

Lipid Profile in Children with Chronic Renal Failure on Conservative Therapy and with Regular Hemodialysis

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ABSTRACT

Background: Abnormalities in lipid metabolism can be detected in children with chronic kidney diseases (CKD) and may constitute a major atherogenic risk factor.

Objectives: To evaluate the prevalence and types of uremic dyslipidemias in children at different stages of renal impairment and modes of treatment.

Methods: We studied total cholesterol, triglycerides (Tg), low density lipoprotein (LDL), and high density lipoprotein (HDL) in 28 children with CKD on conservative therapy (21 males, 7 females with median age 6.5 years), and another 22 children under regular hemodialysis for at least 6 months (13 males and 9 females with median age 12 years). Ten healthy sex-matched children with age ≥ 10 years (median age 12 years) were taken as control.

Results: The characteristic abnormalities in lipid profiles in the conservative group were elevated ($> 95^{\text{th}}$ percentile of normal reference values) Tg in 53.5%, and total cholesterol in 21.4%. However, in the hemodialysis group hypertriglyceridemia and lowered ($< 5^{\text{th}}$ percentile of normal reference values) HDL were detected in 77% and 90.9% respectively. On comparing lipid profiles in a subgroup of conservative children ≥ 10 years old (10 children, 7 males and 3 females with median age 12 years) and control, there was a significant increase in median concentrations of Tg (101 vs. 67.5 mg/dl, $p = 0.021$), and a significant decrease of median HDL concentrations (41.1 vs. 53.5 mg/dl, $p = 0.002$), as well as insignificant differences in median total cholesterol (173.4 vs. 160 mg/dl, $p = 0.125$) and LDL concentrations (101.9 vs. 97 mg/dl, $p = 0.211$) in patients. When the hemodialysis group was compared to the control group, there were a significant increase in Tg concentrations (median 134.5 mg/dl, $p = 0.001$) and a significant decrease in median concentrations of cholesterol (119 mg/dl, $p = 0.002$), LDL (63.5 mg/dl, $p = 0.001$), and HDL (23 mg/dl, $p = 0.0001$) in patients.

Conclusions: Abnormalities in basic lipid profiles were more frequently detected in children with CKD under regular hemodialysis than those on conservative therapy only. It is recommended to evaluate dyslipidemias in these children more than in the general population, and early intervention might be of a protective value for the cardiovascular system.

INTRODUCTION

Cardiac diseases are the major cause of morbidity and mortality among patients with chronic renal failure regardless of their age. Coronary cardiovascular diseases account for approximately 23% of deaths in children and young adults < 30 years old who started treatment of end stage renal disease as children⁽¹⁾. Indeed, studies of

arteries from children with end stage kidney diseases have demonstrated early atherosclerotic cardiovascular changes⁽²⁾.

It is clear that uremic patients are exposed to a multitude of atherogenic risk factors mainly hypertension and abnormal lipid metabolism, in addition to diabetes mellitus and hyperparathyroidism⁽³⁾.

There are few data documenting the

prevalence of dyslipidemia in children and adolescents with chronic kidney diseases (CKD) on continuous ambulatory peritoneal dialysis⁽⁴⁻⁶⁾, and in pediatric kidney transplant recipients⁽⁷⁻⁹⁾, but not, so far, in predialysis and hemodialysis children.

Dyslipidemia in patients with CKD is often multifactorial in origin, primarily due to abnormalities in the composition of lipoproteins and additional secondary factors as urinary protein excretion rate, antihypertensive medications as thiazide diuretics, and β blockers as well as immunosuppressives⁽¹⁰⁾.

The most characteristic feature of dyslipidemia associated with CKD is the accumulation of triglyceride rich lipoprotein particles in very low density lipoprotein (VLDL) and intermediate density lipoproteins that results in increased serum triglycerides in conjunction with low level of high density lipoprotein (HDL)⁽¹¹⁾.

