Elevated serum cholesterol levels are associated with proteinuria over 0.5 g/day in premenopausal women with systemic lupus erythematosus

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Abstract
Background: Systemic lupus erythematosus (SLE) commonly occurs in premenopausal women and is associated with elevated estrogen levels. Patients with SLE may have abnormal serum triglyceride (TG) levels, and lipid reportedly promotes kidney damage in patients with nephrosis. Since estrogen regulates lipid levels, we investigated the serum lipid levels of premenopausal women with SLE and their relationship with proteinuria. **Methods:** This cross-sectional study included 123 premenopausal women with SLE (SLE group), who were classified into 24-h urine protein exceeding 0.5 g (24 h-UPRO > 0.5 g, $n = 22$) and 24 h-UPRO ≤ 0.5 g ($n = 101$) subgroups, and 100 similarly aged healthy women (control group). Clinical characteristics and biomarker levels were compared between these groups. The associated factors of proteinuria over 0.5 g/day were evaluated using multivariate logistic regression. A receiver operating characteristic (ROC) curve was plotted to assess the cholesterol (CH) cut-off associated with increased development of proteinuria over 0.5 g/day. **Results:** The SLE group had significantly higher serum TG levels than that of control group. 24 h-UPRO were significantly correlated with serum creatinine, CH, TG, and uric acid levels. Serum CH level was the greatest associated factor for proteinuria over 0.5 g/day. The area under the ROC curve was 0.843, with a CH cut-off of 4.58 mmol/L. Patients with serum CH above 4.58 mmol/L had a higher proportion of type IV LN, but with no statistical difference. **Conclusions:** In premenopausal SLE patients, serum TG levels were higher than in healthy women, and serum CH levels were the primary associated factor for proteinuria over 0.5 g/day. Proteinura over 0.5 g/day may occur in women with SLE with serum CH levels >4.58 mmol/L. CH levels may be useful for predicting proteinuria.

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Introduction

Systemic lupus erythematosus (SLE), which commonly occurs in premenopausal women, is often associated with elevated estrogen levels.[1] The kidney is one of the most commonly affected organs in SLE. Lupus nephritis (LN) occasionally manifests as nephrotic syndrome and is associated with severe proteinuria, hypoproteinemia, and hyperlipidemia.[2]

Estrogen hyperfunction is a major pathogenesis of systemic lupus erythematosus. Estrogen exerts its effects by activating intracellular receptors, including estrogen receptors (ER) α and β.[3]

In animal models of lupus, it is found that ERα is closely related to the onset and disease activity of SLE, while ERβ helps to alleviate inflammation and disease.[4] Anti-estrogen receptor (anti-ER) α and β antibodies are present in patients with SLE, and anti-ERα may alter estrogen function by acting as an estrogen agonist.[5] High serum levels of anti-ERα have been detected in patients with SLE, and this might contribute to disease activity in patients with SLE,[5] which may worsen renal damage.

Estrogen is involved in uric acid (UA) and lipid metabolism.[6] It was once unclear whether premenopausal women with SLE maintain low serum UA levels under the estrogen hyperfunction background. Our previous study found that their serum UA not only did not maintain low levels, but instead serum UA rose significantly.[7] On the other hand, abnormal UA metabolism often causes dyslipidemia,[8] in contrast, estrogen helps to maintain normal lipid levels.[6] Then, what are the serum lipid levels in premenopausal women with SLE? This topic has not been adequately studied yet. One study reported that patients with SLE often have dyslipidemia. It was found that abnormal serum lipid levels, particularly high triglyceride (TG) levels and low high-density lipoprotein levels, commonly occur in patients with SLE.[9] Additionally, dyslipidemia has been reported to be more severe in patients with LN than in those without LN.[10] However, no previous study has focused on premenopausal patients with SLE.

The role of serum lipids in chronic kidney disease is widely recognized. Nephrotic syndrome mostly results in hepatic lipase deficiency contributing to hypertriglyceridemia, accumulation of atherogenic intermediate density lipoprote, and TG enrichment of low-density lipoprote (LDL). Nephrotic syndrome also results in marked raises in serum cholesterol (CH) and LDL, which are both due to the increased production and deficient catabolism clearance of LDL3 and apolipoprotein B (APOB)-100.[11] These abnormal lipid metabolisms not only promote the progression of atherosclerosis and cardiovascular disease, but also lead to glomerulosclerosis and promote further kidney damage by deposition of lipids in the kidneys and uptake of these abnormal lipoproteins by glomerular mesangial cells.[11] However, there are few reports on the relationship between lipids and proteinuria in SLE patients.

