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Journal

Hemodialysis International, 9(3)

ISSN

1492-7535

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Publication Date

2005-07-01

DOI

10.1111/j.1492-7535.2005.01147.x

Hemodialysis International 2005; **9**: 314–324

A matched comparison of serum lipids between hemodialysis patients and nondialysis morbid controls

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Abstract

The high incidence of cardiac and vascular disease in maintenance hemodialysis (MHD) patients has heightened interest in many investigations concerning the serum lipid levels of these patients. The prevalence and laboratory characteristics of serum lipid concentrations in MHD patients, however, are far from clear. We hypothesized that serum lipids are significantly lower in MHD patients compared to their matched nondialysis counterparts. We compared 2-year averaged serum levels of total cholesterol (TC), low-density lipoprotein (LDL), high-density lipoproteins (HDL), and triglycerides in 285 MHD patients to the same averaged measurements during the same period of time in 285 nondialyzed outpatients from the same geographic area, whose lipid panels were measured in the same laboratory. Matching factors were sex, race and/or ethnicity, diabetes mellitus, and age ($\pm$ 5 years). The MHD patients and their matched controls were 55.6 $\pm$ 13.5 (SD) and 56.3 $\pm$ 13.0 years old, respectively. Each group contained 51% women, 31% African Americans, 52% Hispanics, and 37% diabetics; 16% of MHD patients and 38% of controls were receiving statins. Body mass index (BMI) was significantly lower in MHD patients than in controls (26.2 vs. 31.5 kg/m^2; $p < 0.001$). Serum cholesterol levels were significantly lower in MHD patients than in control subjects including after adjustment for BMI and statin use (TC, -51; LDL, -39; and HDL, -10 mg/dL; $p < 0.001$). Using conditional logistic regression for matched data and after controlling for BMI and statins, all odds ratios for predetermined hypercholesterolemic, but not hypertriglyceridemic, levels were significantly and substantially lower than 1.00, indicating much lower likelihood of hypercholesterolemia in MHD patients. Total and LDL hypercholesterolemia, although very common in nondialysis ambulatory outpatients, are substantially less prevalent in the MHD population, whereas hypertriglyceridemia is approximately equally prevalent between these populations.

Key words: LDL cholesterol, case control, logistic regression, statin

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An abstract of this research was presented at the 34th annual meeting of the American Society of Nephrology, October 18–31, 2004, in St. Louis, MO, USA.

INTRODUCTION

Management of dyslipidemia in maintenance hemodialysis (MHD) patients has been a matter of ongoing debate.[1–4] Hypercholesterolemia, especially increased levels of low-density lipoprotein (LDL), are known to be associated with decreased survival and increased risk of cardiovascular disease in the general population.[5] Based on blind extrapolation of data from the general population, it has generally been assumed that an effective way to reduce the high rate of cardiovascular disease and mortality in more than a quarter of a million MHD patients in the United States is by aggressively lowering their serum cholesterol levels.[6] To that end, the National Kidney Foundation (NKF) Kidney Disease and Dialysis Outcome Quality Initiative (K/DOQI) has recently issued specific guidelines for treatment of hypercholesterolemia in dialysis patients.[7]

A more essential question remains unanswered, that is, whether hypercholesterolemia is significantly prevalent in the MHD population. Increased total serum cholesterol does not appear to be as common in MHD patients as in similar morbid populations who do not receive maintenance dialysis treatment. The prevalence and distribution characteristics of other lipid and lipoprotein fractions, including LDL, high-density lipoproteins (HDL), and triglycerides, are even less well studied in MHD patients. Despite the abundant literature and guidelines advocating aggressive management of hypercholesterolemia in MHD patients, to our knowledge virtually no study has examined the prevalence and laboratory characteristics of lipid disorders in this patient population by comparing them to nondialyzed but similarly morbid individuals. We hypothesized that serum lipid levels are significantly lower in MHD patients when they are compared to their matched nondialysis counterparts.

MATERIALS AND METHODS

Patients

During the first 2 years of the Nutritional and Inflammatory Evaluation in Dialysis (NIED) Study (see NIED Study web site at http://www.niedstudy.org/ for more details, as well as previous publications,[8,9]), that is, between October 1, 2001, and September 30, 2003, a total number of 565 MHD outpatients were recruited from eight DaVita dialysis facilities in Southern Los Angeles County. These eight dialysis facilities along with two other DaVita dialysis units (as backup units for the NIED Study) include approximately 1300 MHD patients and comprise the so-called DaVita South Bay Cohort.[10,11] The facilities are all located within a 15-mi. radius of Harbor-UCLA Medical Center and are administered using uniform treatment practices by DaVita, Inc. Inclusion criteria were treatment with MHD for at least 4 weeks, aged 18 years or older, and no terminal disease with a life expectancy less than 6 months. The study was approved by the Institutional Review Committee of the Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center. After matching procedures (see below), 285 patients remained for the analyses.

