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Original article

Association between Estimated Urinary and Serum Sodium-to-Potassium Ratios and Blood Pressure in Systemic Lupus Erythematosus Patients with Hypertension

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Abstract:

Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder affecting multiple organs, including kidneys and cardiovascular system. Electrolyte disturbances, especially the sodium -to-potassium (Na-to-K) ratios, are gaining attention as indicators of disease activity and cardiovascular risk in SLE individuals. However, there is a lack of extensive research on the connection between Na-to-K ratios, disease activity, and hypertension (HTN) in SLE. **Objectives:** This study researched the association between urinary and serum Na-to-K ratios, blood pressure, and disease activity in SLE cases with HTN. **Methodology:** A case-control analysis was performed on SLE cases with HTN, evaluating demographic, clinical, laboratory, and echocardiographic parameters. Multiple regression and logistic regression analyses were done to identify independent predictors of disease activity and cardiovascular risk. **Results:** The study detected a significant association between urinary Na-to-K ratio and disease activity, as measured by SLE Disease Activity Index, C-reactive protein, and erythrocyte sedimentation rate, with no significant association between serum Na-to-K ratio and disease activity. Elevated urinary Na-to-K ratio correlated with elevated inflammation and disease activity. Additionally, HTN was more prevalent in cases with elevated urinary Na-to-K ratios, indicating a possible link between electrolyte imbalance and cardiovascular complications in SLE. **Conclusion:** The urinary Na-to-K ratio could potentially act as a non-invasive biomarker for tracking disease activity and assessing cardiovascular risk in SLE. Future longitudinal and multi-center investigations are recommended to further validate these associations and explore potential interventional strategies targeting electrolyte balance in SLE management.

Key words: SLE; Sodium to Potassium ratio SLEDAI ; HTN.

Introduction

Systemic lupus erythematosus (SLE) is a long-term female predominant -female to male ratio (9:1)- autoimmune disorder of unclear origin, presenting with a wide range of clinical manifestations with relapsing-remitting course. It is marked by the generation of autoantibodies that target nuclear and cytoplasmic antigens. Its complexity lies in its ability to affect the body in diverse ways, making each case uniquely challenging [1,2].SLE is linked to an increased risk of accelerated atherosclerosis and cardiovascular (CV) events throughout the progression of the disease. Notably, younger individuals with SLE are particularly more susceptible to these risks compared to their age-matched counterparts [3]. Hypertension (HTN), characterized by a systolic blood pressure (SBP) ≥140 mmHg and a diastolic blood pressure (DBP) ≥90 mmHg, is recognized as one of the primary modifiable risk factors for cardiovascular disease (CVD) and overall mortality [4].

In SLE, HTN may develop or worsen due to disease-related factors and long-term use of anti-inflammatory therapies like corticosteroids, immunosuppressants, and NSAIDs[5]. Additionally, SLE is associated with kidney dysfunction, which can lead to secondary HTN and further complicate the disease [6].

Electrolyte imbalances, particularly in sodium (Na^+) and potassium (K^+), are key factors in the progression of SLE and contribute significantly to the development of HTN [7]. High Na^+ concentrations enhance the differentiation of CD4+ cells into pathogenic Th17 cells, which aggravating autoimmune inflammation [8]. In autoimmune conditions, elevated sodium levels induce a stable activation of Th17 cells, with the relationship between salt and Th17 cell induction potentially being stronger in SLE due to the underlying inflammatory processes [9]. Several methods for assessing Na and K intake in cases exist, such as monitoring daily salt intake and measuring 24-hour urine values. However, these approaches are limited by their dependence on patient self-report and adherence to the guidelines [10].

The sodium-to-potassium (Na-to-K) ratio, measured in both serum and urine, has emerged as a potential marker for cardiovascular risk and renal function [11]. Elevated Na-to-K ratios have been linked to HTN and inflammation, both of which are central to SLE pathogenesis [12].

Study objective:

The aim of this research is to explore the relationship between hypertension and serum and urine sodium-to-potassium ratios with disease activity in patients with systemic lupus erythematosus (SLE).

