Predictors of Lipid Abnormalities in Children with New-Onset Systemic Lupus Erythematosus

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ABSTRACT. ***Objective.*** Lipid abnormalities in patients with systemic lupus erythematosus (SLE) are common and likely are one of the causes of premature atherosclerosis in these patients. Our aims were to determine the frequency and pattern of dyslipoproteinemia at presentation of pediatric SLE; and to determine the association between dyslipoproteinemia and markers of disease activity and inflammatory markers at presentation of pediatric SLE.

Methods. Serum lipid measurements were obtained at diagnosis before corticosteroid treatment for an inception cohort of 54 patients. Total cholesterol, triglyceride, LDL-C, and HDL-C levels were regressed on measures of inflammation, disease activity, and disease symptoms.

Results. At least one lipid abnormality was present in the majority of patients (63%), an elevated triglyceride level being the most common lipid abnormality (62%). Triglycerides were best predicted by fibrinogen, nephritis, and pleuritis (model $R^2 = 0.6$). Albumin, C4, and white blood cell count were found to predict HDL-C (model $R^2 = 0.6$). Erythrocyte sedimentation rate, central nervous system involvement, nasal ulcers, and nephritis were found as predictors for LDL-C:HDL-C (model $R^2 = 0.5$). No significant predictors were found for total cholesterol or LDL-C. The European Consensus Lupus Activity Measure disease activity score best predicted abnormal triglyceride and HDL-C levels (OR 1.7, 95% CI 1.2–2.3).

Conclusion. Children with newly diagnosed SLE exhibited the distinct pattern of dyslipoprotein of increased triglycerides and depressed HDL-C that was twice as common in the presence of kidney disease. This lipid profile puts them at risk for premature atherosclerosis. Good disease control and individualized use of lipid-lowering agents based on the observed pattern of lipid abnormalities may lower the risk of premature atherosclerosis in these patients. (First Release Sept 1 2007; J Rheumatol 2007;34:2112–8)

Key Indexing Terms:
LUPUS PEDIATRICS AUTOIMMUNE DISEASE LIPIDS ATHEROSCLEROSIS

Pediatric systemic lupus erythematosus (pSLE) accounts for 20% of all SLE cases[1]. Premature atherosclerosis has been recognized as an important issue for patients with SLE since the mid 1970s[2,3]. Identification of risk factors leading to premature atherosclerosis is an active area of research in SLE and has led to discovery of a role for both traditional and nontraditional risk factors[4-6]. Among the traditional risk factors of atherosclerosis, a history of smoking, diabetes, hypertension, and abnormal lipid profile have been shown to be important[7]. In patients with pediatric SLE, smoking, diabetes, and uncontrolled hypertension are not common and therefore abnormal lipid profiles may be the most important risk factor.

The lipid profile of both children and adults with SLE is the result of a combination of the influences of active disease, therapies, and genetics. Although the influence of genetic predisposition is difficult to either alter or accurately determine, the role of disease activity and therapies, corticosteroid treatment in particular, can be examined. The best way to determine the maximal potential effect of disease activity itself would be to examine patients at the time of presentation of SLE, when they are likely to have high disease activity but no effect of corticosteroid therapy. Studies in patients with active SLE suggested that there is a distinct pattern of lipid abnormalities of increased very low-density lipoprotein (VLDL) and triglycerides and decreased high-density lipoprotein (HDL-C), cholesterol and apolipoprotein A1 levels ("active SLE pattern")[8-14]. Examination of lipid levels at presentation, prior to the introduction of corticosteroid therapy, would allow

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better determination not only of the lipid abnormality associated with active SLE but also of the role of inflammation in altering the lipid profile of SLE patients. Few studies to date have addressed lipid levels at the time of SLE diagnosis in children and even fewer before corticosteroid treatment[11,13,15-17].

The aims of this study were: (1) to determine the frequency and pattern of dyslipoproteinemia at presentation of pediatric SLE; and (2) to determine the association between dyslipoproteinemia and markers of disease activity and inflammatory markers at presentation of pSLE.