Controls

The control subjects were randomly selected from the pool of 2425 nondialysis ambulatory outpatients, who had been followed during the same period of time that the NIED Study was being conducted. These outpatients manifested a variety of different medical and public health problems and were treated in the General Internal Medicine (GIM) Clinic of Harbor-UCLA Medical Center, a major tertiary medical center that provides medical care primarily to an uninsured or poorly insured population of Southern Los Angeles County. The GIM database is based on a software program that tracks diagnoses, medications, allergies, health screening, laboratories, and health habits. Among common diagnoses of patients seen in this clinic are hypertension (61%), diabetes mellitus (36%), and degenerative joint disease (12%). The selection of this population as appropriate controls for this matching study was justified based on the following characteristics: 1) The studied MHD patients also originated from the same geographic area and same zip codes as the outpatient population of the GIM clinic; hence, their racial and socioeconomic features as well as climatic, environmental, cultural, and nutritional constellations were similar. 2) Lipid panels for both MHD patients and GIM controls were measured in the same laboratory center at Harbor-UCLA campus under the same standardized methods and during the same period of time. 3) A nonhealthy population with at least moderate degree of morbidity was required to compare with the multimorbid MHD patient population; therefore, the GIM ambulatory population met these criteria.

Matching

Four simultaneous matching criteria were used: 1) sex—male vs. female; 2) race and ethnicity in four mutually

exclusive categories:—Caucasian, African American, Hispanic, and Asian; 3) the presence or absence of diabetes mellitus, as documented in the medical chart and proven by clinical and laboratory criteria; and 4) age (± 5 years). The one-to-one matching process performed was random, strict, exhaustive, and mutually exclusive. Hence, no control subject was listed more than once as a matched control for a given MHD patient.

A software program was designed to randomly match each MHD patient to one control subject based on the above-mentioned criteria. Of 565 MHD patients who underwent the one-to-one matching process, complete matching could assign perfect controls to 285 MHD patients. The rest (280 MHD patients) could not be matched.

Other pertinent clinical data that were obtained but not matched included the 2-year averaged body weight and height for both MHD patients and the control subjects (based on monthly to quarterly measured values) to calculate the body mass index (BMI) and use of HMG-CoA reductase inhibitors (statins) to treat hypercholesterolemia for at least 3 months, irrespective of the dose and type of the medication.

Laboratory evaluation

In MHD patients, blood samples for the NIED Study were obtained simultaneously and in a uniform fashion in all eight dialysis clinics every 6 months (either every October and April or every January and July). Study blood samples were obtained in gel-separated tubes, centrifuged in the dialysis units, and delivered to the Harbor-UCLA Medical Center, where lipid panels including total cholesterol, HDL, and triglycerides were measured and LDL was calculated. For the control subjects, lipid panels were obtained in the same fashion and measured in the same laboratory center during the same period of time via automated methods. All available lipid values within the 2-year interval of the study were averaged (up to four values for each MHD patient and up to seven values for nondialysis controls).

For MHD patients, the single-pool Kt/V_{urea} was used to represent the weekly dialysis dose. All dialysis-related laboratory measurements were performed in one single laboratory facility (i.e., DaVita Laboratories, Deland, FL, USA), using automated and standardized methods. Laboratory data were extracted and averaged via KLINLAB software. High-sensitivity C-reactive protein (CRP) was measured semiannually by a turbidometric immunoassay in which a serum sample was mixed with latex beads coated with anti-human CRP antibodies forming an insoluble aggregate (manufacturer: WPCI, Osaka, Japan; unit, mg/L; normal range, < 3.0 mg/L).

Statistical and epidemiologic methods

Both nonpaired and paired Student t tests were used to detect significant differences among continuous variables in two groups. Chi-square analysis was used for comparison among categorical variables. We used Pearson's correlation coefficient r for analyses of associations between continuous variables and Spearman's rank test for categorical variables. Linear multivariate regression models were used to calculate the magnitude of differences among lipid panels comparing MHD patients with nondialysis controls, after adjusting for age, BMI, and use of statins. Odds ratios (OR) and their 95% confidence intervals (CI) were calculated to estimate the relative prevalence of hyperlipidemia in MHD patients compared to non-MHD controls after adjusting for additional (nonmatched) features including BMI and use of statins. Conditional logistic regression analysis was the initial method of choice for calculating the above-mentioned OR values in matched data. Any 95% CI not including 1.00 was considered statistically significant. Descriptive and multivariate statistics were carried out with statistical software (Stata, Version 7.0, Stata Corporation, College Station, TX, USA). Fiducial limits are given as means ± SD. A p value of < 0.05 is considered to be statistically significant.