Methods

Study Design

This is a case-control study carried out on 120 individuals during the period from November 2023 to April 2024, attending the in-patients and out-patients clinic of Rheumatology, Rehabilitation and Physical Medicine Department, Echocardiography was done at Cardiology Department, while laboratory investigations were done at Clinical and Chemical Pathology department of Benha University Hospitals. An approval from The Research Ethics Committee of faculty of medicine Banha University was obtained (Code Number: MS 41-9-2023), also an informed consent was obtained from participants included in this study

- **Group A (Cases)**: 60 patients diagnosed as having SLE and hypertension - according to The European League Against Rheumatism (EULAR) and the American college of Rheumatology (ACR) criteria in 2019 [13], and - according to new guidelines from the International Society of Hypertension - as a case group [14].
- **Group B (Controls)**: 60 hypertensive patients, matched at age and sex, as a control group.

Study Population

Participants were excluded if they had other autoimmune disorders, any systemic or chronic diseases, neoplastic conditions, or ischemic heart disease. Additionally, individuals using medications that affect serum or urine Na or K levels, such as diuretics, angiotensin-converting enzyme inhibitors, or angiotensin receptor blockers, were also excluded.

Sample Collection and Processing

A total of 6 ml of venous blood was collected from each participant: 3 ml in serum-separating tubes for biochemical analyses (FBS, serum creatinine, blood urea, serum sodium, and potassium), measured using the Sensa Core ST-200 aQua Electrolyte Analyzer; 1 ml in EDTA tubes for complete blood count; and 2 ml in citrate tubes for ESR. Spot urine samples (~10 ml) were collected in sterile containers and analyzed using the Cobas C311 analyzer. If not processed immediately, samples were stored at −80°C. Electrolyte levels were quantified via the ion-selective electrode (ISE) method. Rigorous internal quality control and external quality assurance protocols were applied. Samples with hemolysis, lipemia, or contamination were excluded to minimize pre-analytical variability.

Outcomes

The study outcomes encompass a range of clinical, laboratory, and imaging parameters. These outcomes include demographic and clinical history data, physical examination data, laboratory investigations and echocardiographic parameters.

Data Collection

1. **Clinical and Laboratory Data**

All Participants provided written informed consent before enrollment in the study, followed by a comprehensive medical history assessment, complete physical examination and necessary laboratory investigations were performed upon each patient. The following data was collected for each individual participant: age, sex, smoking status, weight, HTN duration, SBP, DBP, HTN medications, urea, creatinine, white blood cells (WBC), hemoglobin (Hb), platelets level (PLT), c-reactive protein (CRP), erythrocyte sedimentation rate (ESR), serum and urinary Na, serum and urinary K, Na-to-K ratio in both serum and urine and SLE disease characteristics.

2. **Echocardiography Data**

Participants were positioned in the left lateral decubitus position, examined using a Philips Epic 7 ultrasound system with a 5.5 MHz transducer and doppler imaging technique will be utilized to identify relevant structures. The following parameters were obtained for each patient: ejection fraction (EF), left ventricular (LV) mass index, early to late atrial filling velocity ratio (Mv E/A), early mitral inflow velocity to early diastolic mitral annulus velocity ratio (E/E'), and deceleration time.

3.Assesment of the disease activity of SLE:

Disease activity in SLE patients was assessed using the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K), a validated tool that includes 24 clinical and laboratory parameters, each assigned a specific weight based on their relevance to disease activity. This version allows for the persistent activity of certain manifestations (e.g., proteinuria, alopecia, mucosal ulcers, and rash) to be scored if present at the time of assessment, even if they first appeared more than 10 days prior. The total score ranges from 0 to 105, with higher scores indicating greater disease activity. In this study, SLEDAI-2K scores were categorized as mild (1–5), moderate (6–10), or severe (>10) [15]

Statistical Analysis

- Data were analyzed using SPSS (Version 23.0; IBM Corp., Armonk, NY, USA). Categorical variables were reported as frequencies and percentages, and continuous variables as means ± SD or medians (IQR). Associations were assessed using Chi-square or Fisher's exact tests. Group comparisons were made with independent t-tests or Mann-Whitney

U tests, and among multiple groups using ANOVA or Kruskal-Wallis tests. Pearson's or Spearman's correlation assessed variable relationships. Multiple linear and logistic regression analyses identified predictors of continuous and categorical outcomes, respectively. A P-value ≤ 0.05 was considered significant.

