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ORIGINAL ARTICLE

Serum Homocysteine Levels and Microalbuminuria in Adult Patients with Systemic Lupus Erythematosus

Tamer Mohamed Goda, Adel A.M. Ghorab, Nafesa Mohammed Kamal, Ibrahim Noor Eldeen Ahmed*, Mohamed Gomaa Abdelrahim

Department of Internal Medicine, Faculty of Medicine, Zagazig University

***Correspondingauthor:**

Ibrahim Noor Eldeen Ahmed

Email:
ibrahimbazan93@gmail.com

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ABSTRACT

Background: Currently, there is no clear correlation between serum homocysteine levels in patients with systemic lupus erythematosus (SLE) and microalbuminuria (MAU). Thus, our goals were to measure blood homocysteine levels in patients with SLE, investigate the association between serum homocysteine and microalbuminuria in SLE patients, and evaluate albuminuria as a possible early sign of renal involvement in SLE.

Methods: This cross-sectional study included 48 adult patients with SLE divided equally between 3 groups according to albuminuria, recruited from the Internal Medicine Department, Zagazig University Hospitals and compared to 16 healthy individuals as a control group. Serum Homocysteine was measured in all subjects.

Results: Homocysteine displayed statistically significant higher levels among patients with macroalbuminuria, followed by patients with microalbuminuria, then patients with normo-albuminuria and the control group did not differ statistically significantly. Additionally, compared to patients without renal symptoms, it showed noticeably greater levels in the former group. Serum homocysteine had a 94.5% sensitivity and a 94.4% specificity at a cutoff value of 13.1 nmol/mL for identifying renal impairment in SLE patients.

Conclusion: The frequency of albuminuria in SLE patients is clearly correlated with higher serum homocysteine levels. Serum homocysteine is a good predictor to renal impairment in SLE patients.

Keywords: Homocysteine; Microalbuminuria; Systemic Lupus Erythematosus.

INTRODUCTION

There are many different clinical symptoms of systemic lupus erythematosus, an autoimmune multisystemic illness (SLE) [1]. Systemic lupus erythematosus is one of the most common autoimmune diseases with a unique origin [2].

The mechanisms underlying systemic lupus erythematosus include insufficient T and B cell activation, abnormal self-nucleic antigen presentation, and insufficient removal of apoptotic debris. Environmental and hormonal factors also come into play [3].

Fever, malaise, exhaustion, arthralgia, transitory cognitive impairment, discoid rash, Among the clinical signs of systemic lupus erythematosus are malar rash, photosensitivity, and mouth ulcers [4].

Kidney, neurological, serositis, and arthritis are examples of systemic symptoms. Hematological problems such as anemia, leucopenia, and thrombocytopenia, as well as laboratory criteria such as anti-nuclear antibodies and anti-DNA antibodies. Any four or more of the eleven criteria must be met for a diagnosis. Many diabetic individuals may still experience nephropathy

despite having normal urinary albumin levels,raising concerns about the effectiveness of albuminuria as a precise indicator for nephropathy [5, 6].

After methionine is demethylated, homocysteine, a non-essential amino acid, is produced biochemically. It can either be broken down into cysteine or converted back to methionine. Vitamin B12 is needed as a cofactor and 5-methyltetrahydrofolate as a methyl donor for the methylation reaction that methionine synthase enhances in order to resynthesize methionine [7].

Normal physiological levels of hyperhomocysteinemia (HHCys) range from 5 to 15 μmol/l. Patients with SLE frequently have HHCys, which is thought to be a risk factor for a number of diseases, including atherosclerotic plaque development and atherothrombotic events. Researches indicate that high levels of homocysteine are significantly associated with kidney disease in older adults. These findings imply that homocysteine could serve as an indicator of reduced kidney function in patients with diabetes. Nonetheless, it is still uncertain whether the buildup of homocysteine is a contributing factor leading to initial kidney damage or a mere result of deteriorating kidney function in diabetic individuals. [8].