MATERIALS AND METHODS

Study design and patient population. A single-center observational study of patients with pSLE was performed. The inception cohort consisted of all 54 of 190 patients followed at the Pediatric Lupus Clinic between May 1996 and December 2005 who met the following inclusion criteria: (1) fulfilled at least 4 of 11 American College of Rheumatology classification criteria for the diagnosis of pSLE[18]; (2) onset of disease prior to their 18th birthday; (3) fasting lipid profile levels [cholesterol (CHOL), LDL-C, HDL-C, triglyceride (TG)] performed within 6 months of diagnosis; and (4) lipid testing performed prior to onset of treatment with corticosteroids, or a minimum of 30 days after cessation of all possible corticosteroid use for medical conditions other than pSLE (one patient met this condition). Ethical approval was obtained from the Research Ethics Board at The Hospital for Sick Children.

Lipid profile. Measurements for CHOL, TG, LDL-C, and HDL-C were obtained following an overnight fast. Lipids were analyzed in the biochemistry laboratory using an automated analyzer (Vitros; Ortho-Clinical Diagnostics, Rochester, NY, USA), which uses dry-slide chemistry technology. LDL-C levels were calculated according to the following formula: LDL-C (mmoles/liter) = CHOL – HDL-C – (TG/2.2). LDL-C estimation is not available for triglycerides exceeding 4.00 mmol/l, but no triglyceride level measured in our cohort exceeded this value.

For CHOL, TG, and LDL-C, the percentages of patients with values above the age- and sex-specific normal range were considered abnormal, while for HDL-C, percentages below the normal range were abnormal. As normal serum lipid values are age- and sex-dependent, z-scores were calculated.

Clinical and laboratory measurements. All data were prospectively collected and recorded using a standard protocol. Independent disease symptom variables were dichotomous (present/absent) and included the following: alopecia, photosensitivity, arthritis, central nervous system (CNS) involvement, diffuse lymphadenopathy, digital ulcer, headache, malar rash, other rashes, myositis, oral and nasal ulcers, kidney involvement [includes nephritis diagnosed by biopsy or persistently abnormal urinalysis and nephrotic syndrome diagnosed by proteinuria (> 50 mg/kg/day) and hypoalbuminemia (< 30 gm/l)], pericarditis, pleuritis, Raynaud's phenomenon, and the presence of anti-DNA antibodies and antiphospholipid antibodies (positive for either or both of IgG anticardiolipin antibodies and lupus anticoagulant). The continuous variables examined were the disease activity scores, Systemic Lupus Erythematosus Disease Activity Index (SLEDAI or SLEDAI-2k[19]), and European Consensus Lupus Activity Measure (ECLAM), which were prospectively obtained at the first visit[20-22], and laboratory markers of inflammation: albumin, complement level C3 and C4, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), fibrinogen, hemoglobin level, proteinuria (total grams of protein per 24-hour urine collection), and white blood cell count (WBC). All patients were assessed for disease symptoms at presentation. Not all patients had disease activity scores and inflammatory markers recorded within 7 days of the lipid profile.

Statistical analysis. Univariate regression analysis was used to determine the association of serum lipids with measurements of disease activity and inflammation and to screen continuous variables for colinearity, and chi-square analysis was used for assessing categorical variables for extremely high agreement. A single patient was found to have significantly different values (outliers) for CHOL and LDL-C from the inception cohort. All analyses were performed with and without this patient's data. No significant differences were found and we chose to report all analysis results having excluded this patient. The ratio of LDL-C to HDL-C was found to be positively skewed and therefore data were log-transformed for analysis. Each lipid (continuous dependent variable) was tested against each independent variable (disease activity scores, inflammation measures, disease symptoms) separately to determine the significance of the association. Only associations where $r \geq 0.3$ with p values < 0.05 were considered statistically significant and retained for analysis. In each case the magnitude of the effect (R^2) was considered. Following variable selection, multiple regression models (or logistic models for categorical outcomes) were used to determine which variables were significant predictors of each lipid. Models were first developed using a stepwise regression method. The threshold for entry of variables into the model for the stepwise procedure was $p \leq 0.10$ and for removal of variables from the model, $p > 0.05$. Adjustments were also made by excluding variables from the model that were suspected of being clinically similar, found to be statistically interrelated, and added little information to explain additional variance. In each model, standardized regression coefficients (ß) were reported to show the magnitude of the contribution of each predictor to the regression equation. All statistical test results were considered significant at the 0.05 level and multiple comparisons were corrected using Tukey's studentized range test. SAS 9.1 for Windows (SAS Institute, Cary, NC, USA) was used for all analyses.