Results

This investigation involved 120 participants, divided into two groups. Group A (SLE) consisted of 60 cases with SLE and HTN, aged 18 to 57 years (mean ± SD: 34.1 ± 11.6), with 5 males (8.3%) and 55 females (91.7%). Of these, 56 (93.3%) were non-smokers and 4 (6.7%) smokers. Weight ranged from 54 to 112 kg (mean ± SD: 75.3 ± 14.2). Group B (Control) also comprised 60 individuals with HTN but no other comorbidities, aged 23 to 75 years (mean ± SD: 38.1 ± 12.6), with 13 males (21.7%) and 47 females (78.3%). Among them, 48 (80%) were non-smokers and 12 (20%) were smokers, with weight ranging from 57 to 112 kg (mean ± SD: 79.7 ± 13.1). Clinical characteristics were similar between both groups, except for HTN treatment. A significantly elevated proportion in the Control group used beta-blockers (34, 56.7%) as opposed to the SLE group (16, 26.7%) (P<0.001), while 26 (43.3%) in the SLE group used CCBs, as opposed to 13 (21.7%) in the Control one (P=0.01).

Regarding laboratory values, significant differences were detected between the groups. The Controls had elevated WBC (P=0.01), Hb (P<0.001), and PLT (P=0.03) levels, whereas the SLE group had elevated CRP, ESR, and creatinine levels (P<0.001, <0.001, and =0.03, respectively) . SLE disease duration ranged from 1 month to 8 years, with a median (IQR) of 2 (3). The SLEDAI score ranged from 1 to 33, with a median (IQR) of 6 (8.25). Disease activity distribution was as follows: 70% mild, 15% moderate, 10% high, and 5% very high. Among the 40 cases with LN, 9 (22.5%) had grade 3 nephritis, 1 (2.5%) had grade 3-5, 13 (32.5%) had grade 4, 3 (7.5%) had grade 4-5, and 2 (5%) had grade 5 nephritis. APL results were negative in 3 (50%) cases, and 12 (20%) were positive, while 18 (30%) had no APL testing.

Echocardiographic parameters were similar between groups (Table 1).

No significant differences were observed in serum Na, serum K, serum Na-to-K ratio, or urinary Na levels. However, urinary K was significantly higher in the Control group, while the urinary Na-to-K ratio was significantly higher in the SLE group (P < 0.001 for both). (Table 2). No significant correlations were found between the serum Na-to-K ratio and sex, smoking, antihypertensive type, SLE characteristics, or SLEDAI. However, it correlated positively with Hb and negatively with serum creatinine and urea (P = 0.009, <0.001, and 0.001, respectively). (Table 3, Figure 1).

No significant associations were found between the urinary Na-to-K ratio and demographic variables. However, it was significantly higher in cases with very high SLEDAI scores (P < 0.001) and showed positive correlations with CRP, ESR, and serum creatinine (r = 0.338, P = 0.008; r = 0.293, P = 0.023; r = 0.363, P = 0.004, respectively), and a negative correlation with Hb (r = –0.270, P = 0.037). (Table 4, Figure 2).

Logistic regression analysis revealed significant univariate associations with male sex, smoking, WBC count, Hb, PLT, CRP, ESR, creatinine, urea, urinary K, and urinary Na-to-K ratio (all P < 0.05). In multivariate analysis, only Hb, CRP, ESR, and urinary Na-to-K ratio remained independent predictors (P = 0.02, OR = 0.32; P = 0.02, OR = 1.08; P = 0.001, OR = 1.21; and P = 0.001, OR = 2.34, respectively. (Table 5).

Multiple linear regression analysis identified CRP, ESR, and urinary Na-to-K ratio as independent predictors of SLEDAI (β = 0.07, P=0.02; β = 0.085, P=0.003; and β = 1.923, P<0.001, respectively). (Table 6).