RESULTS

Pertinent demographic and clinical data and 2-year-averaged laboratory values of all 1375 MHD patients of DaVita South Bay cohort as well as the NIED Study subcohort of 565 MHD patients, divided into two groups of matched (n = 285) versus unmatched (n = 280), are summarized in Table 1, for comparison. With the exception of sex and diabetes distribution (less male and less diabetic patients among the matched MHD patients compared to nonmatched), the matched subpopulation of the NIED Study was similar to its base population. Figure 1 shows distribution histograms of four serum lipid values and their descriptive analyses in 285 matched MHD patients. The distribution of HDL and triglycerides appears somewhat skewed.

From a base population of 2425 outpatients who presented to the GIM Clinic at Harbor-UCLA Medical Center at least once during the study period, 285 controls were randomly chosen according to matching criteria (see above). Table 2 compares the pertinent characteristics

Table 1 Relevant characteristics of MHD patients[a]

Variable	All MHD patients from 10 dialysis units (n = 1373)	NIED Study cohort (n = 565)	Matched MHD patients (n = 285)	p value (matched vs. unmatched within NIED)
Sex (% female)	50	46	51	0.02
Race or ethnicity (%)				
Hispanic	48	51	52	0.84
Black	26	30	31	0.62
Asian	8	8	6	0.24
Diabetes mellitus (%)	46	50	37	< 0.001
Use of statins (%)	NA	21	16	0.16
Age (years)	56.1 ± 15.3	54.2 ± 14.8	55.6 ± 13.5	0.57
Time on dialysis (months)	48 ± 44	35 ± 34	37 ± 38	0.22
BMI (kg/m^2)	26.4 ± 8.4	26.2 ± 5.9	26.2 ± 6.0	0.69
Serum total cholesterol (mg/dL)	151 ± 43	144 ± 38	142 ± 38	0.19
LDL (mg/dL)	NA	78 ± 28	76 ± 27	0.55
HDL (mg/dL)	NA	37 ± 12	37 ± 12	0.58
Triglycerides (mg/dL)	NA	147 ± 112	151 ± 124	0.38
Albumin (g/dL)	3.9 ± 0.4	3.9 ± 0.3	3.9 ± 0.3	0.57
CRP (mg/L)	NA	5.5 ± 4.7	5.7 ± 5.2	0.17

[a]DaVita South Bay cohort is the base population and includes 10 outpatient dialysis units with 1373 MHD patients. The NIED Study is a subcohort of the above cohort and includes 565 MHD from 8 DaVita dialysis units, of which 285 MHD patients are matched for the study and 280 are not. The p value compares matched and unmatched data within the NIED cohort
MHD = maintenance hemodialysis; NIED Study = Nutritional and Inflammatory Evaluation in Dialysis Study; BMI = body mass index; LDL = low-density lipoprotein; HDL = high-density lipoprotein; CRP = C-reactive protein; NA = data not available.

of the whole base population with the 285 selected controls. The base population included more women, with less African Americans, Hispanics, and Asians than its matched subgroup. The age, diabetes mellitus, BMI, and mean serum lipid values were similar in both groups.

Table 3 compares pertinent demographic, clinical, and laboratory data between the matched MHD patients and nondialysis controls. The MHD patients and their matched controls were 55.6 ± 13.5 and 56.3 ± 12.9 years old, respectively. Each group included 51% women, 31% African Americans, 51% Hispanics, and 37% diabetics. The BMI was 5.3 kg/m^2 lower in MHD patients. Moreover, 16% of MHD patients used statins compared to 38% of the controls. All serum lipid values were significantly lower in MHD patients compared to controls. Moreover, the frequency of hyperlipidemia using conventional cutoff levels (total serum cholesterol, > 200 mg/dL; LDL, > 100 mg/dL; HDL, > 40 mg/dL; and triglycerides, > 150 mg/dL) was significantly lower in MHD patients than in controls. Figures 2 and 3 depict the latter findings in graphical formats.

