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Assessment of Lipid Profile in Egyptian Children with Chronic Kidney Diseases on Conservative Therapy and Those under Regular Hemodialysis

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The present study aimed to evaluate the prevalence and pattern of uremic dyslipidemias in children at different stages of renal impairment and modes of treatment. We studied total cholesterol, triglycerides (Tg), Low Density Lipoprotein (LDL) and High Density Lipoprotein (HDL) in 28 children with Chronic Kidney Diseases (CKD) on conservative therapy (14 males, 4 females <10 years old and 7 males and 3 females ≥ 10 years old) and other 22 children under regular hemodialysis for at least 6 months (13 males and 9 females with median age 12 years). Ten healthy children with age ≥ 10 years and equal sexes were taken as control. Hypertriglyceridemia and lowered HDL were the characteristic features of uremic dyslipidemia in the majority of hemodialysis children being occurred in 77 and 90.9%, respectively. However, hypertriglceridemia was detected in about 60% of conservative group <10 years and in about 40% of children ≥ 10 years and lowered HDL was observed in only 20% of the latter group. We concluded that abnormalities in basic lipid profiles were more frequent in children with CKD under regular hemodialysis than those on conservative therapy and may constitute a major atherogenic risk factor for the development of cardiovascular diseases.

Key words: Lipid profile, chronic renal failure, cardiovascular risk factors, pediatric nephrology

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INTRODUCTION

Cardiovascular disease is one of the most important causes of morbidity and mortality in children with end stage renal failure (Cengiz *et al*., 2005). 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 (Parekh *et al*., 2002). Indeed, studies of arteries from children with end stage kidney diseases have demonstrated early atherosclerotic cardiovascular changes (Nayir *et al*., 2001).

It is clear that uremic patients are exposed to multitude of atherogenic risk factors mainly hypertension and abnormal lipid metabolism, in addition to diabetes mellitus and hyperparathyroidism (Prichard, 2003).

There are some data documenting the prevalence of dyslipidemia in children and adolescent with Chronic Kidney Diseases (CKD) on continuous ambulatory peritoneal dialysis (Querfeld *et al*., 1991; Querfeld *et al*., 1998) and in pediatric kidney transplant recipient (Singh *et al*., 1998), but not so far in conservative and in hemodialysis treated uremic children.

The aim of this study was to evaluate the prevalence and patterns of dyslipidemias among Egyptian children with chronic kidney diseases treated conservatively only and those under adequate and regular hemodialysis.

MATERIALS AND METHODS

The present study was conducted during July 2004 on children with chronic kidney diseases and variable degrees of renal impairment at 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 m^2 body surface area/min. They were maintained on conservative therapy only but not been commenced in 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 ≥10 years (n = 10 children, 7 males and 3 females with median age 10 years). The causes of their original chronic kidney diseases were listed in Table 1.

The second group of patients (*Hemodialysis Group*) included 22 children (13 males and 9 females with median age 12 years) with End Stage Kidney Disease (ESKD) on regular hemodialysis for at least 6 months prior to study (GFR <10 mL/1.73 m^2 body surface area /min). All of them were receiving at least 3 hours of regular hemodialysis for 3 sessions per week using volumetric controlled machines and low flux polysulfone membrane dialyzers and had Kt/v = 1.2 at the time of the study. The original causes of their chronic kidney diseases were listed in Table 1.

None of children in any group had heavy proteinuria (urinary protein >1 g/m^2/24 h), 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.

A control group of healthy 10 children with age ≥10 years and equal sexes was taken to compare their lipid profile levels with studied patients in conservative group ≥10 years and in hemodialysis group. We did not compare lipid levels in conservative group <10 years to control as it was a hard issue to take overnight fasting samples in healthy children <10 years.

Venous blood samples were taken after an overnight fast of at least 10 h and immediately before hemodialysis session in hemodialysis group. Samples were drawn in tubes with EDETA. Serum was separated by low speed centrifugation. Cholesterol and triglyceride concentrations were determined by automated enzymatic assays using commercially available reagents. HDL was separated by dextran sulphate preparation (Warnick *et al*., 1982) and Low Density Lipoprotein (LDL) cholesterol concentration were calculated using Friedewald formula (Friedewald *et al*., 1972). Glomerular filtration rate was represented by estimated creatinine clearance.

Data were processed and analyzed using Statistical Package of Social Science (SPSS, 1999) under windows

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%)	Shrunken kidneys 11 (50%)
Nephrocalcinosis 3 (16.7%)	Nephrocalcinosis 1 (10%)	Chronic glomerulonephritis 5 (22.7%)
Polycystic kidney disease 2 (11.1%)	Chronic glomerulonephritis 1 (10%)	Dysplastic kidneys 2 (9.1%)
Unknown etiology 2 (11.1%)	Dysplastic Kidneys 1 (10%)	Obstructive uropathy 2 (9.1%)
Chronic glomerulonephritis 1 (5.6%)	Unknown etiology 1 (10%)	Polycystic kidney disease 1 (4.5%)
		Chronic interstitial nephritis 1 (4.5%)

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.

RESULTS

The prevalence of dyslipidemia varied among the different studied groups (Table 2). We define dyslipidemia in children using lipid levels greater than 95th percentiles and decreased levels of less than 5th percentiles of normal reference range for age and gender (Olson, 2000).

In conservative group<10 years old, elevated cholesterol levels > 95th percentiles of reference values (Olson, 2000) were found in 28.6% of males (>203 mg dL^{-1}) and in 25% of females (>200 mg dL^{-1}). However, high triglycerides were observed in 57% of males (>99 mg dL^{-1}) and in 75% of females (>126 mg dL^{-1}).

