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ORIGINAL ARTICLE

Role of low-density lipoprotein receptor rs5925 (1959C>T) gene polymorphism in pathogenesis of dyslipidemia among Egyptian lupus nephritis patients

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ABSTRACT

Objectives: This study aims to investigate the prevalence of low-density lipoprotein receptor (LDL-R) rs5925 genetic variants and to evaluate their relationship with plasma lipid and kidney functions in lupus nephritis patients.

Patients and methods: Between September 2020 and June 2021, a total of 100 lupus nephritis patients (8 males, 92 females; mean age: 31.1±1.1 years; range, 20 to 67 years) and a total of 100 age- and sex-matched healthy volunteers (10 males, 90 females; mean age: 35.8±2.8 years; range, 21 to 65 years) were included. The gene polymorphism rs5925 (LDLR) was performed by polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP). Lipid profile and kidney functions were measured.

Results: Regarding rs5925 (LDLR), C allele was significantly higher among lupus nephritis patients (60%) compared to the control group (45%). While T allele was significantly lower in lupus nephritis patients (40%), compared to the control group (p=0.003). The plasma level of total cholesterol (TC), triglycerides (TG), and low-density lipoprotein cholesterol (LDL-C) were significantly lower in lupus nephritis patients with TT and CT genotypes, compared to those with CC genotype. Moreover, atherogenic index of plasma (AIP) and LDL-C/high-density lipoprotein cholesterol (HDL-C) ratio were significantly lower in patients with TT genotype, compared to the patients with CC genotype. There was a strong and clear association between patients with renal biopsies grades III & IV & V and LDLR C allele (p=0.01, p=0.003, and p=0.004, respectively).

Conclusion: C allele is the significantly prevailed LDLR C1959T variant among lupus nephritis patients. Moreover, LDL-R genetic variant may be one of the non-immunological mechanisms implicated in the disturbed lipid profile among lupus nephritis patients. Profound dyslipidemia may partly underscore the deterioration of kidney function among lupus nephritis patients.

Keywords: Dyslipidemia, gene polymorphism, low-density lipoprotein cholesterol, lupus, nephritis.

Systemic lupus erythematosus (SLE) is an autoimmune inflammatory disease where accelerated atherosclerosis and its consequences are reported as one of the major causes of morbidity and mortality.[1,2] A growing number of evidence suggests that the underlying mechanism may be influenced by the interaction of several factors, including traditional cardiovascular disease (CVD) risk factors, lupus-related factors and medications.[3] However, the precise mechanisms for the development of CVD still remain unclear.

Particularly, dyslipidemia is a major global public health problem, as it is highly prevailed and essential contributor to CVD.[4] Nephrotic syndrome patients have a higher risk to develop cerebrovascular and CVDs. Furthermore,

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risk factors that promote atherogenesis also contribute to impairment in renal function, producing a vicious cycle of renal and vascular complications.[5,6] Although disturbed lipids are a major risk factor for CVD, particularly with renal impairment and are routinely measured for CVD risk stratification, the association between dyslipidemia and lupus nephritis patients remains elusive.

Low-density lipoprotein receptor (LDLR) has an essential function in the lipoprotein metabolism, since low-density lipoprotein cholesterol (LDL-C) is cleared from circulation through LDLR endocytosis.[7] The LDLR gene is located on chromosome 19 and has 18 exons and 17 intervening introns. The LDLR gene mutations are the main genetic cause of familial hypercholesterolemia. Most of the mutations occur in the ligand-binding or epidermal growth factor precursor-like domains.[8,9] Early detection of these mutations minimizes the threat of dyslipidemia and its CVD consequences via usage of suitable therapeutic methods.

The LDLR rs5925 (1959C>T) is present in exon 13, which involves substitution of C for T in the third base of codon Val653Val genetic variant. The LDLR rs5925 has been shown to be linked with increased total cholesterol (TC), triglycerides (TG), and LDL-C in previous studies.[10,11] On the other hand, is associated with lower levels of LDL-C in other studies.[9,10] All these discrepancies may be due to the prevalence of the mutant allele in different ethnicities and its varying impact on the incidence of dyslipidemia.[12,13] However, the precise role of this gene polymorphism in development of dyslipidemia in lupus nephritis patients remains to be elucidated. Therefore, in the present study, we aimed to investigate the prevalence of LDLR rs5925 gene polymorphism among lupus nephritis patients and to evaluate the effect of these genetic variants on plasma lipid phenotypes, kidney functions, and disease activity.