To obtain the adjusted magnitude of differences and the 95% CI in lipid levels between MHD patients and their controls and of these differences to assess the statistical significance after adjustment for pertinent data, linear multiple regression models were used in that serum lipid level was the outcome variable, MHD status (vs. control) was the predicting binomial variable, and age, BMI, and statins were the continuous covariates to adjust for. Table 4 shows the adjusted differences. Serum total cholesterol was 55 mg/dL lower in MHD patients compared to their matched controls, that is, a mean difference of −55 mg/dL. The 95% interval range of this difference was from −48 to −62 mg/dL. After multivariate adjustment for age, BMI, and use of statins, this difference reduced to −51 mg/dL (95% CI, −43 to −58 mg/dL). Similarly, LDL and HDL were also significantly lower in MHD patients, even after multivariate adjustment. Serum triglycerides, however, were not significantly different in MHD patients after multivariate adjustment, because the range of the difference in triglycerides between MHD patients and the controls ranged from −47 to +12 mg/dL.

Table 5 shows the coefficients of correlation among lipid values, age, and BMI in both populations, examined separately. Serum LDL and triglycerides both had strong positive correlations with total cholesterol. There were statistically significant, but moderate and negative, correlations between HDL and triglyceride levels in both groups. The BMI did not correlate with lipid values in

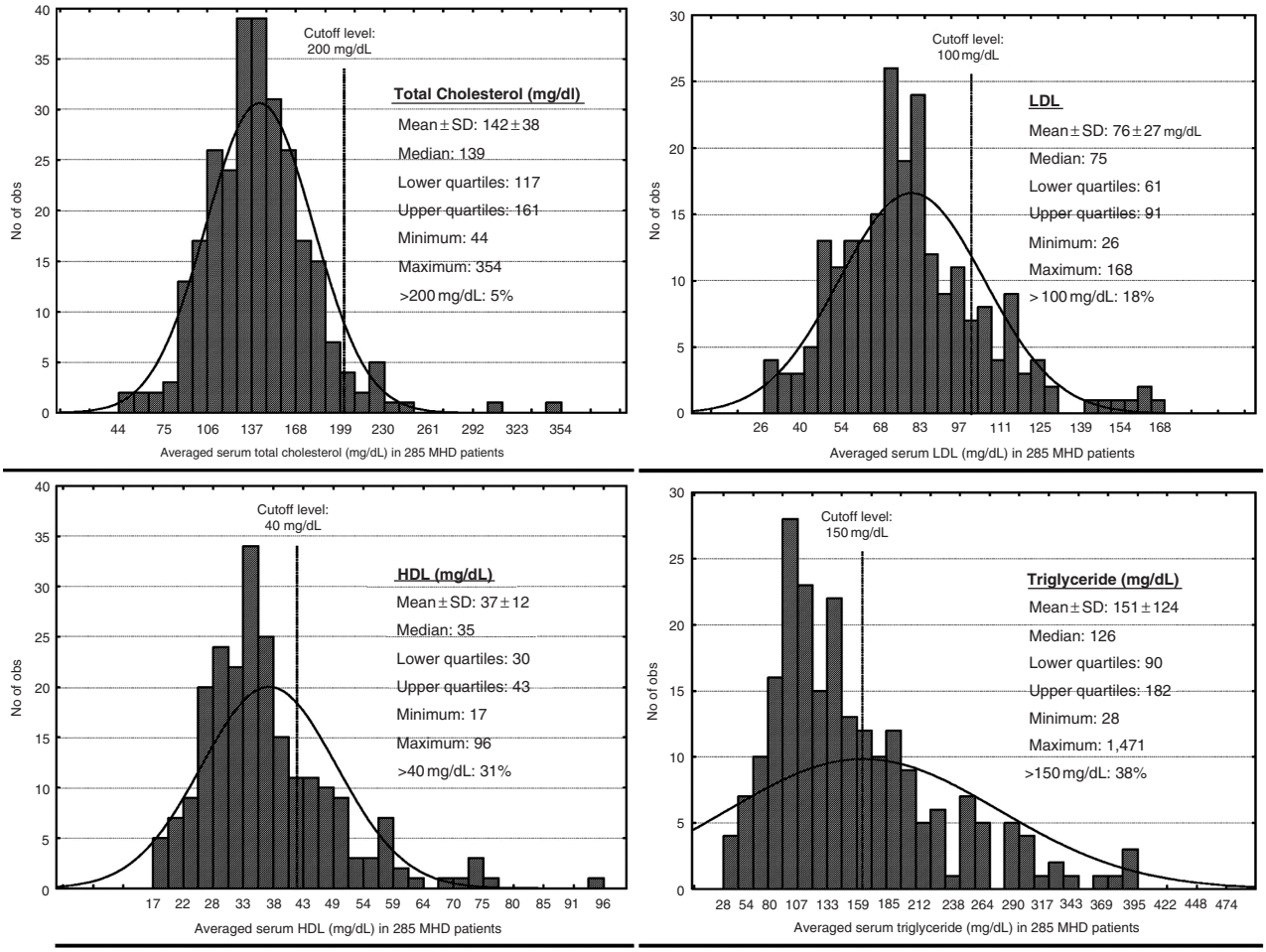

Figure 1 Distribution of serum lipid values in 285 MHD patients.