AIM OF THE WORK

The aim of this study was to evaluate the prevalence and types of dyslipidemias in pediatric patients with chronic kidney diseases treated conservatively only and in those under regular hemodialysis.

SUBJECTS AND METHODS

Subjects

The present study was conducted during July 2004 on children with chronic kidney diseases and variable degrees of renal impairment at the Pediatric Nephrology Unit, Mansoura University Children Hospital, Egypt. All children and/or their parents gave informed written consent to participate in our study. They included 2 main groups according to the degree of renal

impairment and the mode of treatment they were receiving.

The first group of patients (*Conservative Group*) included 28 children with chronic renal failure of varying degrees of renal impairment with glomerular filtration rate (GFR) between 20-50 ml/1.73 m² body surface area/minute. They were maintained on conservative therapy only but had not commenced renal replacement therapy. They were further subdivided into 2 subgroups according to their age into conservative group < 10 years (n = 18 children, 14 males and 4 females with median age 3.5 years), and conservative group \geq 10 years (n = 10 children, 7 males and 3 females with median age 12 years). The causes of their original chronic kidney diseases are listed in Table 1.

The second group of patients (*Hemodialysis Group*) included 22 children (13 males and 9 females, median age 12 years) with end stage kidney disease (ESKD) on regular hemodialysis for at least 6 months prior to the study (GFR < 10 ml/1.73 m² body surface area/minute). All of them were receiving at least 3 hours of regular hemodialysis, 3 sessions per week using volumetric controlled machines and low flux polysulfone membrane dialyzers, and had Kt/V \geq 1.2 at the time of the study. The original causes of their chronic kidney diseases are listed in Table 1.

None of the children in any group had heavy proteinuria (urinary protein > 1 gm/m²/24 hours), severe malnutrition, hypoalbuminemia, diabetes mellitus, or thyroid disease. Also drugs known to influence lipid metabolism as thiazides, and β blockers were not given at the time of the study. All

patients were maintained on non-high fat diets.

A control group of 10 healthy sex-matched children with age ≥ 10 years

(median age 12 years) was taken to compare their lipid profile levels with studied patients in the conservative group ≥ 10 years, and in the hemodialysis group.

Table 1: Etiology of chronic kidney diseases in conservative and hemodialysis groups.

Conservative Group < 10 years (n = 18)	Conservative Group ≥ 10 years (n = 10)	Hemodialysis Group (n = 22)
Obstructive uropathy 10 (55.6%)	Obstructive uropathy 6 (60%)	Unknown etiology 11 (50%)
Nephrocalcinosis 3 (16.7%)	Nephrocalcinosis 1 (10%)	Chronic glomerulonephritis 5 (22.7%)
Polycystic kidney disease 2 (11.1%)	Chronic glomerulonephritis 1 (10%)	Obstructive uropathy 2 (9.1%)
Unknown etiology 2 (11.1%)	Dysplastic Kidneys 1 (10%)	Dysplastic kidneys 2 (9.1%)
Chronic glomerulonephritis 1 (5.6%)	Unknown etiology 1 (10%)	Polycystic kidney disease 1 (4.5%)
		Chronic interstitial nephritis 1 (4.5%)

Methods

Venous blood samples were taken after an overnight fast of at least 10 hours and immediately before the hemodialysis session in the hemodialysis group. Samples were drawn in tubes with ethylene diamine tetra acetic acid (EDETA) at a concentration of 1 mg/dl. Plasma was separated by low speed centrifugation. Cholesterol and triglyceride concentrations were determined by enzymatic assays using commercially available reagents supplied by Humankits, Germany. HDL was separated by phosphotungstic acid and magnesium chloride preparation and low density lipoprotein (LDL) cholesterol concentration was calculated using Friedewald formula⁽¹²⁾. Glomerular filtration rate was represented by estimated creatinine clearance.