RESULTS

All 4 lipid levels were evaluated in 54 patients at the time of diagnosis of pSLE prior to therapy with corticosteroids. Four patients had received antimalarial treatment and 6 patients nonsteroidal antiinflammatory drugs before or at the time of lipid measurement. Mean time from diagnosis to testing was 8.7 days (SD 49.4). Fifty patients (93%) were female and the mean age at time of diagnosis for the cohort was 13.4 years (SD ± 3.1 yrs). There was no statistically significant difference in any of the clinical characteristics at time of diagnosis of the inception cohort and the total hospital pSLE cohort (Table 1). The mean body mass index for 41 of 54 patients was 20.8 (SD 5.1) and it was found to be positively correlated with HDL-C ($r = 0.43$, $p = 0.0047$) and total cholesterol ($r = 0.31$, $p = 0.0465$).

Lipid abnormalities. The mean serum lipid levels and disease measures at diagnosis for the inception cohort are shown in Table 2. At least one lipid abnormality was present in the majority of patients (63%), an elevated triglyceride level being the most common lipid abnormality (62%) and elevated LDL-C the least common (4%). Abnormally low levels of HDL-C and abnormally high CHOL levels were found in 24% and 20% of patients, respectively. Only one patient (2%) had abnormal levels in all 4 lipids and 13 patients (24%) had the "active" lupus lipid profile of abnormally low HDL-C and elevated triglyceride levels[11]. Nine of these patients had kidney involvement and 4 did not have kidney involvement. By grouping the cohort by patients' level of kidney involvement (no kidney involvement, nephritis but not nephrotic, and nephrotic syndrome) we show for CHOL, TG, and LDL-C levels (Figure 1) the percentage of patients with values above

Table 1. Patient characteristics at presentation.

	Inception Cohort	All Patients
N	54	190
M:F (% female)	4:50 (92.6)	33:157 (82.6)
Mean age, yrs ± SD	13.4 ± 3.1	13.2 ± 3.3
Mean BMI, units ± SD	20.7 ± 5.0	20.1 ± 4.4
Symptoms at diagnosis (% present)*		
Mucocutaneous		
Malar rash	79.6	68.4
Non-malar rash	35.2	33.7
Alopecia	29.6	22.6
Photosensitivity	22.2	22.6
Oral ulcers	20.4	24.7
Nasal ulcers	7.4	7.4
Digital ulcer	3.7	3.2
Raynaud's phenomenon	14.8	15.3
Arthritis	59.3	63.7
Kidney involvement	35.2	39.1
Nephritis but not nephrotic	13.0	12.0
Nephrotic syndrome	22.2	27.1
Diffuse lymphadenopathy	16.7	23.2
Central nervous system	13.0	17.9
Headache	9.3	14.7
Pleuritis	3.7	12.1
Pericarditis	3.7	7.9
Myositis	3.7	4.2
Anti-DNA	57.4	62.0
Antiphospholipid	59.3	55.7

* Within 6 months of diagnosis.

Table 2. Clinical and laboratory measures.