MHD patients, but the correlation coefficients were significant (negative for HDL and positive for all of the others) in the nondialysis control population. Age had only a weak correlation with total cholesterol in the control group. Among other correlations somewhat notable but not shown in Table 5 was the one between dialysis vintage and total cholesterol in MHD patients ($r = -0.11$; $r = 0.01$). Other correlation coefficients were not significant.

Table 6 shows OR values and their 95% CI for some conventional hyperlipidemic cutoff levels using conditional logistic regression analyses for the matched data and after controlling for BMI, statins, or both. The OR represents the relative prevalence of hyperlipidemia in MHD patients compared to nondialysis controls. Most OR and their 95% CI were significantly and substantially lower than 1.00, indicating much lower likelihood of hyperlipidemia in MHD patients. For instance, the likelihood of increased serum total cholesterol of >200 mg/dL was 82% to 97% lower in MHD patients compared to the nondialysis control population, after matching for sex, race, age, and diabetes and even after further adjustment for BMI and statin use. Similarly, the likelihood of LDL of >100 mg/dL was 72% to 94% lower in MHD patients after above matching and adjustments. A similar trend was observed for the significantly less prevalent HDL of >40 mg/dL in MHD patients. Hypertriglyceridemia of >150 mg/dL in MHD patients, however, was not significantly different from controls after adjustment for BMI.

DISCUSSION

In an age, sex, race, and diabetes-matched study, we compared 285 ambulatory MHD outpatients to 285 nondialysis ambulatory subjects treated in a general internal

Table 2 Pertinent characteristics of all 2425 outpatients of the General Internal Medicine (GIM) Clinic and its subgroup of 285 matched subjects as controls for the study

Variable	Outpatients of the GIM Clinic (n = 2425)	Selected matched controls (n = 285)
Sex (% females)[a]	64	51
Race or ethnicity (%)		
Hispanic[a]	44	52
Black[a]	26	31
Asian[a]	4	6
Diabetes mellitus (%)	36	37
Use of statins (%)[b]	36	38
Age (years)[b]	59.3 ± 12.7	56.3 ± 12.9
BMI (kg/m^2)	30.6 ± 7.6	31.5 ± 7.8
Serum total cholesterol (mg/dL)	194 ± 53	197 ± 45
LDL (mg/dL)	116 ± 38	116 ± 39
HDL (mg/dL)	48 ± 15	46 ± 16
Triglycerides (mg/dL)	177 ± 136	181 ± 169

[a]$p < 0.01$.
[b]$0.01 < p < 0.05$.
BMI = body mass index; LDL = low-density lipoprotein; HDL = high-density lipoprotein.

medicine clinic in the same geographic area and found striking differences in serum lipids measured in the same laboratory. With the possible exception of hypertriglyceridemia, hyperlipidemia was not prevalent in MHD patients. In contrast, low lipid levels were quite common in these patients. Although the control subjects

Table 3 Comparison between 285 matched MHD cases and 285 nondialysis control subjects (p value is based on t test)[a]

Variables	Matched MHD patients (n = 285)	Matched nondialysis controls (n = 285)	p value
Sex (% female)	51	51	NA
Race or ethnicity (%)			
Hispanic	52	52	NA
Black	31	31	NA
Asian	6	6	NA
Diabetes mellitus (%)	37	37	NA
Age (years)	55.6 ± 13.5	56.3 ± 12.9	0.56
BMI (kg/m^2)	26.2 ± 6.0	31.5 ± 7.8	< 0.001
Use of statins (%)	16	38	< 0.001
Serum total cholesterol (mg/dL)	142 ± 38	197 ± 45	< 0.001
LDL (mg/dL)	76 ± 27	116 ± 39	< 0.001
HDL (mg/dL)	37 ± 12	46 ± 16	< 0.001
Triglycerides (mg/dL)	151 ± 124	181 ± 169	0.008
Hypercholesterolemia > 200 mg/dL (%)	5	43	< 0.001
LDL > 100 mg/dL (%)	18	64	< 0.001
HDL > 40 mg/dL (%)	31	68	< 0.001
Hypertriglyceridemia > 150 mg/dL (%)	38	49	0.01

[a]For each MHD patient, a one-to-one nondialysis control subject was matched for sex, race and ethnicity, diabetes mellitus status, and age (± 5 years).
MHD = maintenance hemodialysis; BMI = body mass index; LDL = low-density lipoprotein; HDL = high-density lipoprotein; NA = data not available.