Statistical Analysis

Data were processed and analyzed using Statistical Package of Social Science (SPSS) under windows version 10. Analysis for difference for quantitative variables was done by Mann Whitney U-Willcoxon Ranks Sum W Test for 2 samples and correlation was done by Kendall tau-b coefficient. Significant difference was considered when $p < 0.05$.

RESULTS

The prevalence of dyslipidemias varied among the different studied groups (Table 2).

In the conservative group < 10 years old, elevated cholesterol levels ($> 95^{\text{th}}$ percentiles of reference values)⁽¹³⁾ were found in 28.6% of males (> 203 mg/dl), and in

25% of females (> 200 mg/dl). However, high triglycerides were observed in 57% of males (> 99 mg/dl), and in 3% of females (> 126 mg/dl).

In the conservative group ≥ 10 years old, elevated total cholesterol (> 202 mg/dl), LDL (> 132 mg/dl), and lowered (< 5th percentiles of normal reference values)⁽¹³⁾ HDL (< 37 mg/dl) were observed in 28.6% of males only. In addition, triglycerides were elevated in 42.9% of males (> 111 mg/dl), and in 33.3% of females (> 120 mg/dl). When compared to the control group (Fig. 1), there was a significant increase in median concentration of triglycerides in patients (101 vs. 67.5 mg/dl, $p = 0.021$), and also a significant decrease of median HDL concentration (41.1 vs. 53.5 mg/dl, $p = 0.002$). However, there were no significant differences in median total cholesterol (173.4 vs. 160 mg/dl, $p = 0.125$), and LDL (101.9 vs. 97 mg/dl, $p = 0.211$) concentrations in patients versus the control group.

In the hemodialysis group, hypertriglyceridemia was observed in the

majority of children of both genders as it occurred in 76.9% of males and 77.8% of females. In addition, lowered HDL, was observed in all females and in 84.5% of males. When compared to the control group (Fig. 2) there was a significant increase in median triglyceride concentrations (134.5 vs. 67.5 mg/dl, $p = 0.001$), and a significant decrease in the median concentrations of cholesterol (119 vs. 160 mg/dl, $p = 0.002$), LDL (63.5 vs. 97 mg/dl, $p = 0.001$), and HDL (23 vs. 53.5 mg/dl, $p = 0.0001$) in patients compared with the control group.

When comparing the conservative group ≥ 10 years old and the hemodialysis group, those receiving regular hemodialysis had significantly higher triglyceride concentrations and lower cholesterol, LDL, and HDL levels (Table 3).

We reported significant positive correlations between GFR and cholesterol, HDL, and LDL. However, triglycerides showed an insignificant negative correlation with GFR (Table 4).

Table 2: Distribution of dyslipidemias among conservative and hemodialysis groups.

Lipid Profile	Predialysis group				Dialysis group	
	< 10 years		> 10 years		Males (n = 13)	Females (n = 9)
	Males (n = 14)	Females (n = 4)	Males (n = 7)	Females (n = 3)		
Cholesterol*	4	1	2	0	1	-
Triglyceride*	8	3	3	1	10	7
LDL*	-	-	2	0	1	1
HDL**	-	-	2	-	11	9

* > 95th percentiles of normal reference values for age and gender

** < 5th percentiles of normal reference values for age and gender

Table 3: Comparison of studied lipid profiles between the conservative group ≥ 10 years and the hemodialysis group.

Lipid Profile (Mean Ranks)	Conservative Group (n = 10)	Dialysis Group (n = 22)	Z	p*
Cholesterol	24.15	13.02	-3.11	0.002
Triglyceride	12.30	18.41	-1.71	0.088
LDL	24.20	13.00	-3.58	< 0.001
HDL	25.30	12.50	-3.13	0.002

* Mann Whitney U-Willcoxon Rank Sum W Test

Table 4: Correlation coefficients between GFR and studied lipid profiles.