Table 1: Echocardiographic observations among the study groups

Variables		SLE group (n=60)	Control group (n=60)	P
LV mass *(mg)*	*Mean ± SD*	153.6 ± 48.3	169.6 ± 52.76	
	Range	(66.08 – 280.5)	(65.9 – 281.74)	0. 09[1]
Mv E/A	*Median (IQR)*	0.8 (0.36)	0.79 (0.53)	
	Range	(1.9 – 3.8)	(0.31 – 2)	0. 89[2]
E/E'	*Median (IQR)*	6.75 (1.7)	7 (2)	
	Range	(2.9 – 8)	(4.2 – 12)	0. 09[2]
EF *(%)*	*Mean ± SD*	61.97 ± 5.86	63.51 ± 6.53	
	Range	(51.3 – 76)	(36 – 76.2)	0.08[2]
Deceleration	*Median (IQR)*	219 (68)	223 (64.35)	
time *(ms)*	*Range*	(162 – 315)	(164 – 333)	0. 79[2]

**[1]Student T-test, [2]Mann-Whitney U test, Non-significant: P >0.05, Significant: P ≤0.05*
***LV mass=Left ventricular mass, Mv E/A=Early to late atrial filling velocity ratio, E/E'=Early mitral inflow velocity to early diastolic mitral annulus velocity ratio, EF=Ejection fraction, IQR=Interquartile Range,* **SLE:** systemic lupus erythematosus

Table 2: Serum and urinary Na-to-K ratio among the studied groups

Variables		SLE group (n=60)	Control group (n=60)	P
Serum Na	*Mean ± SD*	141.33 ± 4.54	140.35 ± 3.91	
(mmol/L)	*Range*	(134 – 150)	(134 – 148)	0.21[1]
Serum K	*Mean ± SD*	4.13 ± 0.68	3.97 ± 0.45	
(mmol/l)	*Range*	(3 – 6.5)	(3 – 5)	0.13[1]
Serum Na-to-K	*Mean ± SD*	35.03 ± 5.22	35.75 ± 4.004	
ratio	*Range*	(23.1 – 47.33)	(27.8 – 47.33)	0.39[2]
Urinary Na	*Median (IQR)*	111.5 (65.25)	110.5 (61.77)	
(mmol/L)	*Range*	(35 – 314)	(19 – 345)	0.89[2]
Urinary K	*Median (IQR)*	27.3 (30.13)	43 (32)	
(mmol/l)	*Range*	(8.6 – 108.7)	(9.78 – 88.7)	**<0.001[2]**
Urinary Na-to-K	*Median (IQR)*	4.33 (2.82)	2.52 (1.11)	
ratio	*Range*	(0.86 – 13)	(0.91 – 4.4)	**<0.001[2]**

**[1]Student T-test, [2]Mann-Whitney U test, Non-significant: P >0.05, Significant: P ≤0.05*
***Na=Sodium, K=Potassium, IQR=Interquartile Range,* **SLE:** Systemic lupus erythematosus

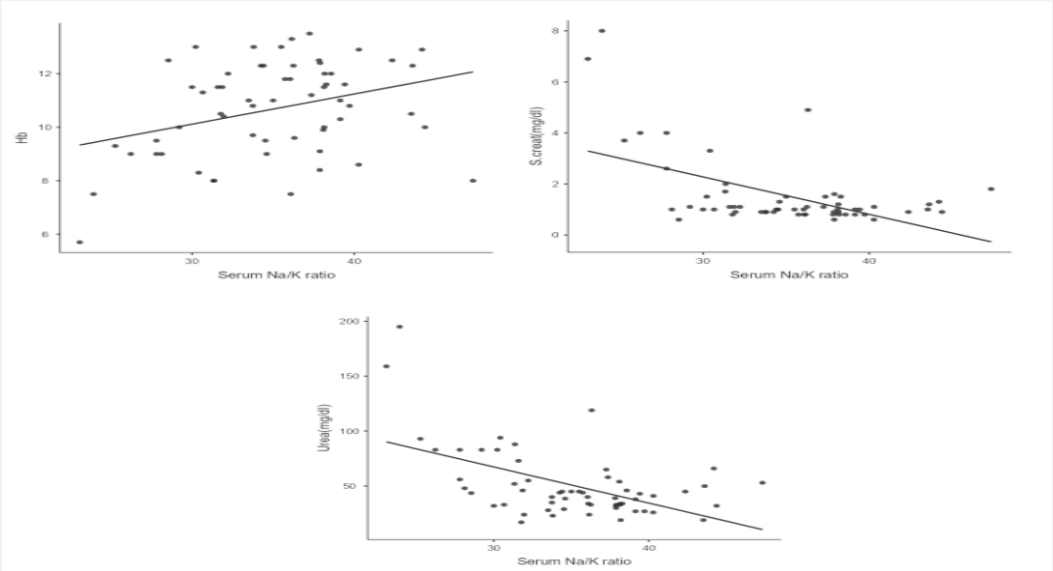

Figure 1: Scatter plots showing the correlation between serum Na-to-K ratio and different parameters among the SLE group