PATIENTS AND METHODS

This single-center, case control study was conducted at Rheumatology Immunology Clinics, Internal Medicine, Faculty of Medicine, Cairo University between September 2020 and June 2021. A total of 100 lupus nephritis patients (8 males, 92 females; mean age: 31.1±1.1 years; range, 20 to 67 years) who were diagnosed according to the criteria of the American College of Rheumatology (ACR) criteria[14] and a total of 100 age- and sex-matched healthy volunteers (10 males, 90 females; mean age: 35.8±2.8 years; range, 21 to 65 years) were included. Data of the liver function tests and complete blood count were all extracted from patient's records. Exclusion criteria were pregnancy, current or recent infection, vasculitis, non-smokers and thyroid gland disorders, and having any lipid-lowering agents or oral contraceptive pills within the previous three months.

Fasting blood samples were withdrawn on ethylenediaminetetraacetic acid (EDTA) sterile tubes under aseptic conditions and divided in two portions. In the first portion, the blood was centrifuged immediately at 4,000×g for 20 min using benchtop centrifuge (Jenway, UK). The separated plasma was kept at -80°C for biochemical analysis. In the second portion, the whole blood was maintained at -80°C for total genomic deoxyribonucleic acid (DNA) analyses.

Biochemical measurements

Total cholesterol was calculated enzymatically using the Stanbio™ kit (Stanbio Laboratory, TX, USA).[15] High-density lipoprotein cholesterol (HDL-C) was quantified by the HDL-C precipitation method.[16] The TG was assessed enzymatically.[17] The LDL-C levels were determined using the Friedewald formula, if TG did not exceed 400 mg/dL.[18] Atherogenic index of plasma (AIP) was evaluated using the following formula: log (TG/HDL-C).[19] Urea and creatinine measurements were measured colorimetrically using biodiagnostic kits.

DNA genotyping

The DNA was extracted from whole blood using DNA extraction kits (Qiagen GmbH Hilden, Germany) using the spin column method. Genotyping for LDLR rs5925 gene polymorphism was performed by polymerase chain reaction (PCR) amplification using the Qiagen Taq PCR Master Mix. The PCR amplification reaction was performed with 25 µL Taq PCR Master Mix; 2.5 µL forward primer (10 µM), 2.5 µL reverse primer (10 µM), 1 µL template DNA

(100 ng/µL), and 19 µL RNase free water. The tubes were caped and centrifuged briefly and, then, incubated in T gradient thermal cycler (Biometra GmbH, Göttingen, Germany). The thermal cycler was adjusted as follows: first denaturing cycle at 94°C for 3 min, followed by 35 cycles of amplification defined by denaturation at 94°C for 1 min, annealing at 59°C for 45 sec and extension at 72°C for 1 min. The resulting PCR amplification products were digested using 5 U of the AvaII restriction enzyme (Invitrogen, CA, USA) and, then, visualized using 3% agarose gel electrophoresis.

Statistical analysis

Statistical analysis was performed using the SPSS version 17.0 (SPSS Inc., Chicago, IL, USA) and GraphPad Prism (GraphPad

Table 1. Demographic characteristics and biochemical parameters of patient and control groups

	Lupus nephritis patients (n=100)			Control subjects (n=100)			
Variables	n	%	Mean±SE	n	%	Mean±SE	*p*
Age (year)			31.1±1.1			35.8±2.8	0.21
Sex							0.6
Male	8	8		10	10		
Female	92	92		90	90		
Weight (kg)			66.4±1.7			70.7±2.3	0.26
Height (cm)			161.8±0.9			165.5±1.3	0.08
Duration of disease (year)			4.7±0.0			-	-
C3 (mg/dL)			60.8±5.6			-	-
C4 (mg/dL)			17.1±1.9			-	-
SLEDAI			32±1.2			-	-
SLICC			3.7±0.2			-	-
ANA							
Positive	100	100				-	-
Ds-DNA							
Positive	100	100				-	-
Hb (g/dL)			9.9±0.3			12.1±0.1	<0.0001
Platelet count (10^9/L)			309.8±77.3			289±76.5	0.7
WBCs (10^9/L)			5.7±0.3			8.6±0.1	<0.0001
ALT (IU/L)			27.3±3.2			25.5±0.5	0.0002
AST (IU/L)			26.6±3.1			24.7±0.8	<0.0001
Albumin (g/dL)			3.1±0.0			5.1±0.1	<0.0001
Creatinine (mg/dL)			1.4±0.1			0.8±0.02	<0.0001
Urea (mg/dL)			80.6±7.6			25.6±5.4	<0.0001
Urine A/C ratio (mg/mmol)			3.8±0.3			2.9±0.1	0.019
Sodium (mmol/L)			144.4±1.4			135.4±2.2	0.001
Potassium (mmoL/L)			3.5±0.1			3.5±0.04	1
TC (mg/dL)			205.7±4.6			165.3±2.3	<0.0001
TG (mg/dL)			167.8±3.4			127.4±2.7	<0.0001
LDL-C (mg/dL)			117.3±4.9			79.3±2.5	<0.0001
HDL-C (mg/dL)			52.6±1.1			61.2±0.75	<0.0001
AIP			0.5±0.0			0.2±0.0	<0.0001
LDL-C/HDL-C			2.5±0.0			0.5±0.1	<0.0001