Variable	Mean (median)	SD (minimum-maximum)	n
Lipids			
CHOL, mmol/l	3.5	0.9	53
Triglyceride, mmol/l	1.6	0.7	53
LDL-C, mmol/l	2.0	0.7	53
HDL-C, mmol/l	0.8	0.4	53
LDL-C:HDL-C	3.0	1.8	53
Disease activity			
SLEDAI	(9.5)	(0–34)	51
ECLAM	(5.0)	(0–10)	51
Inflammation measure			
Albumin, g/l	37.3	7.3	53
C3, g/l	0.8	0.4	51
C4, g/l	0.1	0.1	51
CRP	4.9	14.7	40
ESR	62.1	39.2	51
Fibrinogen	3.2	0.8	32
Hemoglobin, g/l	111.3	19.4	53
WBC	5.6	3.2	53

CHOL: total cholesterol, WBC: white blood cell count ($\times 10^9$/l), ESR: erythrocyte sedimentation rate (mm/h), ECLAM: European Consensus Lupus Activity Measure, SLEDAI: Systemic Lupus Erythematosus Disease Activity Index.

the normal range, while for HDL-C, percentages below the normal range are shown. Very little difference exists between the groups for CHOL or LDL-C. Half the patients with kidney involvement (nephritis or nephrotic syndrome) have abnormally low HDL-C levels and most have abnormally high TG levels. This is twice or more than that observed in patients with no kidney involvement.

Interestingly, 43% of patients had abnormally low CHOL and 31% abnormally low LDL-C levels, while no patient had an abnormally low TG or abnormally high HDL-C level. Mean z-score values were significantly different from 0 for all 4 lipids, although only the mean value of the z-scores for TG levels was found to be outside the normal range of 2 standard deviations (TG level 3.35 SD ± 3.32; $p < 0.0001$). The mean z-scores for the other lipids demonstrated that both the mean CHOL level at –0.93 SD ± 2.90 ($p = 0.0235$) and LDL-C level at –1.33 SD ± 1.52 ($p < 0.0001$) were significantly lower than expected, as was the mean HDL-C level at –1.43 SD ± 1.00 ($p < 0.0001$; Figure 2).

Correlation of lipids with measures of disease. We determined the association of individual disease manifestations, laboratory measures, and disease activity measures listed in Table 2 with the individual lipid levels. We chose to include only "kidney involvement," as nephritis and nephrotic syndrome are closely associated. Only statistically significant associations ($p < 0.05$) with $R^2 \geq 0.09$ were considered. Odds ratios were calculated for binary independent variables (Table 3).

TG levels were significantly associated with both the disease activity measures (SLEDAI and ECLAM) and with fibrinogen, albumin, C3 and C4 levels (the latter 3 were negative associations), serositis (pleuritis, pericarditis), nephritis, and non-malar rash. The only statistically significant associations for cholesterol were with WBC and headache. LDL-C levels were associated with CNS involvement, headache, and myositis, but none of the laboratory or disease activity measures. HDL-C levels were negatively correlated with both disease activity measures and with ESR, nephritis, nasal ulcers, and CNS involvement, and positively associated with albumin, C3, C4, hemoglobin, and WBC. The LDL-C:HDL-C ratio was associated positively with both disease activity scores, ESR, nephritis, and nasal ulcers, and negatively with albumin, hemoglobin and C3, C4 levels, and CNS involvement (Table 3).

Multiple regression analysis of serum lipid levels. Statistically significant ($p < 0.05$, $r > 0.3$) variables were entered into multiple regression analysis (Table 4). Only models with $R^2 \geq 30\%$ were considered. Stepwise multiple regression revealed albumin, C4, and WBC as the significant predictors of HDL-C (model $R^2 = 0.6$). TG were best predicted by fibrinogen, nephritis, and pleuritis (model $R^2 = 0.6$). ESR, CNS involvement, nasal ulcers, and nephritis were found to be significant predictors for LDL-C:HDL-C (model $R^2 = 0.5$). None of the variables we investigated were found to be significant predictors of CHOL or LDL-C.

