12	
TG	M	14	141	122	0.878	M	26	134	73	0.623	M	40	136.32	91.80	0.654
	F	12	135	68		F	19	122	83		F	31	127.11	76.35	
LDL-C	M	14	106	53	0.733	M	26	95	27	0.856	M	40	98.76	37.93	0.927
	F	12	101	27		F	19	96	36		F	31	97.98	32.19	
HDL-C	M	14	29	12	0.528	M	26	37	15	0.450	M	40	33.76	14.35	0.397
	F	12	31	10		F	19	40	12		F	31	36.41	11.04	
VLDL-C	M	14	27	20	0.986	M	26	27	15	0.623	M	40	26.79	16.58	0.722
	F	12	27	14		F	19	25	17		F	31	25.42	15.27	
TC/HDL-c Ratio	M	14	6.9	4.5	0.303	M	26	5.1	2.9	0.361	M	40	5.74	3.55	0.195
	F	12	5.4	1.6		F	19	4.4	1.9		F	31	4.82	1.82	
LDLc/HDLc Ratio	M	14	4.6	3.5	0.303	M	26	3.1	1.9	0.401	M	40	3.65	2.64	0.217
	F	12	3.5	1.3		F	19	2.7	1.4		F	31	3.00	1.37	

Table 6. Correlation between age and lipid profile in hemodialysis patients

Groups	Test / Correlation	T.C	T.G	LDL-C	HDL-C	VLDL-C	TC / HDL-C ratio	LDL-C / HDL-C ratio
Diabetic patients	Pearson correlation	-0.120	0.094	-0.188	0.077	0.070	-0.120	-0.166
	Sig. (2-tailed)	0.560	0.649	0.358	0.709	0.732	0.560	0.417
	Number	26	26	26	26	26	26	26
Non-diabetic patients	Pearson correlation	0.105	0.114	0.100	-0.070	0.113	0.180	0.194
	Sig. (2-tailed)	0.494	0.457	0.513	0.645	0.459	0.236	0.202
	Number	45	45	45	45	45	45	45
All haemodialysis patients	Person correlation factor	0.037	0.113	0.051	-0.147	0.103	0.157	0.151
	Sig. (2-tailed)	0.757	0.349	0.671	0.221	0.394	0.192	0.208
	Number	71	71	71	71	71	71	71

Table 7. Correlation between duration of dialysis and lipid profile.

Group	Test / Correlation	T.C	T.G	LDL-C	HDL-C	VLDL-C	TC / HDL-C ratio	LDL-C / HDL-C ratio
Diabetic patients	Duration							
	Pearson correlation	-0.106	0.037	-0.222	0.323	0.039	-0.178	-0.202
	Sig. (2-tailed)	0.605	0.858	0.276	0.108	0.851	0.383	0.323
	Number	26	26	26	26	26	26	26
Non-diabetic patients	Duration							
	Pearson correlation	-0.152	-0.040	-0.141	-0.057	-0.040	-0.041	-0.016
	Sig. (2-tailed)	0.317	0.794	0.355	0.708	0.792	0.792	0.918
	Number	45	45	45	45	45	45	45
All hemodialysis patients	Duration							
	Pearson correlation	-0.125	-0.035	-0.180	0.123	-0.030	-0.148	-0.151
	Sig. (2-tailed)	0.299	0.773	0.133	0.306	0.802	0.217	0.208
	Number	71	71	71	71	71	71	71