The primary cause of HHCys in patients is genetic abnormality in the transcription of the enzymes that are involved in homocysteine metabolism. A mix of hereditary and nutritional variables, such as deficiencies in specific cofactors necessary for homocysteine metabolism, such as betaine, vitamin B12, vitamin B6, and folic acid, can cause HHCys [9].

METHODS

48 adult SLE patients were gathered from the Internal Medicine Department of Zagazig University Hospitals between January and June of 2024 for this cross-sectional study. They were split equally into three groups, each with sixteen patients, and contrasted with a control group consisting of 18 healthy individuals who were matched for both sex and age. There were 16 patients in Group I who had normo-albuminuria, 16 in Group II who had microalbuminuria, 16 in Group III who had macroalbuminuria, and 16 in Group IV who had control.

This study started after approval of Zagazig University Hospitals' Faculty of Medicine's "Research Ethics Committee" (IRB number 10757-14/5/2023). Every patient gave their signed, informed consent.

Inclusion criteria:

• Individuals with SLE who are between the ages of 18 and 60

• Males and females

Exclusion criteria:

- Individuals under the age of eighteen
- those with thyroid conditions
- And those suffering from long-term liver disorders
- Individuals with renal affection (acute or chronic renal failure) and diabetes

Demographic and anthropometric information, such as age, sex, and body mass index (BMI), medical history, clinical manifestations, and laboratory tests, such as random blood glucose, kidney function test (KFT), which included blood urea, serum creatinine (SCr), albuminuria, GFR, and albumin creatinine ratio (ACR), liver function test (LFT), This included inflammatory markers like erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP); immunological markers like serum complements (C3 and C4), antinuclear antibody (ANA), and anti-dsDNA; and serum albumin, aspartate aminotransferase (AST), and alanine aminotransferase (ALT).

Assessment of disease activity:

Using the SLEDAI-2K severity score, illness activity was evaluated at the time of study enrollment. A SLEDAI-2K score of less than three denotes mild disease, a number between three and six denotes moderate disease, and any score greater than six denotes severe disease.

The SLEDAI-2K evaluation has been verified as a categorical scale and evaluates illness severity on a continuous scale. [10].

Assessment of damage index of the disease:

TheSystemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI) was used to calculate the disease's damage index. gastrointestinal (0–6), musculoskeletal (0–7), skin (0–3), neurological (0–6), pulmonary (0–5), cardiovascular (0–6), peripheral vascular (0–5), ocular (range 0–2), endocrine (diabetes) (0–1), and neuropsychiatric (0–6) (0–1), and cancers (0–2) were the 12 organ systems for which damage was characterized. In theory, damage can only remain constant or rise over time to a maximum of 47 points, where 0 denotes no damage and > 1 denotes damage [11].

Assessment of serum homocysteine:

The enzyme-linked immunosorbent test (ELISA) was used to measure the serum homocysteine levels of each participant. utilizing the human homocysteine ELISA kit (Catalogue No: 201-12-8014), SunRed, Shanghai, China, in compliance with the guidelines and materials provided by the manufacturer.

Statistical analysis:

The 2013 release of IBM SPSS Corp. was used to analyze the data that was input into the computer. Version 22.0 of IBM SPSS Statistics for Windows. NY: IBM Corp., Armonk. One-way ANOVA, the Kruskal Wallis test, the chi-squared test, the independent student t test, linear regression analysis, Spearman's rank-order correlation, Pearson correlation coefficient, and Receiver Operating Characteristic (ROC) curve analysis were all employed.

RESULTS

Table 1 demonstrates that the age and sex differences between the groups under study were not statistically significant. However, compared to patients with normo-albuminuria and the control group, patients with microalbuminuria and macroalbuminuria had significantly higher BMIs, making the difference statistically significant.