We conducted this study to investigate the serum lipid levels of premenopausal women with SLE and their relationships with proteinuria. We evaluated the proteinuria and their influencing factors as 24-h urine protein (24 h-UPRO) >0.5 g is one of the main clinical scores of the kidney used in the diagnostic classification criteria of SLE.[12]

Participants and methods

Participants

Between August 1, 2020 and December 31, 2020, we enrolled 123 premenopausal women with SLE (SLE group) who received regular follow-up at PanYu Central Hospital, and 100 similarly aged healthy women (control group). All patients with SLE fulfilled the requirements of the 1997 revised criteria of the American College of Rheumatology,[13] and the inclusion criteria were female sex and premenopausal status.[14] Women who were pregnant, had severe renal injury or were undergoing hemodialysis, whose serum UA levels had not been measured, or who had diabetes mellitus, who use medications such as statin, NSAIDs or other nephrotoxic drugs, or severe infection were excluded. This study was approved by the Ethics Committee of the PanYu Central Hospital (2019–92), and written consent was obtained from all participants.

Measurement of serum lipid, estrogen, and estrogen receptors antibodies levels

Before blood sample collection, participants followed their regular low fat diet. Fasting blood samples were centrifuged at 4°C to obtain serum samples using established techniques. Serum TG, total CH, high-density lipoprotein (HDL), and low-density lipoprotein (LDL) levels were measured with a chemiluminescent method using a

Beckman Synchron LX20 Chemistry Analyzer (Beckman Coulter Inc., Beckman Coulter Diagnostics, Brea, CA).

Blood collection from all participants was performed two to 5 days after their menstruation ceased. Estrogen was measured via enzyme-linked immunosorbent assay (ELISA) according to the manufacturer's instructions (Sigma, St. Louis, mo.). ER antibodies were measured with ELISA using a previously described technique.[15] Briefly, standards or tested serum samples were added to the appropriate wells (50 μL per well) precoated with antihuman ERα or ERβ monoclonal antibody. Enzymeconjugate were added to standard wells and sample wells (100 μL per well). Plates were sealed and incubated at 37°C for 60 min. After washing the plates, stop solution was add to each well (50 μL per well). The optical density (O.D.) was read at a wavelength of 450 nm using a microtiter plate reader within 15 min. Serum concentrations of ERs were determined by extrapolation from the standard curve (standard ODs vs. concentrations). All reagents and standard controls were provided by Shanghai Meilian Biological Technology Co.

Clinical biomarkers

The following clinical biomarkers were measured in patients with SLE: routine peripheral blood analysis, routine urine analysis, 24 h-UPRO quantification, renal index (creatinine, normal range 40–120 μmol/L; cystatin, normal range 0.63–1.25 mg/L), and serum TG (normal range 0.34–1.70 mmol/L), CH (normal range 3.1–5.17 mmol/L), LDL (normal range 2.08–3.12 mmol/L), HDL (normal range 1.00–2.00 mmol/L), UA (normal range 208–360 μmol/L for premenopausal women), C-reactive protein (CRP, normal range 0–6 mg/l), erythrocyte sedimentation rate (normal range 0–20 mm/H), complement C3 (normal range 900–1800 mg/L), complement C4 (normal range 100–300 mg/L), anti-dsDNA (normal range 0–1), estrogen (normal range of follicular phase: 11–165 pg/mL), anti-ERα, and anti-ERβ.

Clinical characteristics

The age, menstrual status, weight, body mass index (BMI), blood pressure, SLE disease activity index (SLEDAI) score (at the time of enrollment), and current treatment regiments (glucocorticoid dosage) of the women with SLE were recorded. The age, weight, BMI, and menstrual status of the women in the control group were also recorded.