SE: Standard error; C3: Complement 3; C4: Complement 4; SLEDAI: Systemic lupus erythematosus activity index; SLICC: Systemic Lupus International Collaborating Clinics; ANA: Antinuclear antibody; Ds-DNA: Double stranded deoxyribonucleic acid; Hb: Hemoglobin; WBCs: White blood cells; ALT: Alanine transaminase; AST: Aspartate transaminase; TC: Total cholesterol; TG: Triglycerides; LDL-C: Low-density lipoprotein cholesterol; HDL-C: High density lipoprotein cholesterol; AIP: Atherogenic index of plasma; P value <0.05 is significant.

Software, CA, USA). Normal distribution of data was checked using the Kolmogorov-Smirnov test. Descriptive data were expressed in mean ± standard error (SE) or number and frequency. Comparison between the groups was done using the unpaired Student t-test and one-way analysis of variance (ANOVA), followed by the Tukey's honestly significant difference (HSD) post-hoc test for multiple group comparisons. Comparison between the categorical data was performed using the chi-square test (χ^2) and odd ratios (ORs) with 95% confidence interval (CI). A *p* value of <0.05 was considered statistically significant.

RESULTS

Demographic characteristics and laboratory measurements of the patients and the controls are shown in Table 1. In lupus nephritis patients, plasma level of creatinine and urea and the value of urinary albumin/creatinine ratio were significantly higher compared to the controls, indicating an impairment in renal functions of these patients. Regarding lipid profile, plasma level of TC, TG, and LDL-C levels were significantly higher (p<0.0001), while HDL-C was significantly lower in lupus nephritis patients than normal individuals (p<0.0001). Additionally, AIP and LDL-C/HDL-C values were higher among lupus nephritis patients (p<0.0001).

The distribution of LDLR C1959T genotypes and alleles in the studied groups is shown in Table 2. The frequency of the CC genotype was significantly higher in lupus nephritis patients. However, CT and TT genotype were significantly lower in lupus nephritis patients (44% and 18%, respectively) compared to the control group (47% and 31%, respectively) (p=0.03 and p=0.005, respectively). Moreover, C allele was significantly higher among lupus nephritis patients (60%) compared to the control group (45%). The T allele was significantly lower in lupus nephritis patients (40%) compared to the controls (55%) (p=0.003).

The different biochemical values of the lupus nephritis patients were categorized according to the different LDL-R C1959T genotypes: CC, CT and TT (Table 3). Comparing C4, Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) and systemic Lupus Erythematosus International Collaborating Clinics (SLICC), they were significantly lower in lupus nephritis patients with TT genotype compared to the CC and CT genotypes. In addition, C3 was significantly lower in TT genotype compared to the CC genotype, but did not show any significant difference with CT genotype.

Regarding the lipid profile, the plasma level of TC, TG, and LDL-C were significantly lower in lupus nephritis patients with TT and CT genotypes compared to those with CC genotype. In the same disturbed direction, the AIP and LDL-C/HDL-C ratio were significantly lower in patients with TT genotype compared to the patients with CC genotype. The mean plasma level of HDL-C did not show any significant differences among the three genotypes.