In conservative group < 10 years old, elevated total cholesterol (>202 mg dL^{-1}), LDL (>132 mg dL^{-1}) and lowered < 5th percentiles of normal reference values (Olson, 2000) HDL (<37 mg dL^{-1}) were observed in 28.6% of males only. However, triglycerides were elevated in 42.9% of males (>111 mg dL^{-1}) and in 33.3% of females (>120 mg dL^{-1}). When compared to control group (Table 3), there were significant increase in median concentrations of triglycerides in patients (p = 0.021) and also significant decrease of median HDL concentrations (p = 0.002). However, there were no significant differences in median total cholesterol (p = 0.125) and LDL (p = 0.211) concentrations.

In 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 control group (Table 3) there were significant increase in median triglyceride concentrations (p = 0.001) and significant decrease in median concentrations of cholesterol (p = 0.002), LDL (p = 0.001) and HDL (p = 0.0001).

When comparing conservative group ≥10 years old and hemodilaysis group, those receiving regular hemodialysis had insignificant higher triglyceride concentrations and significant lower cholesterol, LDL and HDL levels (Table 4).

Table 2: Distribution of dyslipidemia among conservative and hemodialysis groups

	Conservative group					
	< 10 years		≥10 years		Hemodialysis group	
Abnormal lipid profile	Males (n = 14)	Females (n = 4)	Males (n = 7)	Females (n = 3)	Males (n = 13)	Females (n = 9)
Cholesterol*	4	1	2	-	1	-
Triglyceride*	8	3	3	1	10	7
LDL*	-	-	2	-	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 between lipid profiles among conservative group ≥10 years versus control and hemodialysis group versus control

Median lipid profile concentration (mg dL^{-1})	Conservative group = 10 years (n = 10)	Hemodialysis group (n = 22)	Control group (n =10)	p_1*	p_2**
Cholesterol	173.4	119	160	0.125	0.002
Triglyceride	101	134.5	67.5	0.021	0.001
LDL	101.9	63.5	97	0.211	0.001
HDL	41	23	53.5	0.002	0.0001

Significant difference (p<0.05) by mann whitney U Willcoxon rank test, *p_1 = Significance of difference between conservative group ≥10 years and control, **p_2 = Significance of difference between hemodialysis group and control

Table 4: Comparison of studied lipid profiles between conservative group ≥ 10 years and hemodialysis group

Lipid profile (Mean rank)	Conservative group ≥10 years (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 5: 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

We reported significant positive correlations between GFR and cholesterol, HDL and LDL. However, triglycerides showed insignificant negative correlation with GFR (Table 5).

DISCUSSION

Atherosclerotic process is believed to be accelerated in uremia thus putting children with chronic renal failure at high risk for developing premature coronary vascular diseases when they combine common atherogenic risk factors as hypertension and hyperlipidemia (Flynn, 2006).

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 (Wanner, 2001).

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 (K/DOQUI, 2001). For so in our study we define dyslipidemia in children using lipid levels with reference to percentiles of normal reference range for age and gender.

In the present study, we demonstrate the prevalence and patterns of uremic dyslipidemia in Egyptian children with chronic kidney diseases on groups of children not commenced in renal replacement therapy and those under regular hemodialysis to determine the magnitude of the major atherogenic risk factor for development of premature cardiovascular diseases.

Hypertriglyceridemia and lowered HDL were the characteristic features of uremic dyslipidemia in the majority of hemodialysis children being occurred in 77% and 90.9%, respectively. However, in conservative children hypertriglceridemia 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.

Present findings are consistent with Asayama *et al.* (1984), who founded increased triglyceride concentrations and lowered HDL levels in different groups of children with chronic renal failure not on dialysis and others on hemodialysis and were attributed to defective triglyceride removal due to reduced activities of plasma lipoprotein lipase enzyme.

Querfeld (1993) founded that in addition to the characteristic hypertriglyceridemia and lowered HDL in uremic children, serum levels of total cholesterol, VLDL, LDL and apolipoprotein B are frequently elevated in children with chronic renal failure. In contrast, our patients on regular hemodialysis experienced low cholesterol and LDL concentrations. The explanation of these observations is questionable. It could 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 by some investigators (Oda and Keane, 1998). The role of nutritional status in our study was of little concern as any child with severe malnutrition or hypoalbuminemia was excluded from the study.

Many reports demonstrated abnormal lipid metabolism in adult hemodialysis patients and were characterized also by increased triglycerides and reduced HDL cholesterol (Kasiske and Keane, 1991) and LDL was usually not elevated (Keane, 1994).

Most studies tried to elucidate he pathogenesis of such lipid abnormalities in hemodialysis patients were in adults and founded 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, decrease lipoprotein lipase activity and hepatic triglyceride lipase (O'Neal *et al.*, 1996). In addition, the 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 (Oda and Keane, 1998) and decreased antioxidant activities might be an additional factor (Maggi *et al.*, 1994).

Although our results showed significant abnormalities in basic lipid profile in both predialysis and hemodialysis children, other studies focused that disturbances in lipid metabolism associated with uremia were mainly in the form of dyslipoproteinemias and such abnormalities will be reflected on apolipoprotein composition rather than lipid profiles (Attman *et al.*, 1993; Ma *et al.*, 1992).

Uremic dyslipidemias may contribute not only to accelerated atherosclerosis but may enhance the progression of renal disease in patients with residual renal function (Querfeld, 1993). Others suggest a limited role for dyslipidemia in the progression of CKD (Massy *et al.*, 1999). However, we reported insignificant negative correlation between GFR and triglycerides and significant positive correlations with cholesterol, LDL and HDL.

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 than recommended in general population on terms of basic lipids and may be extended to terms of apolipoprotein profiles. Early treatment of significant uremic hyperlipidemia in children might be of protective value, but the long term clinical effects have yet to be established.

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