Statistical analyses

This is a cross-sectional study. According to a previous study, the proportion of Chinese SLE patients with elevated cholesterol is about 55%, with an expected error value of 1/5.[16] According to the sample size formula of the cross-sectional study, the needed sample size of this study was calculated to be 71 patients with SLE. Statistical analysis was performed using SPSS version 19.0 for Windows (IBM Corp., Armonk, NY). Data are presented as frequencies and percentages for categorical variables and as mean and standard deviation for continuous variables, unless otherwise stated. Two independent samples t-Test or the Mann–Whitney U test was used for comparison between two independent groups according to distributions. The chi-square test was used to compare categorical variables. A Pearson correlation was used to analyze the relationship between 24 h-UPRO and clinical biomarkers. Associated factors for proteinuria over 0.5 g/day were evaluated using multivariate logistic regression. A receiver operating characteristic (ROC) curve was constructed to analyze the predictive value of serum CH level for proteinuria over 0.5 g/day. All significance tests were two-tailed and were conducted at the 5% significance level.

Results

The SLE group was divided into 24 h-UPRO > 0.5 g ($n = 22$, 24-h UPRO >0.5 g) and 24 h-UPRO ≤ 0.5 g ($n = 101$) subgroups according to the 24 h-UPRO levels. The mean age ($p = 0.087$) and BMI ($p = 0.095$) were comparable between the SLE and control groups (Table 1) and between the SLE subgroups ($p = 0.814, 0.738$, Table 2). The mean disease course was comparable between the two SLE subgroups ($p = 0.778$, Table 2). Although the proportion of hypertension in the 24 h-UPRO > 0.5 g subgroup was higher than that in the 24 h-UPRO ≤ 0.5 g subgroup, there was no significant difference ($p = 0.057$, Table 2). Serum TG levels were significantly higher in the SLE group than in the control group ($p < 0.001$), but the CH levels were comparable between these groups ($p = 0.062$, Table 1). Among patients with SLE, only eight had a 24 h-UPRO exceeding 3.5 g. Most of patients with SLE were mild to moderately activity according to SLEDAI scores. 78.05% of the patients were below 15 (62 of 123 were below 10, 34 were between 10 and 14, 27 were above 14). LN was diagnosed in 56 (45.53%) of these 123 SLE patients, of which 22 had the renal pathology reports.

Of the 123 patients with SLE, 43 (34.96%) had hyperuricemia. Patients with hyperuricemia had significantly higher mean serum CH levels (5.57 ± 2.44 mmol/L) than those with normal UA levels (3.98 ± 1.30 mmol/L; $p < 0.001$).

SLEDAI, serum UA, creatinine, positive urinary blood rate, and CH, TG, LDL, and HDL levels were significantly higher in the 24 h-UPRO >0.5 g subgroup than in the 24 h-UPRO ≤ 0.5 g subgroup of patients with SLE ($p < 0.05$; Table 2). Complement c3 of the 24 h-UPRO > 0.5 g subgroup was significantly lower than that of the 24 h-UPRO ≤ 0.5 g subgroup ($p < 0.05$, Table 2). Estrogen and

Table 1. Comparison of clinical characteristics between the SLE and control groups.

	SLE group (*n* = 123)	Control group (*n* = 100)	*p*-value
Age (years)	28.92 ± 7.38	30.58 ± 6.90	t = −1.722, *p* = 0.087
BMI	20.50 ± 1.15	20.95 ± 2.42	t = −1.680, *p* = 0.095
UA level (μmol/L)	340.17 ± 155.98	303.25 ± 66.32	t = 2.413, *p* = 0.017
CRE level (μmol/L)	71.16 ± 31.10	76.30 ± 10.42	t = −1.721, *p* = 0.087
CH level (mmol/L)	4.54 ± 1.93	4.91 ± 0.88	t = −1.875, *p* = 0.062
TG level (mmol/L)	1.67 ± 1.10	1.02 ± 0.0.49	t = 5.898, *p*<0.001
LDL level (mmol/L)	2.82 ± 1.32	3.16 ± 0.89	t = −2.184, *p* = 0.030
HDL level (mmol/L)	1.69 ± 0.98	1.57 ± 0.37	t = −0.258, *p* = 0.796
C3 level (mg/L)	687.22 ± 343.12		
C4 level (mg/L)	120.46 ± 91.01		
ESR (mm/H)	40.63 ± 36.31		
CRP level (mg/L)	7.56 ± 15.79		
SLEDAI score	10.39 ± 6.29		
Anti-dsDNA level	2.26 ± 1.02		
24h UPRO (g/24 h)	0.72 ± 2.21		