Table 2 demonstrates that there were statistically significant differences between the groups under study in terms of GFR, albuminuria, and ACR. GFR was much higher in individuals with normo-albuminuria than in those with microalbuminuria and macroalbuminuria, although it was significantly lower than in the control group. All groups did, however, vary statistically significantly in terms of albuminuria and ACR. In contrast to the control group and patients with normo-albuminuria, patients with microalbuminuria and macroalbuminuria had considerably lower serum albumin levels.

Table 3 demonstrates that patients with macroalbuminuria had considerably higher ESR and CRP than the other groups. Patients with microalbuminuria and macroalbuminuria had significantly lower C3 values than the control group, suggesting a statistically significant difference between the study groups in terms of C3, C4, ANA, and anti-dsDNA. Patients with macroalbuminuria, microalbuminuria, and normo-albuminuria had considerably lower C4 values. In contrast to patients with normo-albuminuria in the control group, patients with microalbuminuria and macroalbuminuria had considerably greater levels of ANA and anti-ds DNA.

Table 4 demonstrates that there was a statistically significant difference in homocysteine levels between the groups under study. Patients with macroalbuminuria had the highest significant levels, followed by those with microalbuminuria and those with normo-albuminuria. The normoalbuminuric group and the control group did not vary statistically significantly.

Table 5 and Figure 1 demonstrate that serum homocysteine had a 94.5% sensitivity and a 94.4% specificity at a cutoff point of 13.1 nmol/mL to identify renal impairment in patients with SLE.

Table 6 shows that SLEDAI-2K was considerably higher in patients with macroalbuminuria, followed by

microalbuminuria,and then normo-albuminuria, but there was no statistically significant difference between those with macroalbuminuria and microalbuminuria. The SDI did not, however, differ significantly across the groups that were the subject of the investigation.

Table 7 demonstrates the strong positive association between homocysteine and anti-ds DNA, age, ACR, ESR, CRP, C3, C4, ANA. Nonetheless, there was a noteworthy inverse relationship between homocysteine and GFR. Table 1 supplementary shows that among these parameters, age, SLE duration, SCr ACR and C4 were significant predictors of serum homocysteine.

Table 1: Demographic and anthropometric data among the studied groups

Demographic and anthropometric data		Cases			Group IV (n = 16)	Test of sig. P-value
		Group I (n = 16)	Group II (n =16)	Group III (n = 16)		
Age (years) Min.–Max		19 – 51	18 – 57	20 – 55	22 – 57	F =1.28 P = 0.28
Mean ± SD		34.41 ± 8.68	32.45 ± 7.79	34.39 ± 8.63	38.75 ± 10.04	
Median		47.0	47.5	48.5	44.0	
Sex N (%)	Male	1 (6.3%)	1 (6.3%)	1 (6.3%)	2 (12.5%)	$\chi 2$=0.81 P=0.85
	Female	15 (93.7%)	15 (93.7%)	15 (93.7%)	14 (84.5%)	
BMI (kg/m^2) Min.–Max		19 - 25	21 – 26	22 – 25	21 – 25	F=2.77 P=0.04
Mean ± SD		22.71 ± 1.57	23.7 ± 1.38	23.83 ± 0.93	22.53 ± 1.28	
Median		23	24	23	23	
Sig. bet. Groups		P_1=0.02, P_2 =0.01, P_3 =0.69, P_4=0.76, P_5=0.008, P_6=0.004				

BMI: Body mass index, F: One-Way ANOVA test, SD: Standard deviation, $\chi 2$: Chi square test, p: p-value >0.05: Non-significant; p-value <0.05: Significant; p-value< 0.01: Highly significant, p_1: p value for comparing between Group I and Group II, p_2: p value for comparing between Group I and Group III , p_3: p value for comparing between Group I and Group IV, p_4: p value for comparing between Group 1I and Group III, p_5: p value for comparing between Group II and Group IV, p_6: p value for comparing between Group III and Group IV.