Multiple logistic regression analysis of combined abnormality

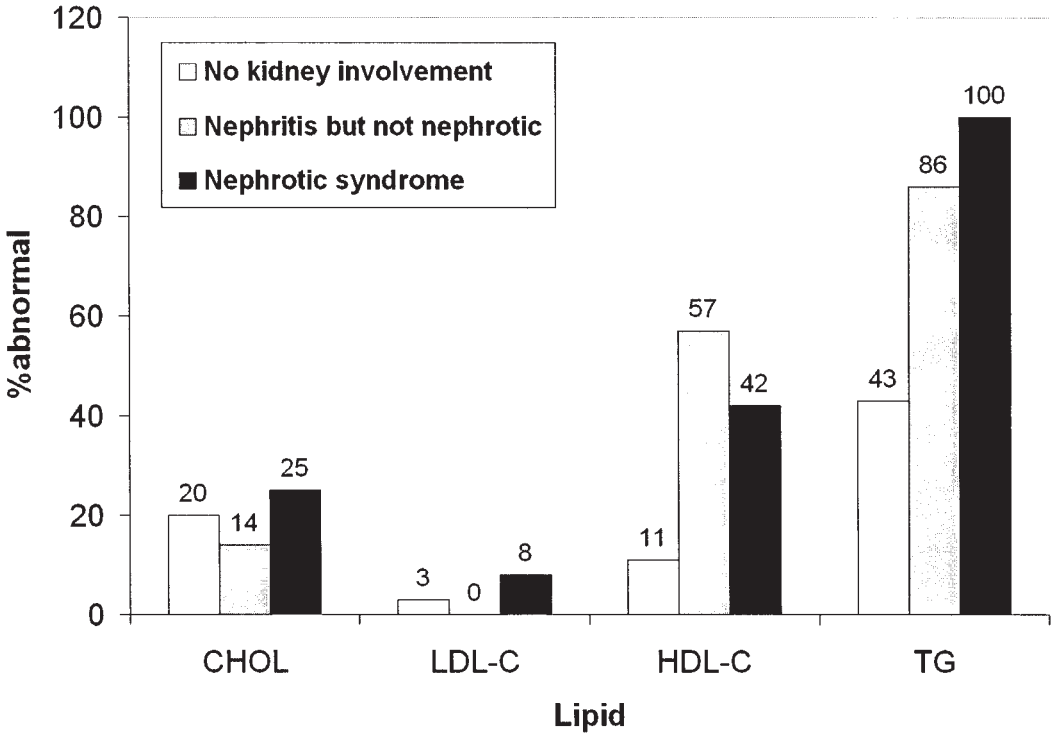

Figure 1. Abnormal serum lipid measurements (%) for patients with no kidney involvement, nephritis but not nephrotic, and nephrotic syndrome; y-axis is the percentage of patients with an abnormal lipid value adjusted for age and sex. Actual percentages are listed above the respective bars.