Abbreviations: SLE, systemic lupus erythematosus; BMI, body mass index; UA, uric acid; CRE, creatinine; CH, cholesterol; TG, triglyceride; LDL, low-density lipoprotein; HDL, high-density lipoprotein; C3, complement c3; C4, complement c4; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; SLEDAI, Systemic lupus erythematosus disease activity index; anti-DNA, anti-double stranded DNA; 24h UPRO, 24-h urine protein.

Table 2. Clinical characteristics of premenopausal women with SLE.

		24 h-UPRO >0.5 g group (*n* = 22)	24 h-UPRO ≤ 0.5 g group (*n* = 101)	*p*-value
Age (years)		28.18 ± 7.38	29.07 ± 9.40	0.814
BMI		20.67 ± 1.28	20.49 ± 1.13	0.738
Hypertension (%)		4 (18.18)	6 (5.94)	0.057
Disease course (months)		18.50 ± 21.05	19.55 ± 19.64	0.778
SLEDAI score		16.76 ± 5.43	9.08 ± 5.64	<0.001
UA level (μmol/L)		510.19 ± 181.87	306.15 ± 123.44	<0.001
CRE level (μmol/L)		108.38 ± 43.48	63.50 ± 21.14	<0.001
Cystatin level (mg/L)		2.80 ± 4.05	1.95 ± 7.84	0.628
CRP level (mg/L)		8.83 ± 14.02	7.29 ± 14.18	0.687
ESR (mm/H)		41.95 ± 28.83	40.36 ± 37.78	0.856
C3 level (mg/L)		477.62 ± 254.65	747.90 ± 328.71	0.001
C4 level (mg/L)		85.81 ± 64.20	127.60 ± 94.27	0.055
Anti-dsDNA level		2.32 ± 1.20	2.24 ± 0.98	0.776
CH level (mmol/L)		6.72 ± 2.62	4.09 ± 1.40	<0.001
TG level (mmol/L)		2.64 ± 1.71	4.09 ± 1.40	0.006
LDL level (mmol/L)		4.34 ± 1.71	2.51 ± 0.97	<0.001
HDL level (mmol/L)		1.23 ± 0.50	1.00 ± 0.34	0.010
Estrogen level (pg/mL)		69.14 ± 50.10	70.69 ± 54.46	0.905
Anti-ERα level (ng/mL)		58.59 ± 30.25	55.80 ± 32.35	0.717
Anti-ERβ level (ng/mL)		92.32 ± 45.46	72.79 ± 43.30	0.064
24h UPRO (g/24 h)		3.98 ± 4.04	0.05 ± 0.10	<0.001
Positive UBLD (%)		18 (81.82)	35 (34.65)	<0.001
Glucocorticoid dosage (%)	≤ 10 mg/d	8 (36.36)	42 (41.58)	0.379
	11–30 mg/d	1 (4.55)	11 (10.89)	
	> 30 mg/d	13 (59.09)	48 (47.52)	

Abbreviations: 24h UPRO, 24-h urine protein; SLE, systemic lupus erythematosus; CH, cholesterol; BMI, body mass index; SLEDAI, Systemic lupus erythematosus disease activity index; UA, uric acid; CRE, creatinine; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; C3, complement c3; C4, complement c4; Anti-dsDNA, anti-double stranded DNA; CH, cholesterol; TG, triglycerides; LDL, low-density lipoprotein; HDL, high-density lipoprotein; ER, estrogen receptor; UBLD, urinary blood.

estrogen receptor antibodies were comparable between the two subgroups (p = 0.905, 0.717, 0.064, Table 2). The proportions of patients using low-dose glucocorticoid (prednisone ≤ 10 mg/d), medium-dose glucocorticoid (11–30 mg/d), and high-dose glucocorticoid (>30 mg/d) were similar in the two SLE subgroups (p = 0.379, Table 2).