Table 2: Kidney function among the studied groups

		Cases			Group IV (n = 16)
		Group I (n = 16)	Group II (n =16)	Group III (n = 16)	
Kidney function					
Blood urea (mg/dl)	Min.–Max	13.0 – 35.0	15.0 – 38.0	14.0 – 61.0	7.0 – 18.0
	Mean ± SD	24.53 ± 7.30	26.35 ± 6.85	31.71 ± 11.25	11.53 ± 5.85
	Median	26	24.5	33.5	27
F (P-value)		2.61 (0.06)			
Serum creatinine (mg/dl)	Min.–Max	0.48 – 0.88	0.48 – 1.20	0. 48– 1.90	0.47 – 0.91
	Mean ± SD	0.62 ± 0.13	0.79 ± 0.20	0.91 ± 0.35	0.54 ± 0.23

	Median	0.6	0.79	0.82	0.76
F (P-value)		1.08 (0.36)			
GFR (ml/min)	Min-Max	87 – 140	61 – 136	35 – 126	109 –138
	Mean ± SD	105.12 ± 17.3	100.4 ± 22.7	91.67 ± 28.4	116.94 ± 14.8
	Median	122	99	89.5	106
H (P-value)		9.29 (0.026)			
Sig. bet. Groups		P_1=0.03, P_2=0.005, P_3=0.04, P_4=0.35, P_5=0.56, P_6=0.26			
Albuminuria (mg/day)	Min-Max	3-25	33 – 213	315 – 635	3 – 18
	Mean ± SD	17.65 ± 5.68	147.06 ± 60.7	476.7 ± 93.1	7.81 ± 5.9
	Median	18	151.3	459.5	9
H (P-value)		62.94 (0.001)			
Sig. bet. Groups		P_1<0.001, P_2<0.001, P_3=0.002, P_4<0.001, P_5<0.001, P_6<0.001			
ACR (mg/gm)	Min.–Max	4 - 27	38 – 278	374 – 711	5 – 21
	Mean ± SD	18.82 ± 8.85	189.2 ± 94.2	575.6 ± 142.5	16.06 ± 4.9
	Median	19	198.5	581.5	13.2
H (P-value)		63.32 (0.001)			
Sig. bet. Groups		P_1<0.001, P_2 <0.001, P_3 =0.001, P_4<0.001, P_5<0.001, P_6<0.001			
Liver function					
Albumin (gm/dl)	Min.–Max	3.6 – 4.5	2.7 – 3.8	2.2 – 3.4	3.8 – 4.9
	Mean ± SD	4.04 ± 0.25	3.69 ± 0.36	3.1 ± 0.49	4.3 ± 0.26
	Median	4.1	3.7	3	4.3
F (P-value)		22.43 (<0.001)			
Sig. bet. Groups		P_1=0.001, P_2=0.001, P_3=0.14, P_4 =0.47, P_5<0.001, P_6 <0.001			
ALT (IU/L)	Min.–Max	12 – 19	10 – 18	11 – 22	13 – 18
	Mean ± SD	15.24 ± 1.92	14.1 ± 1.96	15.67 ± 2.61	14.88 ± 1.69
	Median	15	14	15.5	14
F (P-value)		1.56 (0.21)			
AST (IU/L)	Min-Max	14 – 22	14 – 20	14 – 24	15 – 23
	Mean ± SD	17.71 ± 2.25	16.68 ± 0.95	18.39 ± 2.5	17.65 ± 2.39
	Median	17	18.8	18	17
F (P-value)		2.24 (0.09)			

ACR: Albumin creatinine ratio, F: One-Way ANOVA test, H: Kruskal Wallis test, GFR: Glomerular filtration rate, ALT: Alanine transaminase, AST: Aspartate transaminase, F: One-way ANOVA, SD: Standard deviation, p: p-value >0.05: Non-significant; p-value <0.05: Significant; p-value< 0.01: Highly significant, p_1: p value for comparing between Group I and Group II, p_2: p value for comparing between Group I and Group III , p_3: p value for comparing between Group I and Group IV, p_4: p value for comparing between Group 1I and Group III, p_5: p value for comparing between Group II and Group IV, p_6: p value for comparing between Group III and Group IV.