Table 3: Association between serum Na-to-K ratio and clinical variables

Variables		Serum Na-to-K ratio *Mean ± SD*	P
Sex	Male	32.9 ± 5.9	
	Female	35.2 ± 5.17	0.34
Smoking status	Non-smokers	34.9 ± 5.25	
	Smokers	37 ± 4.99	0.06
Beta blockers	No	35.4 ± 4.63	
	Yes	34 ± 6.65	0.37
Calcium channel blockers	No	34.8 ± 5.01	
	Yes	35.3 ± 5.56	0.74
α methyl dopa	No	35.3 ± 5.31	
	Yes	32.4 ± 3.61	0.2
Others	No	35.3 ± 4.99	
	Yes	33.3 ± 6.42	0.29
Lupus nephritis *(n. %)*	Absent	36.2 ± 4.99	
	Present	34.4 ± 5.29	0.21[1]
Grade *(n. %)*	Not yet	36.3 ± 3.35	
	Grade 3	37.7 ± 3.71	
	Grade 3-5	35.5	
	Grade 4	34 ± 5.5	0.06[2]
	Grade 4-5	30.1 ± 5.43	
	Grade 5	25.4 ± 3.34	
	Died	28.3 ± 4.29	
Antiphospholipid syndrome *(n. %)*	Negative APL	35.4 ± 5.09	
	Positive APL	33.1 ± 5.07	0.37[1]
	APL antibodies not done	35.6 ± 5.52	
SLEDAI score	Mild activity	35.8 ± 3.83	
	Moderate activity	36.2 ± 4.59	
	High activity	34.7 ± 6.55	0.07[2]
	Very high activity	28.8 ± 5.68	

[1]*Student T-test,* [2]*One way ANOVA test, Non-significant: P >0.05, Significant: P ≤0.05,* ***APL****=antiphospholipid syndrome,* ***SLEDAI****=Systemic lupus* erythematosus disease activity index, ***Na***=Sodium, ***K***= Potassium.

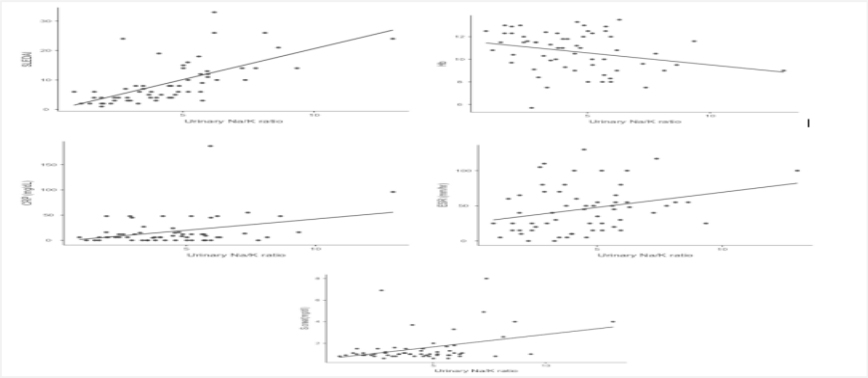

Figure 2: Scatter plots showing the correlation between urinary Na-to-K ratio and different parameters among the SLE group

Table 4: Association between urinary Na-to-K ratio and clinical variables

Variables		Urinary Na-to-K ratio *Median (IQR)*	P Value
Sex	Male	3.3 (1.28)	
	Female	4.48 (2.85)	0.24
Smoking status	Non-smokers	4.37 (2.87)	
	Smokers	3.89 (1.51)	0.38
Beta blockers	No	4.64 (2.91)	
	Yes	3.33 (1.86)	0.16
Calcium channel blockers	No	4.33 (3.03)	
	Yes	4.33 (2.67)	0.56
α methyl dopa	No	3.99 (2.94)	
	Yes	5.12 (0.93)	0.08
Others	No	4.48 (2.82)	
	Yes	3.98 (2.89)	0.29
Lupus nephritis *(n. %)*	Absent	3.83 (2.56)	
	Present	4.57 (2.83)	0.42[1]
Grade *(n. %)*	Not yet	3.88 (1.68)	
	Grade 3	4.83 (1.74)	
	Grade 3-5	4.86	
	Grade 4	3.71 (3.28)	0.15[2]
	Grade 4-5	8.64 (2.87)	
	Grade 5	5.43 (2.71)	
	Died	4.85 (0.76)	
Antiphospholipid syndrome *(n. %)*	Negative APL	4.71 (2.86)	
	Positive APL	3.89 (3.07)	0.63[1]
	APL antibodies not done	3.5 (2.1)	
SLEDAI score	Mild activity	2.89 (2.03)	
	Moderate activity	4.52 (1.82)	
	High activity	5.8 (1.13)	**<0.001[2]**
	Very high activity	7.17 (2.31)	