Pearson correlation analysis showed that 24h UPRO was significantly positively correlated with serum creatine (r = 0.447, p < 0.001), CH (r = 0.458, p < 0.001), UA level (r = 0.287, p < 0.001), TG level (r = 0.255, p = 0.04), LDL

Figure 1. Results of the multivariate logistic regression analysis of associated factors of proteinuria over 0.5 g/day (dependent variable). Independent variables included age, disease course, SLEDAI score, anti-dsDNA, complement C3, uric acid, triglycerides, cholesterol, estrogen, anti-ERα, anti-ERβ levels, hypertension, and glucocorticoid dosage.

level (r = 0.975, p < 0.001), and SLEDAI (r = 0.401, p < 0.001).

Logistic regression analysis with adjustment for potential confounders such as age, disease course, blood pressure, glucocorticoid dosage, anti-dsDNA, SLEDAI score, and complement C3, UA, CH, TG, estrogen, anti-ERα, and anti-ERβ levels revealed that CH level was an associated factor for proteinuria over 0.5 g/day (odds ratio: 2.00, 95% confidence interval: 1.31–3.06; Figure 1).

The area under the ROC curve predicting proteinuria over 0.5 g/day based on CH level was 0.843. The cut-off derived from the ROC curve was 4.58 mmol/L (sensitivity: 86.4%, specificity: 69.3%; Figure 2).

Twenty-two patients with renal pathology reports were divided into the high CH group (>4.58 mmol/l) or normal CH group according to the blood CH levels, and the differences in the proportion of each pathological type between the two groups were compared. The results showed that the proportion of type IV LN in the high CH group was higher than that in the normal CH group, but the difference was not statistically significant (Table 3).
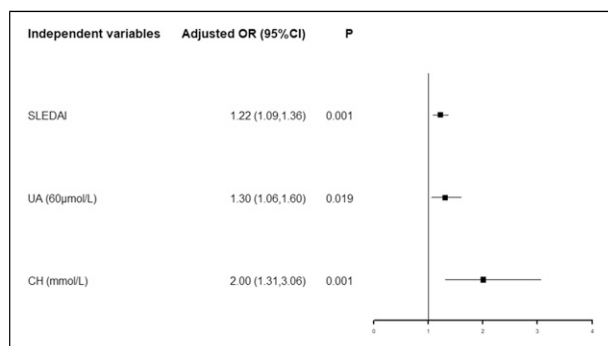
Discussion

We have great interest in the blood lipid levels of premenopausal women with SLE with a high estrogen background. We found that the serum TG levels of these SLE patients were higher than those of healthy premenopausal women and the serum CH levels had significant
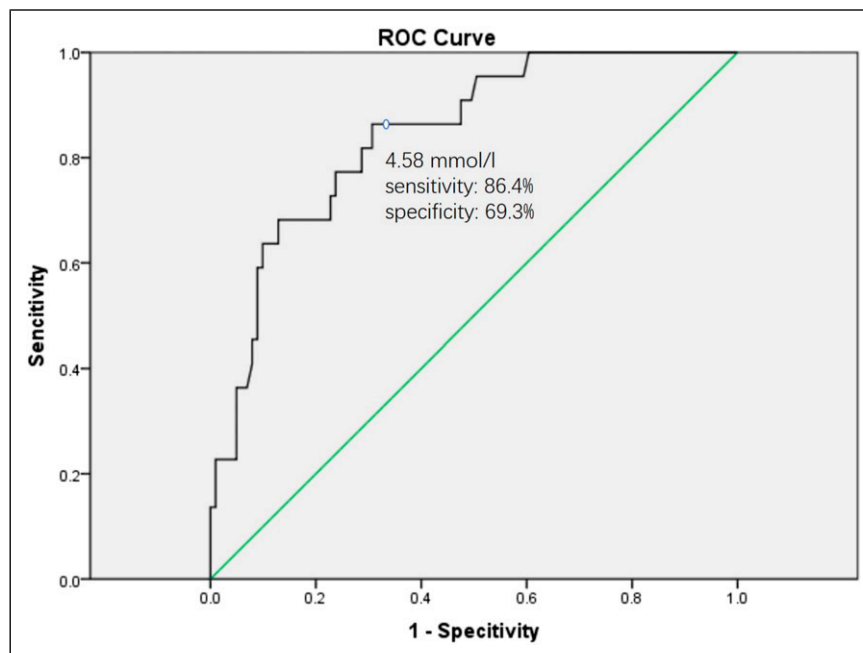

Figure 2. Receiver operating characteristic curve of cholesterol level for predicting proteinuria over 0.5 g/day.