Table 3: Inflammatory and immunological markers among the studied groups

		Cases			Group IV (n = 16)
		Group I (n = 16)	Group II (n =16)	Group III (n = 16)	
Inflammatory markers					
ESR (mm/hr)	Min.–Max	5 – 60	8 – 100	5– 90	2 – 6
	Mean ± SD	29.35 ± 7.3	33.80 ± 6.85	36.61 ± 11.25	3.88 ± 1.22
	Median	25	28	29.5	12
H (P-value)		37.29 (<0.001)			
Sig. bet. Groups		P_1=0.73, P_2= 0.71, P_3<0.001, P_4 =0.94, P_5<0.001, P_6 <0.001			
CRP (mg/L)	Min.–Max	2– 23	4– 24	6– 29	2– 5
	Mean ± SD	7.44 ± 4.6	8.33 ± 4.7	8.59 ± 7.07	3.75 ± 0.99
	Median	6.8	7	7	4
H (P-value)		20.25 (<0.001)			
Sig. bet. Groups		P_1=0.52, P_2= 0.83, P_3=0.001, P_4 =0.76, P_5<0.001, P_6 =0.003			
Immunological markers					
Serum C3 (mg/dl)	Min.–Max	80 – 100	70 – 90	40 – 80	90 – 150
	Mean ± SD	103.5 ± 16.56	87 ± 11.29	68.38 ± 20.78	113.47 ± 18.7
	Median	90	88	70	110
F (P-value)		3.25 (0.027)			
Sig. bet. Groups		P_1=0.07, P_2= 0.13, P_3=0.04, P_4 =0.76, P_5=0.001, P_6 =0.04			
Serum C4 (mg/dl)	Min.–Max	17 –28	10 – 25	8 –20	18 – 34
	Mean ± SD	20.88 ± 3.26	16.6 ± 3.42	9.72± 3.42	26.29 ± 5.45
	Median	20	17	9	26
F (P-value)		57.61 (0.001)			
Sig. bet. Groups		P_1=0.04, P_2< 0.001, P_3<0.001, P_4 <0.001, P_5<0.001, P_6 <0.001			
ANA (IU/dL)	Min-Max	100 – 140	100 – 420	100 – 310	100 – 110
	Mean ± SD	100 ± 14.49	233 ± 74	234.4 ± 46.81	100 ± 0.1
	Median	105	230	230	100
H (P-value)		36.44 (0.001)			
Sig. bet. Groups		P_1<0.001, P_2< 0.001, P_3=0.74, P_4 =0.97, P_5<0.001, P_6 <0.001			
Anti-dsDNA (IU/mL)	Min.–Max	8 - 30	15 – 42	19 – 47	2 – 8
	Mean ± SD	16.8 ± 6.8	27.1 ± 7.2	28.7 ± 5.81	4.75 ± 1.29
	Median	20	26	28	10
H (P-value)		40.27 (0.001)			
Sig. bet. Groups		P_1<0.001, P_2 <0.001, P_3 =0.004, P_4=0.43, P_5<0.001, P_6<0.001			

CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, ANA: Antinuclear antibody, Anti-ds DNA: Anti-double stranded DNA, C3: Complement 3, C4: Complement 4, F: One-Way ANOVA test, H: Kruskal Wallis test, SD: Standard deviation, p: p-value >0.05: Non-significant; p-value <0.05: Significant; p-value< 0.01: Highly significant, p_1: p value for comparing between Group I and Group II, p_2: p value for comparing between Group I and Group III , p_3: p value for comparing between Group I and Group IV, p_4: p value for comparing between Group 1I and Group III, p_5: p value for comparing between Group II and Group IV, p_6: p value for comparing between Group III and Group IV.