[1]Mann-Whitney U test, [2]Kruskal-Wallis test, Non-significant: P >0.05, Significant: P ≤0.05, ***ALP****=antiphospholipid syndrome,* ***SLEDAI****=Systemic lupus* erythematosus disease activity index, ***Na***=Sodium, ***K***= Potassium.

Table 5: Logistic regression analysis for predictors of SLE

Variables	Univariate analysis		Multivariate analysis	
	P	Odds* (CI 95%)	P	Odds (CI 95%)
Age	0.08	1.03 (0.99 – 1.06)	-	-
Sex (male)	**0.048**	3.04 (1.01 – 9.16)	0.31	1.92 (0.55 – 6.77)
Weight (Kg)	**0.09**	1.02 (0.99 – 1.05)	0.14	0.98 (0.95 – 1.01)
Smoking	**0.04**	3.5 (1.06 – 11.57)	0.21	0.42 (0.11 – 1.63)
SBP (mmhg)	0.46	0.99 (0.97 – 1.02)	-	-
DBP(mmhg)	0.87	0.99 (0.97 – 1.02)	-	-
HTN duration	0.18	1.09 (0.96 – 1.23)	-	-
WBCs (×10³/µL)	**0.04**	0.85 (0.72 – 0.99)	0.07	0.54 (0.28 – 1.04)
Hb (g/dl)	**<0.001**	0.41 (0.28 – 0.58)	**0.02**	0.32 (0.13 – 0.81)
PLT (×10³/µL)	**0.03**	0.99 (0.99 – 1.00)	0.37	0.99 (0.99 – 1.005)
CRP(mg/L)	**0.002**	1.08 (1.03 – 1.14)	**0.02**	1.08 (1.01 – 1.14)
ESR(mm/hr)	**<0.001**	1.13 (1.06 – 1.19)	**0.001**	1.21 (1.07 – 1.34)
Creatinine(mg/dl)	**0.03**	2.28 (1.09 – 4.8)	0.49	1.56 (0.45 – 5.42)
Urea(mg/dl)	**0.03**	1.02 (1.002 – 1.04)	0.26	0.96 (0.88 – 1.03)
Serum Na *(mmol/L)*	0.21	1.06 (0.97 – 1.15)	-	-
Serum K *(mmol/L)*	0.14	1.64 (0.85 – 3.15)	-	-
Serum Na-to-K ratio	0.39	0.97 (0.89 – 1.05)	-	-
Urinary Na*(mmol/L)*	0.62	1.002 (0.99 – 1.01)	-	-
Urinary K *(mmol/L)*	**0.002**	0.97 (0.96 – 0.99)	0.67	1.006 (0.98 – 1.03)
Urinary Na-to-K ratio	**<0.001**	2.42 (1.68 – 3.49)	**0.001**	2.34 (1.39 – 3.89)
LV mass (g)	0.07	0.99 (0.99 – 1.00)	-	-
Mv E/A	0.8	1.14 (0.43 – 3.01)	-	-
E/E'	0.32	1.07 (0.94 – 1.23)	-	-
EF %	0.18	0.96 (0.91 – 1.02)	-	-
Deceleration time *(ms)*	0.99	1.00 (0.99 – 1.01)	-	-

** Odds: odds ratio***SBP=**systolic blood pressure, **DBP=**Diastolic blood pressure, **HTN=** Hypertension, **Na**=Sodium, **K**=Potassium, **WBCs=**White blood cells, **Hb=**Hemoglobin, **PLT=**Platelet, **ESR=**Erythrocyte sedimentation rate, **CRP=**C- reactive protein, ***LV mass****=Left*

*ventricular mass, **Mv E/A**=Early to late atrial filling velocity ratio, **E/E'**=Early mitral inflow velocity to early diastolic mitral annulus velocity ratio, **EF**=Ejection fraction,* **SLE:** systemic lupus erythematosus.