Concerning kidney function tests, both creatinine and urinary A/C ratio were significantly lower in lupus nephritis patients with TT genotype

Table 2. Genotype and allele frequency distribution of LDLR C1959T genotypes and alleles in patient and control groups

	Lupus nephritis patients (n=100)		Control subjects (n=100)			
LDLR C1959T	n	%	n	%	χ^2 (df)	*p*
CC	38	38	21	22		
CT	44	44	49	47	4.24 (1)[a]	0.03[a]
TT	18	18	30	31	7.68 (1)[b]	0.005[b]
C allele	120	60	91	45		
T allele	80	40	109	55	8.43 (1)	0.003[c]

Comparison was done using Chi square test (χ^2). a: CC versus CT; b: CC versus TT; c: C allele versus T allele; P value <0.05 is significant.

Table 3. Demographic characteristics and biochemical parameters of different LDLR C1959T genotypes among lupus nephritis patients

	LDLR C1959T Genotypes among lupus nephritis patients		
	CC (n=38)	CT (n=44)	TT (n=18)
Variables	Mean±SE	Mean±SE	Mean±SE
Age (year)	33.1±1.3	31.7±1.1	32.9±1.8
Weight (kg)	73.6±2.4	67.2±1.8	69.7±3.2
Duration of disease (year)	5.2±.3	4.1±0.26	4.2±0.3
C3 (mg/dL)	70.4±6.8	64.3±5.9	43.6±4.9[a]
C4 (mg/dL)	24.2±2.3	19.2±2.1	10.3±1.9[ab]
SLEDAI	34.9±1.3	33.1±1.4	27.2±1.2[ab]
SLICC	5.1±0.3	4.1±0.3[a]	2.9±0.3[ab]
TC (mg/dL)	221.7±7.4	200.1±46.6[a]	166.5±9.3[a]
TG (mg/dL)	183.5±4.8	161.5±4.4[a]	147.1±5.2[a]
LDL-C (mg/dL)	137.2±8.5	110.9±6.4[a]	94.8±9.8[a]
HDL-C (mg/dL)	55.3±1.9	50.5±1.8	49.5±2.4
AIP	0.6±0.0	0.53±0.02	0.5±0.0[a]
LDL-C/HDL-C	2.8±0.3	2.7±0.2	1.8±0.3[ab]
Creatinine (mg/dL)	1.6±0.2	1.7±0.2	1.0±0.1[ab]
Urea (mg/dL)	87.9±10.4	92.1±9.1	84.5±11.4
Urine A/C ratio (mg/mmol)	3.7±0.5	3.2±0.5	1.7±0.3[a]

SE: Standard error; C3: Complement 3; C4: Complement 4; SLEDAI: Systemic lupus erythematosus activity index; SLICC: Systemic Lupus International Collaborating Clinics; TC: Total cholesterol; TG Triglycerides; LDL-C: Low-density lipoprotein; HDL-C: High density lipoprotein cholesterol; AIP: Atherogenic index of plasma; a: Is significant difference from CC at p<0.05; b: Is significant difference from CT at p<0.05; Comparison was done using ANOVA followed by Tukey's HSD post-hoc test.

Table 4. The frequency of patients with hypercholesterolemia, hypertriglyceridemia, and elevated LDL-C among lupus nephritis patients with different LDLR C1959T genotypes

	CC (n=38)		CT (n=44)		TT (n=18)			
Genotypes	n	%	n	%	n	%	χ^2 (df)	*p*
TC ≤200 mg	14	37	27	61	12	67	**4.9[a]**	**0.02[a]**
TC >200 mg	24	63	17	39	6	33	**4.3[b]** 0.15 c	**0.03[b]** 0.6 c
TG ≤150 mg	10	26	26	59	13	72	**8.8[a]**	**0.002[a]**
TG >150 mg	28	74	18	41	5	28	**10.6[b]** 0.9 c	**0.001[b]** 0.3 c
LDL-C ≤100 mg	10	26	22	50	13	72	**4.8[a]**	**0.02[a]**
LDL-C >100 mg	28	74	22	50	5	28	**10.6[b]** 2.5c	**0.001[b]** 0.1c
HDL-C ≥40 mg	32	84	31	70	13	72	2.1[a]	0.1[a]
HDL-C <40 mg	6	16	13	30	5	28	0.007[b] 1.1[c]	0.9[b] 0.2[c]

a: Between CC & CT; b: Between CC & TT; c Between CT & TT. LDL-C: Low-density lipoprotein; TC: Total cholesterol; TG: Triglycerides; Comparison was done using Chi square test (χ^2); P value <0.05 is significant.