Table 4: Serum homocysteine level among the studied groups

		Cases			Group IV (n = 16)
		Group I (n = 16)	Group II (n =16)	Group III (n = 16)	
Serum homocysteine (nmol/mL)	Min.–Max	9.2 – 11.5	11.10 – 17.0	13.0 – 17.6	7.7 – 11.2
	Mean ± SD	10.11 ± 0.66	12.80 ± 1.85	14.61 ± 3.25	10.07 ± 0.36
	Median	10.1	11.8	13.6	10.2
F (P value)		92.45 (0.001)			
Sig. bet. Groups		P_1<0.001, P_2 <0.001, P_3 =0.87, P_4< 0.001, P_5<0.001, P_6 <0.001			

SD: Standard deviation, p: p-value >0.05: Non-significant; p-value <0.05: Significant; p-value< 0.01: Highly significant, p_1: p value for comparing between Group I and Group II, p_2: p value for comparing between Group I and Group III, p_3: p value for comparing between Group I and Group IV, p_4: p value for comparing between Group 1I and Group III, p_5: p value for comparing between Group II and Group IV, p_6: p value for comparing between Group III and Group IV.

Table 5: ROC curve of homocysteine as marker of renal involvement in SLE

AUC	P-value	Cut off point	Sensitivity	Specificity	95% CI
0.959	0.0001*	>13.1	94.5%	94.4%	0.912-1.000

AUC: Area under the curve, CI: Confidence interval, ROC: Receiver operator characteristic, SLE: Systemic lupus erythematosus, p: p-value >0.05: Non-significant; p-value <0.05: Significant; p-value< 0.01: Highly significant

Table 6: Evaluation of disease activity and damage indices among the studied groups

		Cases			Test of sig. P. value
		Group I (n = 16)	Group II (n =16)	Group III (n = 16)	
SLEDAI-2K	Min.–Max	2 – 12	4 – 16	2 – 22	H=7.93 P=0.02
	Mean ± SD	5.25 ± 3	7.75 ± 3.71	9.87 ± 5.86	
	Median	4	6	8	
H (P value)		2.36 (0.06)			
Sig. bet. Groups		P_1=0.04, P_2= 0.01, P_3=0.32			
SDI	Min.–Max	0 – 4	0 – 4	0 – 5	H=7.93 P=0.02
	Mean ± SD	0.81 ± 1.28	1.25 ± 1.65	1.19 ± 0.51	
	Median	0	0	0.5	
Damage n (%)		6 (37.5%)	7 (43.8%)	8 (50%)	χ2=0.51 P=0.78

SLEDAI-2K: Systemic lupus erythematosus activity index-2000, SDI: Systemic Lupus International Collaborating Clinics (SLICC)-Damage Index, H: Kruskal Wallis test, SD: Standard deviation, p: p-value >0.05: Non-significant; p-value <0.05: Significant; p-value< 0.01: Highly significant, p_1: p value for comparing between Group I and Group II, p_2: p value for comparing between Group I and Group III, p_3: p value for comparing between Group 1I and Group III.

Table 7: Correlation of serum homocysteine and other parameters

Parameters	Serum homocysteine (nmol/L)	
	r	P-value
Age (years)	0.45	0.001
BMI (kg/m^2)	0.17	0.15
Blood urea (mg/dL)	0.30	0.008
Serum creatinine (mg/dL)	0.35	0.004
GFR (ml/min)	-0.41	0.001
ACR (mg/gm)	0.84	0.001
Albumin (gm/dL)	0.05	0.69
ALT (IU/L)	0.2	0.09
AST (IU/L)	0.19	0.11
ESR	0.44	0.001
CRP (mg/L)	0.24	0.05
C3 (mg/dl)	0.26	0.03
SLEDAI-2K	0.27	0.07

ACR: Albumin creatinine ratio, ALT: Alanine transaminase, ANA: Antinuclear antibody, Anti-ds DNA: Anti-double stranded DNA, AST: Aspartate transaminase, BMI: Body mass index, C3: Complement 3, C4: Complement 4, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, GFR: Glomerular filtration rate, r: Correlation coefficient, SLEDAI-2K: Systemic lupus erythematosus activity index-2000, SDI: Systemic Lupus International Collaborating Clinics (SLICC)-Damage Index, p: p-value >0.05: Non-significant; p-value <0.05: Significant; p-value< 0.01: Highly significant

. DISCUSSION

In individuals with SLE, low serum albumin levels and albuminuria are important diagnostic indicators that have a good predictive value, even when renal histological lesion severity is considered [2]. However, in the mechanisms of autoimmune disorders like SLE, homocysteine can activate the immune system and cause pro-inflammatory molecules to develop [7].