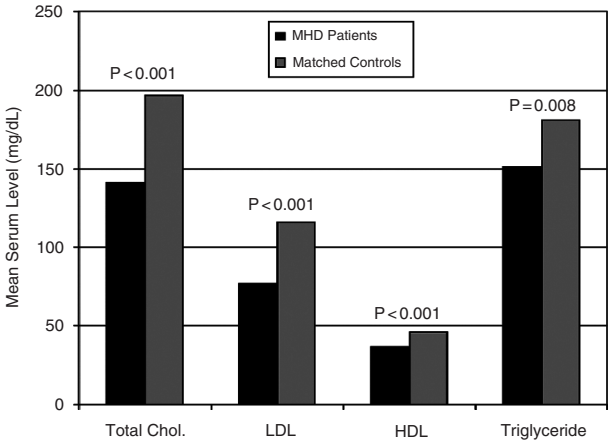

Figure 2 Comparing serum lipid levels between 285 matched MHD cases and 285 nondialysis control subjects (p value is based on t test). For each MHD patient, a one-to-one nondialysis control subject was matched for sex, race and ethnicity, diabetes mellitus status, and age (± 5 years).

had higher BMI and used statins more frequently, our conducted multivariate analyses showed that the substantially lower serum levels of total cholesterol, LDL, and HDL in MHD patients remained significantly lower even after adjustment for BMI and statins, whereas the difference between triglyceride levels was not significant. Only 5% of MHD patients in our study had a total cholesterol level greater than 200 mg/dL, and only 18%

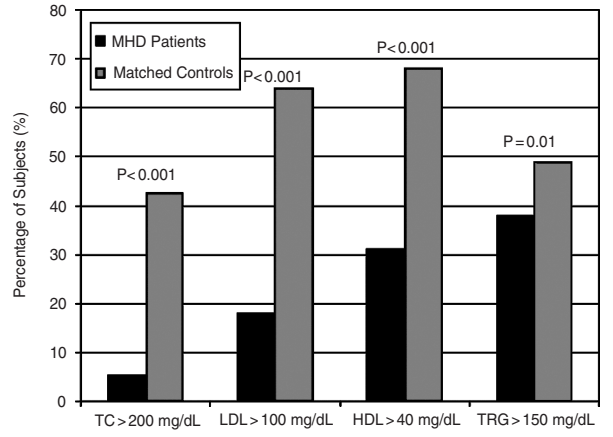

Figure 3 Comparing the prevalence of hyperlipidemia, based on conventional cutoff levels, between 285 matched MHD cases and 285 nondialysis control subjects (p value is based on t test). For each MHD patient, a one-to-one nondialysis control subject was matched for sex, race and ethnicity, diabetes mellitus status, and age (± 5 years). TC = total cholesterol; TRG = triglycerides.

had an LDL greater than 100 mg/dL. Our findings of 82% to 97% less likelihood of total hypercholesterolemia of >200 mg/dL and 73% to 94% less likelihood of serum LDL of >100 mg/dL in MHD patients compared to nondialysis controls indicate that hypercholesterolemia is substantially less prevalent in this MHD population. To our knowledge, this is the first time that a matched study has systematically examined the prevalence and laboratory characteristics of hyperlipidemia in dialysis population.

In the past three decades, a substantial number of publications, lectures, and guidelines have advocated aggressive management of hyperlipidemia in the chronic dialysis population.[2,3,7] The true prevalence of hyperlipidemia in dialysis patients may have been overstated in these publications. This may have occurred because most MHD patients die of cardiovascular disease, in which hyperlipidemia is blindly assumed to play a major role. Neither a causal nor an epidemiologic association between hyperlipidemia and accelerated atherosclerosis in MHD patients has been shown, however.