Table 5. Association between renal biopsy grades and LDLR C1959T different genotypes

	CC (n=38)		CT (n=44)		TT (n=18)		CC-CT/TT	
Renal biopsy grades	n	%	n	%	n	%	OR (95% CI)	*p*
I+II	1	3	1	2	5	28	ref	
III	12	31	16	37	7	39	10 (1.59-62.7)	0.01
IV	16	42	19	43	5	28	17.5 (2.6-115.6)	0.003
V	9	24	8	18	1	5	42.5 (3.1-571.8)	0.004

OR: Odd ratio; CI: Confidence interval; P value <0.05 is significant.

compared to the CC genotype, while no significant difference was seen in urea among the three genotypes.

The frequency of patients with hypercholesterolemia (TC >200 mg/dL) was higher in patients with CC genotype reaching 63% compared to the CT and TT genotype (39% and 33%, respectively) (p=0.02 and p=0.03, respectively). The frequency of patients with hypertriglyceridemia (TG >150 mg/dL) was higher in patients with CC genotype reaching 74% compared to CT and TT genotype (41% and 28%, respectively) (p=0.002 and p=0.001, respectively). The frequency of patients with elevated LDL-C >100 mg/dL was higher in patients with CC genotype reaching 74% compared to the CT and TT genotype (50% and 28%, respectively) (p=0.02 and p=0.001, respectively). On the other hand, the frequency of patients with decreased HDL-C <40 mg/dL was not significantly different among the three genotypes as shown in Table 4.

Furthermore, ORs were calculated to estimate the interaction between different grades of renal biopsy and LDLR C1959T different genotypes. The results showed a strong and clear association between patients with Grades III & IV & V and LDLR C allele. Thus, the patients carrying C allele were 10 times more likely to develop renal lesion Class III with 95% CI: 1.59-62.7 (p=0.01) and 17.5 times more likely to develop renal lesion Class IV with 95% CI: 2.6-115.6 (p=0.003). Finally, the patients carrying C allele were 42.5 times more likely to develop renal lesion Class V with 95% CI: 3.1-571.8 (p=0.004) as shown in Table 5.

DISCUSSION

The patients with SLE, particularly those with nephritis, have an increased risk of atherosclerosis and CVD compared to the healthy individuals. Dyslipidemia, which is the key player in atherosclerosis, is common in patients with SLE.[20] It has a multifactorial origin, that is why elucidating which factors contribute to this lipid disorder is complex. To the best of our knowledge, this is the first study to highlight the prevalence of LDL-R rs5925 genetic variants and their relationship with plasma lipids and kidney functions among lupus nephritis patients. The rationale for selection of this gene polymorphism is based on its highly variable prevalence in different populations and in different pathological conditions.

The current study revealed that frequency of the CC genotype was significantly higher in lupus nephritis patients. In addition, CT and TT genotypes were significantly lower in lupus nephritis patients compared to the control group. Moreover, C allele was significantly higher among lupus nephritis patients (60%) compared to the controls (45%). Also, T allele was significantly lower in lupus nephritis patients (40%) compared to the controls (55%). The current study is the first citation of this gene polymorphism among lupus nephritis patients; however, previous studies reported its prevalence in normal subjects and other pathological conditions. Rojas *et al.*[13] reported that the frequency of T allele was higher than C allele reaching 55% among healthy individuals. Similarly, Ríos-González *et al.*[21] reported that the prevalence of the T allele in normal subjects and hypertensive patients were 53.1% and 54.7%, respectively. On the other

hand, Long et al.[10] reported that the occurrence of T allele was 34.5% and 19.3% in two different ethnic groups. Moreover, previous studies showed the high incidence of T allele in myocardial infarction,[22] gallstone patients,[23] but it was lower in patients with cerebral infarction.[24] These results indicate that the racial/ethnic factor may have a critical role in the distribution of the C and T allele variants of LDL-R rs5925 gene polymorphism.

The relatively high prevalence of these two alleles encourages us to examine the impact of the LDL-R C1959T genetic variation on the lipid profile. In the current study, the plasma level of TC, TG, and LDL-C were significantly lower in lupus nephritis patients with TT and CT genotypes compared to those with CC genotype. Moreover, AIP and LDL-C/HDL-C ratio were significantly lower in patients with TT genotype compared to the patients with CC genotype. On the other hand, Ahn et al.[20] reported that the T allele was significantly associated with both TC and LDL-C differences, while the heterozygotes having cholesterol levels in-between the two types of homozygous variants, but all of these effects were sex-specific and confined to women.