The majority of the patients in the current study are female, and there were no appreciable differences in age or sex across the groups under investigation.

In the study by Gheita et al. [12], the bulk of the 3661 Egyptian patients were female (90.03%), with a female to male ratio of 9.03:1.

It is true that there is a significant female bias in SLE, and there are a number of reasons for this. To start, sex hormones significantly influence a person's vulnerability to SLE. Second, more than 1,000 genes, Numerous genes on the X chromosome encode proteins, such as microRNAs, which are known to either directly or indirectly regulate immunological responses.

Third, the fact that 15% to 23% of X-linked genes in females are still active after incomplete X inactivation raises the potential that overexpression of X-linked genes, such TLR-7, may be associated to females' increased susceptibility to SLE [13].

Despite the fact that every patient in this study had a BMI that was supposedly normal, those with microalbuminuria and macroalbuminuria had considerably higher BMIs than those with normo-albuminuria and the control group.

This was in line with Lee and Song's [14] meta-analysis of 18 studies, which included 1048 controls and 1333 SLE patients. They demonstrated that while SLE patients had greater leptin levels, their BMIs were higher than those of the control group. In addition to activating monocytes, Leptin also encourages the development of T lymphocytes into Th1 phenotype by prompting dendritic cells and macrophages to release proinflammatory cytokines like TNF-α and interleukin-6 (IL-6).

In a review paper, Chagnac and Friedman [15] found a correlation between elevated

albuminuria and BMI, indicating that obesity is a risk factor for moderately elevated albuminuria on its own.

In contrast to patients with normoalbuminuria and the control group, this study showed significantly lower GFR, significantly more albuminuria, and significantly higher ACR in patients with albuminuria, which led to significantly lower blood albumin.

Similarly, 87 SLE patients in the USA were examined by Chedid et al. [21], who discovered considerably reduced GFR and significantly higher proteinuria.

The ESR is only a measurement of the rate at which erythrocytes fall when anticoagulated blood is placed in a vertical tube, whereas CRP is a plasma protein that is present in all humans and is produced by hepatocytes in response to interleukin-6 during inflammation [22].

Both ESR and CRP were significantly higher in the SLE groups in this study, with a median of 29.5 mm/hr and 7 mg/L, respectively. The presence of inflammation, either due to flaring or the onset of infection, was indicated by the significantly greater levels of both markers in patients with macroalbuminuria compared to the other groups.

This was similar to a cross-sectional research by Emorinken et al. [23] that included 52 Nigerian patients with SLE who exhibited elevated ESR with a mean of 105.87 ±18.86 mm/hr.

TNF-α and IL-6 are two examples of inflammatory cytokines that are responsible for this elevated production of inflammatory markers [24].

Additionally, among 160 SLE cases in Sweden, Karlsson et al. [25,26] discovered that, despite elevated IL-6, Compared to lupus flares, CRP levels are frequently higher during infections and stay low or only slightly raised during SLE flares.

C3 and C4 levels were significantly lower in SLE patients (87.5 and 91.7%, respectively) than in the control group, and much lower in albuminuric individuals, illustrating a characteristic presentation of immunological markers among SLE patients. Similarly, ANA and anti-ds DNA levels were substantially greater in SLE patients (62.5% and 66.7%, respectively) than in the control group, which had somewhat higher levels in albuminuric patients.

This was consistent with Qu et al. [27], who found that among 194 Chinese SLE patients and 120 healthy volunteers, immunological abnormalities of SLE were mostly characterized by a substantial increase in ANA and anti-dsDNA levels, but a significant decrease in C3 and C4 levels in blood.