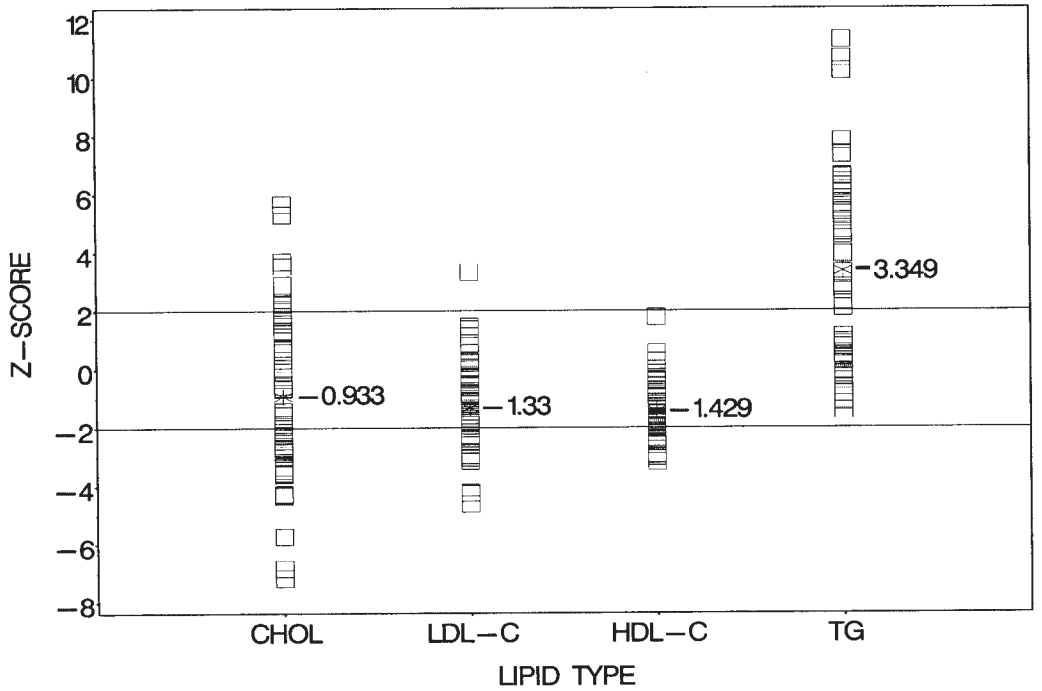

Figure 2. Z-score values for serum lipid measurements; y-axis shows z-score with standard deviations as units. Mean z-score values are labeled with the numeric value. Horizontal lines represent ± 2 standard deviations from z-score of 0.

Table 3. Univariate analysis of variance of serum lipid levels at diagnosis with inflammation measures and disease symptoms.

Lipid	Symptom	R^2 (OR)	p (95% CI)	n
Cholesterol	WBC	0.12	0.0096	53
	Headache	(6.1)	(1.2–31.2)	53
LDL-C	Myositis*	(0.03)	(0.001–0.9)	53
	Headache	(5.3)	(1.1–26.2)	53
	CNS*	(0.2)	(0.03–0.9)	53
HDL-C	Albumin	0.42	< 0.0001	53
	ECLAM*	0.41	< 0.0001	51
	C3	0.36	< 0.0001	51
	Kidney involvement	(0.001)	(< 0.001–0.05)	53
	SLEDAI*	0.30	< 0.0001	51
	C4	0.27	< 0.0001	51
	ESR*	0.27	0.0001	51
	Hemoglobin	0.26	0.0001	53
	WBC	0.16	0.0028	53
	Nasal ulcers*	(< 0.001)	(< 0.001–0.3)	53
	Other rash*	(0.1)	(0.02–0.9)	53
	aPL*	(0.1)	(0.02–0.7)	53
Triglyceride	Albumin*	0.35	< 0.0001	53
	Kidney involvement	(9.8)	(2.8–35.0)	53
	SLEDAI	0.29	< 0.0001	51
	ECLAM	0.27	< 0.0001	51
	Fibrinogen	0.14	0.0319	32
	C3*	0.14	0.0071	51
	Other rash	(3.2)	(1.3–7.6)	53
	Pleuritis	(22.2)	(1.1–468.7)	53
	C4*	0.13	0.0095	51
	Anti-DNA	(2.5)	(1.1–5.8)	53
LDL-C:HDL-C	Kidney involvement	(13.6)	(2.8–65.2)	53
	Nasal ulcers	(276.4)	(2.9– >999.9)	53
	Albumin*	0.23	0.0003	53
	C4*	0.23	0.0004	51
	C3*	0.23	0.0004	51
	ECLAM	0.22	0.0005	51
	ESR	0.22	0.0005	51
	HGB*	0.17	0.0023	53
	SLEDAI	0.12	0.0119	51
	CNS*	(0.09)	(0.008–1.0)	53
	Anti-DNA	(4.0)	(1.2–13.6)	53
	aPL	(4.0)	(1.2–13.6)	53

* Negative association.

Table 4. Multiple regression analyses.

Lipid	Variable	Regression Coefficient	p	R^2
HDL-C	Albumin	0.027	< 0.0001	0.577
	C4	1.139	0.0187	
	WBC	0.029	0.0127	
Triglyceride	Fibinogen	0.308	0.0129	0.629
	Kidney involvement	0.879	0.0002	
	Pleuritis	1.392	0.0010	
LDL-C:HDL-C	CNS	–0.420	0.0197	0.499
	ESR	0.004	0.0231	
	Nasal ulcers	0.633	0.0088	
	Kidney involvement	0.292	0.0498	

of increased TG and decreased HDL-C. Variables statistically significantly associated with the active lupus lipid profile[11] of (also the most common combined lipid abnormality) were entered into stepwise logistic regression analysis. The ECLAM disease activity score was found to be the best statistically significant predictor, with an odds ratio of 1.7 (95% CI 1.2–2.3), while the SLEDAI had an odds ratio of 1.1 (95% CI 1.0–1.2). None of the other variables remained in the model.