Lipid Profile	r*	p
Cholesterol	0.47	0.001
Triglyceride	-0.26	0.069
LDL	0.48	0.001
HDL	0.49	0.001

* Kendall tau-b Correlation Coefficients

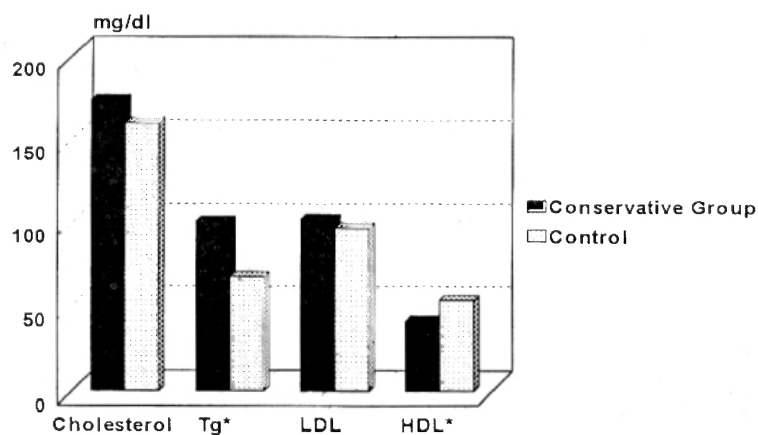


Fig. 1: Comparison between median concentrations of studied lipid profiles in the conservative group ≥ 10 years and the control group.

* Significant difference ($p < 0.05$) by Mann Whitney U-Willcoxon Rank Test.

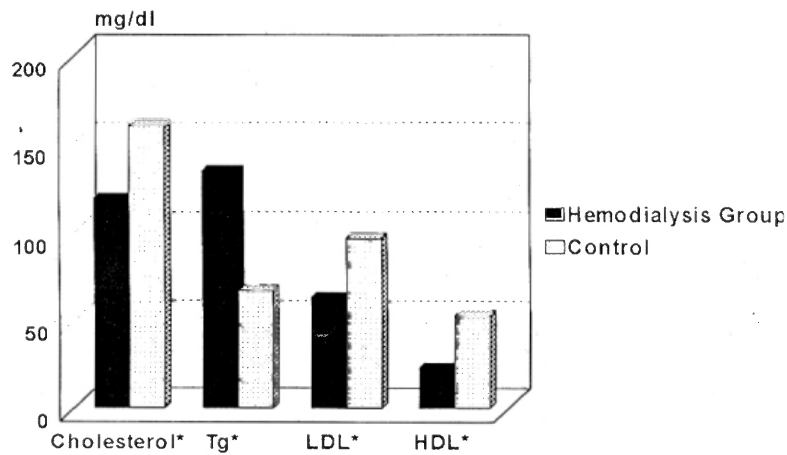


Fig. 2: Comparison between median concentrations of studied lipid profiles in the dialysis and control groups.

* Significant difference ($p < 0.05$) by Mann Whitney U-Willcoxon Rank Test.

DISCUSSION

The atherosclerotic process is believed to be accelerated in uremia thus putting children with chronic renal failure at a high risk for developing premature coronary vascular diseases when they combine common atherogenic risk factors as hypertension and hyperlipidemia⁽¹¹⁾.

Abnormalities in lipid metabolism can be detected in patients with CKD as early as renal function begins to decline, and lipid levels may change during the course of different kidney disease treatments⁽¹⁰⁾.

It is important to note that lipid levels in the general population change with age and puberty and differ by gender and these changes dictate that the definitions of dyslipidemia be different in children and adults⁽¹⁴⁾. In our study we define hyperlipidemia in children using lipid levels greater than the 95th percentiles⁽¹³⁾ for age and gender.

Our results demonstrate the prevalence and types of uremic dyslipidemia in children. Such findings are consistent with

the few previous studies which examined abnormalities in lipid metabolism in children on continuous ambulatory peritoneal dialysis and pediatric kidney transplant recipients and extended these findings to the group of children who did not yet commence renal replacement therapy and those under regular hemodialysis.