In the current study compared to patients with normo-albuminuria and the control group, patients with albuminuria had the highest significant amounts of homocysteine. In order to detect renal impairment in SLE patients, the ROC curve found an AUC of 0.959, a cutoff point of serum homocysteine equal to 13.1 nmol/mL, with a sensitivity of 94.5% and a specificity of 94.4%.

In 36 publications, comprising 2919 SLE patients and 3120 healthy controls, the homocysteine levels of SLE patients were considerably higher than those of the control group, per Sam et al.'s systematic review and meta-analysis [29].

Additionally, Mohannad et al. [30] evaluated the levels of homocysteine in 60 SLE patients and 30 age-matched controls. They found that the homocysteine levels were considerably higher in SLE patients than in the control group.

Another study by Wei et al. [31] found that 150 Chinese individuals with SLE and albuminuria had significantly higher serum homocysteine levels than those without albuminuria. With cutoff values of 9.0 nmol/mL, the serum homocysteine ROC curve showed an AUC of 0.730, 72.2% sensitivity, and 61.9% specificity.

In human vascular cells and monocytes, homocysteine has the ability to promote the formation of chemokines and chemokine receptors, The increased amounts of homocysteine may be explained by substances such as IL-1β, IL-6, IL-8, IL-12, IL-18, IL-1

receptor antagonist, CRP, adhesion molecules, and metalloproteinases [32].

Furthermore, by promoting endothelial cell apoptosis (which lowers the production of H2S), a potent antioxidant and vasorelaxation factor, and causing oxidative stress (which damages nitric oxide-dependent vasodilatation), these elevated levels of homocysteine among SLE patients may contribute to endothelial dysfunction. By breaking down elastin fibers, increasing the production of collagen by activating metalloproteinases, and promoting the growth of smooth muscle cells, it may also make blood vessels more rigid [33].

The people with macroalbuminuria did not differ statistically significantly from one another and microalbuminuria in this investigation, however SLEDAI-2K was considerably greater among those with albuminuria than among those with normoalbuminuria.

This was parallel to Shamim et al. [34] who examined 23 children with SLE diagnoses in Pakistan and found that those who presented with renal involvement—as indicated by proteinuria, pyuria, and hematuria—had higher average SLEDAI scores.

Age, ACR, ESR, CRP, C3, C4, ANA, and anti-ds DNA all showed a strong positive correlation with homocysteine in the current study. While homocysteine and GFR had a significant negative connection, SLEDAI and SDI did not correlate with homocysteine. Moreover, age, SCr, ACR, and C4 all strongly predicted blood homocysteine.

This was comparable to Sam et al. [29], whose findings showed a strong association between homocysteine levels and several markers of disease activity in SLE patients, such as CRP, ESR, anti-dsDNA, C3, and C4.

Furthermore, in a study with 829 adult SLE patients, Petri and Fu [35] discovered a substantial correlation between homocysteine levels and renal disease, low glomerular filtration rate, and proteinuria.

Furthermore, Mohannad et al. [30] discovered no meaningful relationship between homocysteine levels and the SLEDAI scores of SLE patients.

Conversely, Zeña-Huancas et al. [36] examined 145 SLE patients in Peru and discovered that in both univariable and multivariable models, the highest homocysteine levels predicted the accumulation of new damage.

This study has been found to have certain limitations. First, the study's comparatively small sample size is a limitation. Nonetheless, the Community Department determined and authorized the sample size. Second, The investigation was only carried out at one location, which would have limited how broadly the findings could be applied. Lastly, it is impossible to assess causal correlations due to the cross-sectional nature of this study and the lack of follow-up.

CONCLUSION

The frequency of albuminuria in SLE patients is clearly correlated with higher serum homocysteine levels. With a cutoff point of 13.1 nmol/mL, serum homocysteine was found to have a 94.5% sensitivity and a 94.4% specificity in predicting renal impairment in SLE patients.

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