atherogenic index TC/HDL-C ratio was significantly higher in hemodialysis patients compared to normal controls. This result is in agreement with other previous studies (9,13). The results of this study also showed that the atherogenic index LDL-C/HDL-C ratio was significantly higher in hemodialysis patients compared to normal controls. This result is in agreement with what was found previously (9). We found that both hemodialysis groups (diabetic and non-diabetic) have a significantly higher triglycerides and VLDL-C levels and significantly lower HDL-C level compared to normal controls. The atherogenic indices TC/HDL-C and LDL-C/HDL-C ratios are also significantly higher in both groups of hemodialysis patients compared to controls. There were no statistically significant differences in total cholesterol or LDL-C levels. These results in general are in line with the results of comparing lipid profile of all hemodialysis patients to normal controls indicating that patients with diabetic nephropathy generally share the characteristic features of dyslipidemia of chronic renal failure as found previously in some other studies (3,5). From the results it was found that both groups of hemodialysis patients (diabetics and non-diabetics) have significantly higher levels of triglycerides compared to normal healthy controls indicating that , regardless of the cause , CRF leads to hypertriglyceridemia as reported in similar studies (3,4). The results of this study also showed that there were no significant differences in triglycerides and VLDL-C levels between diabetic and non-diabetic patients. This is in agreement with previous study (5). However, these results are not in line with other studies which found that plasma triglycerides were more pronounced in diabetic than in non-diabetic patients (3,4). The results of this study also showed that diabetic hemodialysis patients had significantly lower HDL-C levels compared to non-diabetics, so despite the similarities in lipid profile between diabetic and non-diabetic hemodialysis patients, some abnormalities are more marked in diabetic hemodialysis patients than in non-diabetic patients reflecting the additional impact of diabetes on lipid profile (3). So renal failure accompanied by diabetes severely affected the level of HDL-C. The results of this study showed that there were no significant differences in total cholesterol or LDL-C concentrations between diabetic or non-diabetic renal failure patients or in comparison with normal healthy controls. This support the results of many studies that end-stage renal disease - regardless of the cause does not necessarily cause increase in total cholesterol or LDL-C levels (8,10-12,15,19). The results showed that diabetic hemodialysis patients had significantly higher TC/HDL-C and LDL-C/HDL-C ratios compared to non-diabetic hemodialysis patients who also had significantly higher ratios compared to normal controls, thus diabetic hemodialysis patients have great chance for developing atherosclerotic cardiovascular disease compared to non-diabetic patients who are at great risk of developing atherosclerotic cardiovascular disease compared to normal controls. This may be contributory to the high mortality rate among diabetic hemodialysis patients compared to non-diabetic. Thus, cardiovascular complications may contributed to the high mortality rate among hemodialysis patients especially diabetics. Cardiovascular abnormalities must be investigated for all hemodialysis patients especially those who had bad lipid profile such as diabetics. Future studies must concentrate on the causes of the high mortality rate among hemodialysis patients in Jenin District, an issue which may have not been recognized before especially that many deaths occurred at home. The results showed that there was no significant differences in lipid profile between males and females in all hemodialysis groups (diabetic, non-diabetic, and all patients).These results are in agreement with other previous studies (16,17). The results also showed that there was no significant correlation between age and lipid profile in hemodialysis patients .These results agree with what was found previously in some other studies (16.17). The results of this study showed that there was no significant correlation between duration of dialysis and lipid profile in hemodialysis patients. This result is in agreement with what was found previously (16). From these results, it is found that lipid profile of hemodialysis patients points to high risk of atherosclerosis compared to normal healthy controls indicating that hemodialysis treatment contributes significantly to the dyslipidemic profile of CRF patients by altering serum lipids and lipoproteins concentrations, thus all hemodialysis patients in Jenin District regardless of the cause of renal failure, age, sex, or duration of dialysis - should be screened for complete lipid profile and patients with bad lipid profile should be subjected to lipid lowering therapy in order to decrease the chance of atherosclerosis and its complications such as cardiovascular disease.

In conclusion, lipid profile of hemodialysis patients in Jenin district is generally similar to that found elsewhere characterized mainly by hypertriglyceridemia and low HDL-C levels compared to normal healthy controls. Although TC and LDL-C levels were not different between hemodialysis patients and controls but patients had higher atherogenic indices suggesting that our hemodialysis patients have increased atherosclerotic cardiovascular disease. Furthermore, diabetic hemodialysis patients had

higher risk for developing atherosclerotic cardiovascular disease compared to non-diabetic patients. This is likely to contribute to the increased mortality rates observed among diabetics. However, lipoprotein disturbances in patients with CRF treated by hemodialysis appear to be independent of age, gender, and duration of dialysis. Further studies to investigate cardiovascular abnormalities and the causes of death among hemodialysis patients specific to our population are called for.

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