Table 6: The multiple linear regression analysis of SLEDAI-2000 and different predictors of systemic lupus erythematosus

Model fit measures	**R=0.787**	**R^2=0.619**	
Model coefficients	**Estimate**	**t**	**P**
SLE duration	0.013	0.046	0.96
WBCs *(×10³/μL)*	0.237	0.929	0.36
Hb *(g/dl)*	-0.932	-1.889	0.07
PLT *(×10³/μL)*	0.017	1.613	0.11
CRP *(mg/L)*	0.07	2.42	**0.02**
ESR *(mm/hr)*	0.085	3.15	**0.003**
Serum Na-to-K ratio	0.375	0.99	0.59
Urinary Na-to-K ratio	1.923	5.99	**<0.001**

*Mann-Whitney U test, [2]Kruskal-Wallis test, Non-significant: P >0.05, Significant: P ≤0.05, **ALP**=antiphospholipid syndrome,* **SLE:** systemic lupus erythematosus, **WBCs**=White blood cells, **Hb**=Hemoglobin, **PLT**=Platelet ***SLEDAI**=Systemic lupus* erythematosus disease activity index, ***Na***=Sodium, ***K***= Potassium.

Discussion

In this study, HTN duration, SBP, and DBP were comparable between SLE and control group (P > 0.05 for all comparisons). This finding is consistent with previous studies proving that, despite the higher risk of HTN in SLE patients, their blood pressure levels may not significantly differ from non-SLE hypertensive individuals with similar risk profiles [(16)].

There was a significant difference in antihypertensive medication use between both groups. Beta-blockers were more frequently used in the controls (56.7%) as opposed to the SLE (26.7%) (P < 0.001), while calcium channel blockers (CCB) were more commonly prescribed in the SLE (43.3%) than in the controls (21.7%) (P=0.014). This may be due to the preference for CCB, particularly amlodipine, in SLE cases given their vascular and renal protective effects [(17)]. In contrast, beta-blockers, are less favored due to potential exacerbation of Raynaud's phenomenon and fatigue [(18)]. No significant differences were detected in the use of alpha-methyldopa or other antihypertensive drugs between the groups.

SLE patients had significantly lower WBC counts, Hb levels, and PLT counts (P = 0.011, P < 0.001, and P = 0.032, respectively), in line with previous findings reporting leukopenia, anemia, and thrombocytopenia as common manifestations due to immune-mediated destruction, bone marrow suppression, or chronic inflammation [(19,20)]. Furthermore, CRP and ESR levels were elevated in SLE patients, supporting prior observations that ESR correlates with disease activity, whereas CRP may indicate concurrent infections [(21)]. Additionally, we detected elevated levels of creatinine and urea in the SLE group, suggesting a degree in renal injury, which is common in SLE due to high frequency of lupus nephritis[(22)].

Our study found no significant differences between SLE patients and controls in serum Na, K, or the Na-to-K ratio, aligning with previous findings that electrolyte disturbances in SLE are usually mild unless there is notable renal involvement or corticosteroid use [(23)]. Most SLE patients were hypertensive and on antihypertensive drugs, which may explain the stable serum levels [(24)]. However, urinary K was significantly lower and the urinary Na-to-K ratio significantly higher in SLE cases (P <

0.001), possibly reflecting impaired renal K handling due to tubular dysfunction, chronic inflammation, or medication effects [25]. The elevated urinary Na-to-K ratio is clinically relevant, as it's linked to increased cardiovascular risk, hypertension severity, and kidney disease progression in SLE [26, 27].

No significant differences were observed in echocardiographic parameters between SLE and control groups. Specifically, LV mass showed no significant difference (P = 0.071), likely due to the comparable HTN duration and control in both groups. Similarly, diastolic function indices (E/A and E/E′ ratios) did not differ significantly, proving no major diastolic dysfunction in SLE patients compared to controls. Although previous studies reported subclinical myocardial changes in SLE, our findings suggest these alterations may be more evident in patients with longer disease duration or additional cardiovascular risk factors [28,29].