Hypertriglyceridemia and lowered HDL were the characteristic features of uremic dyslipidemia in the majority of hemodialysis children occurring in 77% and 90.9% respectively. However, in conservative children hypertriglyceridemia was detected in about 60% of children < 10 years, and in about 40% of children ≥ 10 years. In addition, elevated cholesterol levels were present in nearly 28% of conservative children in both age categories with high LDL in 28% only of those ≥ 10 years.

Consistent with our results, Asayama et al.⁽¹⁵⁾, found that increased triglyceride concentrations and lowered HDL levels in groups of children with chronic renal failure not on dialysis, and others on hemodialysis

were associated with defective triglyceride removal due to reduced activities of plasma lipoprotein lipase enzyme.

Querfeld⁽¹⁶⁾ stated that in addition to the characteristic uremic hypertriglyceridemia and lowered HDL in children, serum levels of total cholesterol, VLDL, LDL, and apolipoprotein B are frequently elevated in children with chronic renal failure. However, in our study patients on regular hemodialysis experienced low cholesterol and LDL concentrations. The explanation of these observations may be related to the effects of efficient dialysis, or to the polysulfone nature of the membrane dialyzers that had been postulated to have improved lipolytic activities⁽¹¹⁾. The role of nutritional status in hemodialysis children was of little concern as any child with severe malnutrition or hypoalbuminemia was excluded from the study.

Other studies exhibited impaired lipid metabolism in children receiving continuous ambulatory peritoneal dialysis⁽⁴⁻⁶⁾, and pediatric transplant recipients⁽⁷⁻⁹⁾ that were characterized by increased triglycerides, and cholesterol with decreased HDL.

Furthermore, many reports demonstrated abnormal lipid metabolism in adult hemodialysis patients and were characterized also by increased triglycerides and reduced HDL cholesterol⁽¹⁷⁾. LDL was usually not elevated⁽¹⁸⁾.

Studies in adults which tried to elucidate the pathogenesis of such lipid abnormalities in hemodialysis patients, found that the principal cause of hypertriglyceridemia was increased production of apoprotein B and marked decrease in the metabolism of very low density lipoproteins

rich in triglycerides as a result of decreased endothelial cell delipidation of VLDL, decreased lipoprotein lipase activity, and hepatic triglyceride lipase⁽¹⁹⁾. In addition, loss of carnitine which plays an important role in facilitating the transport of fatty acids across the inner mitochondrial membrane prior to β oxidation is common in hemodialysis patients⁽¹¹⁾, and decreased antioxidant activities might be an additional factor⁽²⁰⁾.

Although our results showed significant abnormalities in basic lipid profile in both conservative and hemodialysis children, other studies in adults stressed that disturbances in lipid metabolism associated with uremia were mainly in the form of dyslipoproteinemias rather than dyslipidemias, and such abnormalities will be reflected on apolipoprotein composition rather than lipid profiles^(21,22).

Uremic dyslipidemias may contribute not only to accelerated atherosclerosis but may enhance the progression of renal disease in patients with residual renal function⁽¹⁶⁾. However, we reported an insignificant negative correlation between GFR and triglycerides and significant positive correlations with cholesterol, LDL, and HDL. Others suggested a limited role for dyslipidemia in the progression of CKD⁽²³⁾.

In conclusion, abnormalities in lipid profile can be detected in children with chronic kidney diseases with varying degrees of renal insufficiency. Hypertriglyceridemia and lowered HDL were the main characteristic features of uremic dyslipidemia in both conservative and hemodialysis children. It is prudent to evaluate dyslipidemia in children with CKD

more frequently than recommended in the general population and this may be extended to apolipoprotein profiles. Early treatment of significant uremic hyper-

lipidemia in children might be of protective to the cardiovascular system value, but the long term clinical effects have yet to be established.

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