Association of organ disease with abnormal TG and HDL-C levels. When we examined the association of active nephritis and abnormal lipid levels we found that 86% (6/7) of patients with nephritis but not nephrotic syndrome, and 100% (12/12) of patients with nephrotic syndrome also had abnormal TG levels, while only 42% (4/7) of patients with nephritis but not nephrotic syndrome and 47% (5/12) of patients with nephrotic syndrome had abnormally low HDL-C levels. Abnormal levels of both TG and HDL-C were found in 57% (5/7) of those with nephritis but not nephrotic syndrome and in 42% (5/12) of patients with nephrotic syndrome. To determine the association of CNS involvement and abnormal TG and HDL levels, we eliminated the 3 patients who had both CNS and kidney involvement, which left only 4 patients with CNS involvement without kidney disease. Only 25% of these patients had abnormal TG levels and none had abnormally low HDL-C levels.

To further explore the role of nephritis and proteinuria in determining abnormal TG levels we categorized patients with kidney involvement, i.e., those with nephrotic syndrome, nephritis but not nephrotic syndrome, and no kidney involvement. Measures of proteinuria as total grams of protein per 24-hour urine collection were obtained for 26 patients (median 0.31 g, range 0.04–7.4 g). Those patients that were not tested were assumed to have values < 0.02 g/24 h, as there was no indication of nephritis. Post-hoc ANOVA analysis indicated that low serum albumin levels were associated with kidney involvement ($R^2 = 0.55$, $p < 0.0001$), TG levels ($R^2 = 0.35$, $p < 0.0001$), and disease activity measured by SLEDAI ($R^2 = 0.52$, $p < 0.0001$). After adjustment for serum albumin levels using ANCOVA, there was still a statistically significant association of a high TG level and the presence of kidney disease ($p = 0.0119$). We found that the mean TG level was significantly higher in patients with nephrotic syndrome as compared to "nephritis but not nephrotic" and no kidney involvement; however, there was no significant difference between "nephritis but not nephrotic" and no kidney involvement. The adjusted mean (least-square mean) TG levels were significantly higher in nephrotic syndrome (2.24 mmol/l) compared to nephritis but not nephrotic syndrome (1.63 mmol/l) and no kidney involvement (1.40 mmol/l). In comparison we did not find any association of HDL with kidney involvement, categorized into having nephrotic syndrome, nephritis but not nephrotic, or no kidney involvement, using the same methodology.

DISCUSSION

SLE is an autoimmune disease characterized by chronic

inflammation and frequently requires treatment with prolonged courses of high-dose corticosteroids. Both these factors have been associated with development of an abnormal lipid profile and premature atherosclerosis. This association has been confirmed by studies in SLE showing that both cardiovascular and cerebral vascular events are significantly more common in young adults with SLE than the general population[2,3]. Although multiple studies have demonstrated that patients with SLE have abnormal lipid profiles, it has been difficult to differentiate the precise role of the inflammation and of the therapy on patients' lipid profiles[13]. The best way to determine the maximal role of inflammation on lipid profiles in SLE is to study lipid levels at diagnosis of SLE prior to therapy. Our study is a continuation of work by Sarkissian, *et al*[13], and 9 of our 54 patients were included in both studies. In our current study, we found that in a large inception cohort of patients with pSLE, the majority had at least one lipid abnormality. An elevated TG level was the most common lipid abnormality seen in the majority of patients (61%), while a high LDL-C level was the least common (seen in only 4%). All patients with nephritis and/or nephrotic syndrome were found to have abnormally high TG levels, which were associated with abnormally low HDL-C levels in about 50%. Post-hoc analysis suggested TG levels were highest in patients with active kidney disease, even after adjustment for the potential confounding effects of albumin. These findings suggest that there may be another process contributing to an elevated TG level intrinsic to SLE nephritis, other than the effects of a reduced albumin level that is typical of nephrotic syndrome (which itself has been associated with elevated triglyceride levels[15,23,24]). A previous pediatric study demonstrated that elevated TG and depressed HDL-C levels were associated with kidney disease, although they did not attempt to differentiate the effect of nephrotic syndrome from the potential confounding effect of nephrotic-range proteinuria[15]. In contrast, we found no association of HDL-C levels and kidney disease, suggesting that the process(es) driving low albumin levels may also be responsible for decreased HDL-C levels. Further, although only 4 patients had only CNS without kidney involvement, the majority of these patients (75%) did not have abnormal TG or HDL-C levels despite having active major organ involvement and high disease activity scores. This observation suggests that disease activities resulting from kidney or CNS involvement may differ in their effects on serum lipids.