Our study detected no association between the serum Na-to-K ratio and the SLEDAI score, contradicting other research that reported that hyponatremia has been associated with elevated disease activity . A trend toward a lower Na-to-K ratio was observed in cases with very high disease activity compared to those with mild or moderate activity. This may reflect inflammation-induced electrolyte imbalances and renal involvement in severe SLE [30].This aligns with investigations that have shown that elevated inflammatory markers, such as CRP and IL-6, can lead to electrolyte imbalance[31].

This study found a significant correlation between the Na-to-K ratio and hemoglobin levels (r = 0.334, P = 0.009), suggesting a potential link between electrolyte balance and anemia in SLE. This aligns with research indicating that anemia in SLE often results from chronic inflammation and renal dysfunction, which affect erythropoiesis and electrolyte regulation [32]. No significant association was found between urinary Na-to-K ratio and antihypertensive drug use, consistent with conflicting evidence in the literature regarding medication effects on this ratio [33]. This lack of association may reflect variations in renal function, disease activity, or drug dosages among patients.

No significant associations were found between the urinary Na-to-K ratio and SLE disease characteristics, including lupus nephritis and Anti-Phospholipid Syndrome (P > 0.05). This suggests that variations in urinary electrolyte ratios may not directly influence renal affection or vascular complications in SLE [34,35].

A significant association was found between urinary Na-to-K ratio and SLE disease activity as measured by the SLEDAI score (P < 0.001), with higher ratios observed in cases with greater activity. The ratio also correlated positively with CRP (P = 0.008), ESR (P = 0.023), and serum creatinine (P = 0.004), and negatively with hemoglobin levels (P = 0.037). These findings suggest that increased disease activity and inflammation in SLE may impair renal electrolyte handling, in line with existing evidence linking electrolyte disturbances to lupus nephritis and immune-mediated renal dysfunction [36].

Our logistic regression analysis identified Hb, CRP, ESR, and NA-to-K ratio as independent predictors of SLE. Lower Hb levels were significantly associated with SLE, reflecting the common occurrence of anemia in these patient[37]. Elevated ESR and normal CRP were also strong predictors, reinforcing their role as inflammatory markers in disease activity.

Notably, the urinary Na-to-K ratio emerged as a significant predictor, proving its potential as a novel biomarker linked to renal dysfunction and immune dysregulation. While variables such as sex, smoking, WBC, and creatinine were significant in univariate analysis, they lost significance in the multivariate model, implying that their influence may be mediated by other factors. These observations illustrate that monitoring Hb, CRP, ESR, and urinary Na-to-K ratio could aid in early detection and risk stratification of SLE, though further validation is required[38].

Multiple linear regression analysis identified urinary Na-to-K ratio, CRP, and ESR as independent predictors of SLE disease activity (SLEDAI-2000), with a well-fitting model ($R^2 = 0.619$). The urinary Na-to-K ratio showed a strong positive association with SLEDAI-2000 ($\beta = 1.923$, $P < 0.001$), highlighting its role in electrolyte-mediated immune dysregulation [39]. CRP ($\beta = 0.07$, $P = 0.02$) and ESR ($\beta = 0.085$, $P = 0.003$) were also significant predictors. In contrast, SLE duration, WBC count, platelet count, and serum Na-to-K ratio were not predictive. These results support the urinary Na-to-K ratio as a promising, non-invasive marker for SLE activity monitoring, warranting further research [40].

Strength and Limitation

This study's strengths are that it explores the association between urinary and serum Na-to-K ratios and blood pressure in hypertensive SLE cases, addressing underexplored areas. By incorporating using comprehensive clinical and laboratory data with robust statistical analyses. The sample size and lack of strong matching between the individuals of control and case groups in age and sex may have restricted the detection of subtle associations, particularly in subgroup analyses. Additionally, dietary Na and K intake were not assessed, and factors like medication effects and hydration status were not fully accounted for, which could influence the results.

Conclusion

Although this study has certain limitations, it offers important insights into the connection between electrolyte balance, blood pressure, and disease activity in hypertensive cases with SLE. The urinary Na-to-K ratio stands out as a potential non-invasive marker for monitoring disease progression. To further confirm and build on these results, future research should incorporate larger, longitudinal investigations along with dietary assessments.

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