Likewise, the present study revealed that the number of patients with hypercholesterolemia, hypertriglyceridemia, and elevated LDL-C >100 mg/dL were higher in patients with CC genotype compared to the CT and TT genotype. These data suggest the hypothesis that the C allele may have deleterious effect on lipid profile among lupus nephritis patients. These results are consistent with other studies which reported that individuals carrying LDLR mutated allele (T) have lower values of TC, TG, and LDL-C compared to CC homozygous genotype.[9,13] These findings may give more explanation of the disturbed lipid profile among lupus nephritis patients, particularly those carrying C allele. It is worthy noticed that this common genetic variation in the LDLR is involved in determining the inter-individual fluctuations in cholesterol levels together with other genetic variations at other genetic loci and other factors such as race, sex, diet, and lifestyle.

In the current study, the mean plasma level of HDL-C did not show any significant differences among the three genotypes, consistent with previous literature which reports that mutations that abolish the expression of the LDLR have relatively little impact on HDL-C.[17] Similarly, the frequency of patients with decreased HDL-C <40 mg/dL was not significantly different among the three genotypes.

Dyslipidemia is a feature of SLE patients with progressive renal injury and nephrotic syndrome.[25] Focusing on of LDL-R genetic variants predisposing dyslipidemia and kidney functions, our study reports that creatinine was significantly lower in lupus nephritis patients with TT genotype compared to CC genotype, while no significant difference was seen urea level among the three genotypes. These data give additional evidence that lupus nephritis patients carrying C allele may be at a higher risk in developing nephritis. Thus, these observations support the concept that the prevalence of the C allele and its modulatory role on lipid particles may provoke the disturbed kidney functions. Several authors have shown the association between dyslipidemia and lupus nephritis, where hyperlipidemia enhances the renal immune complex-mediated complement activation and leads to development of nephritis. Furthermore, the present study is in accordance with Sajjad et al.[2] who reported that SLE patients with renal diseases had elevated levels of TC, TG, and LDL-C. Additionally, the study showed that urinary A/C ratio was significantly lower in lupus nephritis patients with TT genotype compared to the CC genotype, in agreement with previous studies which reported that proteinuria was an independent risk factor for progressive renal injury in lupus nephritis and there was a strong relationship between cholesterol concentrations and proteinuria.[26]

More importantly, the current study showed a strong and clear association between patients with Grades II & IV & V and LDL-R C allele. These data reflecting that the C allele may have a critical role in the progression of nephritis. Accordingly, we can hypothesize that dyslipidemia may be the link between LDL-R C allele and development of nephritis among SLE patients. Similarly, the present study demonstrated that C allele had critical repercussions on flares and complications of SLE, where the SLEDAI and SLICC scores were highly elevated in CC genotype compared to the TT genotype. These results may be accounted for the ongoing dyslipidemia and the prevalence of nephritis among SLE patients carrying C allele.

Nonetheless, the present study has some limitations such as other genetic mutations in the LDLR gene either pathological or non-pathological should be investigated to assess the interaction of them along with other factors related to family history, dietary pattern, and physical activity. Moreover, we need to shed more light into the role of this gene polymorphism in other pathological diseases and other populations with different ethnicities.

In conclusion, it is well known that dyslipidemia is a multifactorial trait caused by several environmental and genetic factors and their interactions. Thus, variations in plasma lipid levels may be attributed to different dietary patterns, lifestyle factors, as well as genetic background. Our study results support that C allele is the significantly prevailed LDLR C1959T variant among lupus nephritis patients. Moreover, LDL-R genetic variant may be one of the non-immunological mechanisms associated with the disturbed lipid profile among lupus nephritis patients. Profound dyslipidemia may relatively underscore the deterioration of kidney function among lupus nephritis patients. Although the role of LDLR as a genetic risk factor has not been confirmed yet, it may mediate its effect via interaction with other genetic mutations in the LDLR gene. Therefore, the current findings indicate a new genetic risk factor for dyslipidemia and preventive strategies may be introduced early and before situations predisposing to atherogenicity have progressed.

Ethics Committee Approval: The study protocol was approved by the Research Ethics Committee for Clinical Studies of Cairo University, Faculty of Medicine (no: MD-196-2020). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each participant.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Study conception, material preparation, writing: Y.A.A.; Study conception and design: S.A.A.; Study conception and design, material preparation: H.E.S.; Data collection and analysis, writing: M.A.A.E.; Data collection and analysis, writing: H.L.E.

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