The "active lupus pattern" of elevated TG and decreased HDL-C was initially described in pediatric patients in 1988, and later in adult patients[8,11]. The main limitations to the previous studies were the relatively small number of patients and the fact that not all patients were seen at presentation, and serum lipid measurements were not made exclusively before treatment. In our cohort of 54 patients, 24% had the combination of abnormal TG and HDL-C levels. This lipid profile was the result of active SLE, and in particular active nephritis, as it was seen prior to initiation of prednisone therapy and at presentation, which is generally associated with significantly active disease, as seen in our patients who had a median SLEDAI score of 9.5. These findings expand previous results in adults that also suggested that lipid profile abnormalities in lupus are aggravated by disease activity[8]. Previous studies have also suggested that dyslipoproteinemia of active SLE may be secondary to the effects of tumor necrosis factor-α and/or autoantibodies[14,25]. Further, disease activity (by ECLAM or SLEDAI) was found to best predict "lupus dyslipoproteinemia." The active lupus pattern of dyslipoproteinemia is not restricted to patients with SLE, as it is also seen in other instances associated with acute inflammation, including sarcoidosis and macrophage activation syndrome[26,27]. We suggest that the best way to alleviate these lipid abnormalities and decrease the risk of cardiovascular disease is by good control of the patient's SLE.

As may be expected in the absence of corticosteroid therapy, measures of inflammation were found to be related to most lipid levels. Elevated inflammatory markers including fibrinogen, CRP, ESR, and albumin levels have been shown to be predictors for risk of cardiovascular disease[28,29]. Interestingly, global measures of disease activity did not correlate with all lipids, and the best predictors for lipid levels were frequently measures of organ-specific disease. It therefore appears that in the absence of corticosteroid therapy, an abnormal lipid profile was likely secondary to active SLE with major organ involvement. This was supported by the association of LDL-C:HDL-C ratio with markers of both kidney and neuropsychiatric diseases. Both the LDL-C and total cholesterol levels were most often either normal or depressed but not increased in these patients. This also contributed to a LDL-C:HDL-C ratio in the normal range, a finding that is generally associated with a low risk of coronary artery disease[30]. However, because elevated TG levels, a risk factor for cardiovascular disease (as reviewed[31]), were found in the majority of patients (62%), early recognition of this lipid abnormality may be important in decreasing the risk of cardiovascular disease.

We acknowledge the limitations imposed by the relatively small sample size of our study. The possible effects of diet and physical activity on our lipid prediction models were not considered in this study. Although there were some missing data for some of the laboratory measurements, which contributed to a larger standard error, we are confident that our results reflect the true relationship that exists between the "active lupus pattern" and clinical and laboratory measures.

Children with newly diagnosed SLE exhibited the distinct pattern of dyslipoproteinemia of increased TG and depressed HDL-C that was twice as common with the presence of kidney disease. This lipid profile puts them at risk for premature atherosclerosis. We suggest that disease control will correct these lipid abnormalities and that the individual patient's observed pattern of lipid levels should be determined to correctly select a lipid-lowering strategy. It is likely that good dis-

ease control is the optimum way to prevent premature atherosclerosis in pediatric SLE.

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