Table 3. Differences in pathological type of LN with different cholesterol levels.

	Pathological type of LN (%)					
	II	III	IV	IV+V	V	p-value
Normal cholesterol group (n = 9)	1 (11.11)	2 (22.22)	1 (11.11)	2 (22.22)	3 (33.33)	0.862
High cholesterol group (n = 13)	0	1 (7.69)	6 (46.15)	2 (15.38)	4 (30.76)	

High cholesterol was defined as blood cholesterol over 4.58 mmol/l, LN: lupus nephritis.

correlations with proteinuria. The ROC curve indicated that a serum CH level exceeding 4.58 mmol/L can predict proteinuria over 0.5 g/day.

Here, although the mean serum CH level of premenopausal women with SLE was not significantly higher than that of healthy women, the serum TG level was. These results are similar to those of other studies,[17–19] which showed that dyslipidemia can occur in patients with chronic kidney disease as well as SLE and that the most common lipid abnormality is an elevated TG level. Moreover, elevated blood lipid levels may indicate disease activity in patients with SLE.[20] Patients with SLE may have elevated TG level because of antibodies to lipoprotein lipase.[21]

On the other hand, in our study, the serum CH levels of patients with hyperuricemia were significantly higher than those of patients with normal UA levels. Moreover, the TG levels in the SLE group were significantly higher than those in the healthy group. Estrogen and anti-ER antibodies levels were comparable between the two SLE subgroups, and they were not the associated factors for proteinuria over 0.5 g/day. These results indicate that UA may be involved in CH metabolism, with high UA levels leading to elevated CH levels, and that urine protein levels may be not affected by estrogen levels or anti-ERs. This may be because most premenopausal women with SLE with elevated UA levels have renal injury leading to elevating blood lipids or because hyperuricemia can affect the metabolism of lipids.[8] Therefore, our study showed that the blood lipid levels of premenopausal women with SLE are high despite the presence of high estrogen background.

Further analysis of the factors influencing proteinuria in premenopausal women with SLE suggested that serum creatinine, UA, CH, TG, and LDL levels were significantly positively correlated with 24 h-UPRO. Furthermore, logistic regression analysis revealed that CH level was the greatest associated factor for proteinuria over 0.5 g/day. The area under the ROC curve for predicting proteinuria over 0.5 g/day based on CH level was 0.843, and the ideal cut-off was 4.58 mmol/L (sensitivity: 86.4%, specificity: 69.3%). Among the 22 cases with renal pathology reports, the proportion of type IV LN in patients with CH over the cut-off point (4.58 mmol/l) was higher than that in patients

with CH levels lower than that point, but it was not statistically significant probably because of the small sample size. Consequently, the serum CH levels of premenopausal women with SLE may be useful for predicting proteinuria over 0.5 g/day. Further research is needed on the protective effect of lipid-lowering drugs on renal function in patients with SLE with CH levels > 4.58 mmol/L. Although other studies have found elevated TG levels in SLE patients or elevated CH and TG levels in renal impairment groups, they did not further explore the relationship between blood lipids and proteinuria.[9,13,20] To our knowledge, this is the first paper to report the relationship between CH and proteinuria in patients with SLE, although it is an old topic in other chronic kidney diseases.