Recently, Liu *et al.*[3] showed that a positive association between serum cholesterol and mortality existed only in those MHD patients who did not have the malnutrition–inflammation complex syndrome. The study had several limitations including younger age and higher rate of transplantation of their patients, however.[4] Moreover, in the absolute majority of MHD patients as well as in the entire cohort of the same study, there was indeed an inverse association between serum cholesterol and mortality[3] that was consistent with reports by other investigators.[12,13]

Increased release or activation of inflammatory cytokines, such as interleukin-6 or tumor necrosis factor-α,[14] may suppress appetite[9] and lead to hypoalbuminemia, hypocholesterolemia, and what we have referred to as "cachexia in slow motion."[15] These processes may also engender atherosclerosis.[16] Nevertheless, the degree to which malnutrition in dialysis patients is related to inflammation is not clear. Some studies suggest that protein-energy malnutrition and inflammation each independently contribute to hypoalbuminemia and hypocholesterolemia and subsequently increase morbidity and mortality.[17] Both malnutrition and inflammation are strongly associated with each other and can change many nutritional measures including serum lipids in the same direction.[16] Hence, *hypo*cholesterolemia may be a much more relevant issue in dialysis patients and their poor clinical outcome and high mortality than *hyper*cholesterolemia. Consistent with this notion, no improved cardiovascular outcomes were observed

Table 4 The magnitude of the differences (and their 95% confidence intervals) in serum lipids in 285 MHD patients when compared to 285 (sex, race, diabetes, and age) matched control subjects (p values are from multivariate regression models)

	Serum lipid type and its mean value in control subjects			
Difference	Total cholesterol (197 mg/dL)	LDL (116 mg/dL)	HDL (46 mg/dL)	Triglycerides (181 mg/dL)
Baseline difference based on matching only	−55[a] (−61 to −48)	−38[a] (−45 to −32)	−9[a] (−7 to −12)	−30 (−3 to −57) p = 0.03
Difference for MHD patients (mg/dL)				
+ Adjusted for age	−55[a] (−62 to −48)	−38[a] (−46 to −32)	−9[a] (−7 to −12)	−30 (−3 to −57) p = 0.03
+ Adjusted for age and BMI	−53[a] (−61 to −46)	−40[a] (−46 to −33)	−10[a] (−8 to −13)	−23 (+6 to −52) p = 0.12
+ Adjusted for age, BMI, and statin use	−51[a] (−58 to −43)	−39[a] (−46 to −32)	−10[a] (−8 to −13)	−17 (+12 to −47) p = 0.26

[a]$p < 0.001$.
MHD = maintenance hemodialysis; LDL = low-density lipoprotein; HDL = high-density lipoprotein; BMI = body mass index.

among dialysis patients administered atorvastatin or placebo in the 4D trial, which was presented at 2004 meeting of the American Society of Nephrology.[15] Similarly, in patients with chronic heart failure, too, a paradoxically inverse association between serum lipid concentrations and clinical outcome has been observed.[18,19] With the emergence of the new concept of ''reverse epidemiology''[20] in that a low, rather than a high, serum cholesterol appears paradoxically to be associated with higher mortality rates in MHD patients,[12] the characteristics of lipid disorders in dialysis patients need to be revisited using well-designed studies.

The strikingly low prevalence of hypercholesterolemia that we have found in our study is not a new finding but may be an underappreciated one.[13,21–23] More than a quarter of a century ago, Brunzell *et al.*[22] reported that in 94 male dialysis patients, serum triglyceride levels were higher but cholesterol levels were lower than normal controls ($p < 0.001$). Lowrie and Lew[13] examined more than 12,000 MHD patients and found low prevalence of hypercholesterolemia, but these investigators did not compare MHD patients to a control group. Hence, our study aims to revive this important notion that hypercholesterolemia is not a prevalent problem in dialysis patients.

Table 5 Pearson correlation coefficients among serum lipid levels, BMI, and age

	MHD patients (n = 285)				Nondialysis controls (n = 285)			
Variable	TC	LDL	HDL	TRG	TC	LDL	HDL	TRG
LDL	+0.75[a]				+0.69[a]			
HDL	+0.21[a]	+0.14[b]			+0.14[b]	+0.01		
TRG	+0.43[a]	+0.07	−0.19[a]		+0.60[a]	+0.10	−0.26[a]	
BMI	−0.01	−0.09	−0.08	−0.04	+0.16[b]	+0.16[b]	−0.21[a]	+0.25[a]
Age	−0.04	−0.08	+0.01	+0.04	+0.14[b]	+0.10	+0.06	−0.01

[a]$p < 0.001$.
[b]$0.001 < p < 0.05$.
BMI = body mass index; MHD = maintenance hemodialysis; TC = total cholesterol; LDL = low-density lipoprotein; HDL = high-density lipoprotein; TRG = triglycerides.

Table 6 Odds ratios (OR) and their 95% confidence intervals (CI) to reflect the relative prevalence of hyperlipidemia for predetermined hyperlipidemic levels comparing 285 MHD patients with 285 matched nondialysis control subjects[a]

	OR (95% CI) and P value of selected hyperlipidemic cutoffs			
Prevalence	Total cholesterol > 200 mg/dL	LDL > 100 mg/dL	HDL > 40 mg/dL	Triglycerides > 150 mg/dL
Based on matched data	0.07[b] (0.03–0.16)	0.13[b] (0.07–0.22)	0.21[b] (0.12–0.34)	0.52 (0.34–0.78) p = 0.002
+ Adjusted for BMI	0.08[b] (0.03–0.18)	0.12[b] (0.06–0.25)	0.18[b] (0.10–0.34)	0.67 (0.41–1.10) p = 0.11
+ Adjusted for statin use	0.08[b] (0.03–0.16)	0.14[b] (0.08–0.25)	0.22[b] (0.13–0.37)	0.57 (0.36–0.88) p = 0.01
+ Adjusted for BMI and statin use	0.08[b] (0.03–0.18)	0.13[b] (0.06–0.27)	0.19[b] (0.10–0.36)	0.78 (0.46–1.31) p = 0.34

[a]Analyses are based on conditional logistic regression models for data matched on age, sex, race, and diabetes. Additional multivariate adjustments for BMI and statins use are shown as well.
[b]$p < 0.001$.
MHD = maintenance hemodialysis; LDL = low-density lipoprotein; HDL = high-density lipoprotein; BMI = body mass index.

A potential limitation of our study is that there was a high rate of diabetes and a high representation of Hispanics. Diabetic or Hispanic patients, however, tend to be even more hypercholesterolemic than others.[24] Another limitation of the matching process is the effect of matching variables per se cannot be examined; however, the residual effect of the continuous age on lipid was studied (Table 5), because match on age was incremental. Another potential issue is that the BMI in the control group was 5.3 kg/m^2 higher than the MHD patients (26.2 ± 6.0 kg/m^2). Two-thirds of the general population in California, however, is now deemed overweight (BMI, > 25 kg/m^2), with half of those classified as obese (BMI, > 30 kg/m^2).[25] Although this prevalence of obesity in the general population is still lower than that in our selected control group, comparing dialysis patients to the healthy general population would be flawed, because the otherwise healthy population of California would not provide a commensurate group to match to the multimorbid dialysis population. Indeed, the prevalence of obesity in our GIM clinic was similar to other ambulatory clinics.[26] Moreover, to overcome the confounding effect of BMI, we did use multivariate models to adjust for obesity. After statistical adjustments, although there was no statistically significant difference for hypertriglyceridemia, the striking difference for total cholesterol and its components remained almost intact.

Undoubtedly, hyperlipidemia is a known risk factor of cardiovascular disease in the general population and warrants aggressive treatment. Blind extrapolation of data from nondialysis populations to the dialysis patients may be inappropriate, however, because hyperlipidemia is not a prevalent problem in the dialysis population. Indeed, the strong and paradoxical association that has been found between low serum cholesterol levels and high mortality rate in MHD patients should prompt more focused attention to examining the pathophysiology of this reverse epidemiology. To that end, the prevalence of hyperlipidemia in MHD patients needs to be further examined. Our study should provide increased awareness to the underappreciated fact that in MHD patients, hypercholesterolemia is indeed infrequent. This observation, in combination with the finding that a low, rather than a high, serum cholesterol is associated with mortality, may have major clinical implications in this important but not adequately studied area.

ACKNOWLEDGMENTS

The Nutritional and Inflammatory Evaluation in Dialysis (NIED) study is supported by the National Institute of Diabetes, Digestive, and Kidney Disease Grant DK61162 for K.K-Z., a research grant from Amgen for K.K-Z. and J.D.K., and the General Clinical Research Center (GCRC)

Grant M01-RR00425 at Harbor-UCLA Medical Center from the National Centers for Research Resources, National Institutes of Health. The authors are indebted to DaVita, Inc., for authorizing and supporting the NIED Study in their facilities. The authors are also thankful to Ms. Stephanie Griffith, at the Harbor-UCLA GCRC Core Laboratories, for managing blood samples and measuring inflammatory markers; to Dr Charles McAllister at DaVita, Inc., for his ongoing support of the NIED Study; and to Mr Robert S. Lehn at DaVita Laboratories, Deland, FL, USA, for his technical support in database management.

Manuscript received October 2004; revised January 2005.

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