There are several possible reasons for the relationship between elevated serum CH level and proteinuria. The first is that hypercholesterolemia is a manifestation of nephrotic syndrome. Lupus nephritis usually manifests as nephrotic syndrome, which is often accompanied by elevated CH levels. In our study, the mean 24 h-UPRO of patients with SLE was 2.82 ± 3.82 g, and it was less than 3.5 g in most of the patients (only eight patients exceeded that level). This suggested that, in some patients, although 24 h-UPRO quantitation did not fit the diagnostic criteria for nephrotic syndrome, hypercholesterolemia had occurred. The second reason is that elevated CH levels may occur in patients with renal injury that does not fit the diagnostic criteria of nephrotic syndrome and can lead to damage of the glomeruli and renal tubules. Although excessive lipids in the blood do not damage normal glomeruli,[22] renal injury may occur in cases of hyperplasia or inflammation of the glomerular basement membrane.[23] Glomerular damage is mainly caused by lipids containing APOB, such as CH, LDL, and very-low-density lipoprotein.[24] Glomerular damage occurs following the infiltration of APOB into the glomerulus via the apolipoprotein receptor in the glomerular mesangium.[25] In addition, the APOB in CH can be deposited in the glomerulus following its uptake by lipoproteins through the monocyte-macrophage non-receptor-mediated "scavenger" mechanism.[22] APOB-containing lipoproteins accumulate and degenerate in the glomeruli, triggering a series of cytokine-mediated cellular responses such as the release of tumor necrosis factor-alpha (TNF-α)

and interleukin-1 beta (IL-1β).[26] This eventually leads to the release of growth factors and an increase in mesangial matrix synthesis.

Abnormal CH homeostasis in renal tissue is another mechanism of lipid-associated renal injury. Both genetic and non-genetic pathways are involved in defective CH trafficking. Genetic disorders leading to abnormalities in proteins such as apolipoprotein E, apolipoprotein M, lecithin-cholesterol acyltransferase, Niemann-Pick C1, Niemann-Pick C2, and ATP-binding cassette transporter (ABC)-A1 can cause CH accumulation in glomerular or tubular cells, leading to renal injury.[27] Additionally, increased or decreased expression of certain non-genetic factors in renal tissue may lead to CH accumulation. For example, in animal experiments,[28,29] chronic renal failure was induced by 5/6 nephrectomy in rats, and de novo lipid accumulation with abnormal expression of certain factors was observed in the remaining renal tissue; the expression of liver X receptor (LXR), ABC-A1, ABC-G1, CH acyl-transferase, scavenger receptor (SR)-B1, SR-A1, LDL receptor protein (LDLR), carbohydrate-responsive element-binding protein, fatty acid synthase, and acetyl-CoA carboxylase increased, whereas the expression of sterol regulatory element-binding protein (SREBP)-1, SREBP-2, 3-hydroxy-3-methylglutaryl-CoA reductase, peroxisome proliferator-activated receptor alpha (PPAR-α), fatty acid-binding protein, and carnitine palmitoyl-transferase 1A decreased. Changes in these factors may be related to CH accumulation in renal tissue. As for the mechanism of CH leading to renal injury, renal tissue inflammation and chronic hypoxia induced by hypoxia-inducible factors are the major mechanisms underlying tubulointerstitial injury and renal fibrosis.[30] On the other hand, in hepatocytes, TNF-α- or IL-1β-mediated inflammatory stress significantly reduces intracellular CH efflux by inhibiting PPAR, LXR, and ABC-A1 expression and increasing LDLR and SREBP-2 expression, suggesting that inflammatory stress may exacerbate non-alcoholic fatty liver disease.[31] Studies have shown that TNF-α and IL-1β are expressed in mesangial cells and regulate CH-mediated LDLR activity.[22] In other words, inflammatory cytokines may also contribute to lipid-mediated renal injury.

There were some limitations to our study. First, given the research objective, our research participants were limited to premenopausal women with SLE. Therefore, the relationship between CH levels and renal injury in other groups of patients with SLE remains to be investigated. Second, due to the cross-sectional nature of the study, the predictive value of serum CH level for proteinuria is limited. To this end, we have carried out a cohort study to further investigate the predictive value of serum CH level for renal injury. Third, because this was a single-center study, there may be biases in the disease activity and severity of patients with SLE, leading to deviations in the prediction threshold of cholesterol on kidney damage.

Conclusions

In premenopausal women with SLE, serum TG levels were higher than in healthy women, and proteinuria may occur in patients with serum CH levels >4.58 mmol/L. This suggests that CH is closely associated with proteinuria over 0.5 g/day, and maintaining a low CH level with lipid-lowering therapy may be beneficial for the treatment LN with CH level over 5.17 mmol/l. Further prospective studies are needed to determine whether SLE patients with CH levels between 4.58 and 5.17 mmol/l can benefit from lipid-lowering therapy.

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