RENAL AND BONE PROFILES IN SAUDI INDIVIDUALS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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SUMMARY: The renal and bone profiles were investigated in Saudi systemic lupus erythematosus (SLE) patients and the results were compared with normal age and sex matched controls. The results showed that one or more renal profile abnormalities were present in 48.5% of the patients though the severity of renal involvement differed from one patient to another. The rest of the patients (i.e. 51.5%) had no renal involvement. One or more bone profile abnormalities were encountered in 33.3% of the SLE patients, majority of these patients had only a single abnormal test (24.2%). This case-control study shows the very heterogeneous presentation of SLE patient, in biochemical analyses, even among the individuals of same ethnic origin.

Key Words : Systemic lupus erythematosus, IgA, IgG, IgM.

INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune disorder with striking diversity regarding clinical manifestations, pathophysiology and prognosis. It is largely defined on the basis of its clinical manifestations. Though there are certain laboratory abnormalities which are characteristics of SLE, none is considered diagnostic in the absence of relevant clinical patterns of the disease (1–3). Among the abnormalities commonly encountered in SLE patients are renal lesions, in the form of focal or diffuse glomerulonephritis and membranous lupus nephritis (4). Clinically detectable evidence of renal involvement is seen in almost half of the SLE patients. However, the extent of renal involvement varies from one individual to another. Joint involvement including stiffness, pain and inflammation is another common feature of SLE and has been reported in 46% to 92% of SLE patients (6).

We investigated the renal and bone profiles in Saudi SLE patients and compared the results with those obtained in normal healthy, age and sex matched controls. In this paper we present our findings and discuss the results in the light of those reported for SLE patients in other populations.

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MATERIALS AND METHODS

Thirty-two Saudi SLE patients attending the Rheumatology Clinics at Riyadh Al-Kharj Hospital (RKH), Riyadh and diagnosed applying the criteria of the American Rheumatism Association (7), were investigated. An equal number of age and sex matched healthy volunteers were selected as controls. The patients group comprised of 23 females with age ranging from 13–65 years and 9 males with age ranging from 35–72 years as shown in Table 1.

Ten milliliters of blood was collected in plain tubes, from the patients prior to initiation of any therapy and from the control group and allowed to stand at room temperature. Serum was separated by centrifugation at 3000 RPM for 5 minutes, and stored frozen at -20°C until required for analysis. The estimation of parameters commonly included as renal profile tests, and the bone profile, were conducted using auto analyzer "Parallel Analytical System" (American Monitor Corporation, Indianapolis, IN 46268, USA). Wherever possible the samples were run in duplicates. To control the methodological error of the procedure in

Table 1: Age and sex distribution in SLE patients.

Sex	Age (years)	Prevalence (%)
Male (n=9)	<30	0
	30-40	22.2
	40-50	44.4
	50-60	22.2
	60-70	0
	70-80	0
Female (n=23)	<10	0
	10-20	21.74
	20-30	34.78
	30-40	21.74
	40-50	4.35
	50-60	8.70
	60-70	4.35
	70-80	4.35

application in the laboratory, both internal and external quality controls were utilized.

In addition, in some patients and controls the immunoglobulins IgG, IgM and IgA and the complements C3 and C4 were also estimated. The immunoglobulins were estimated using the COBAS Biosystem and the complements were estimated using the Immuno-chemistry System (ICS) (Beckman Instrument, Inc., Brea CA 92621).

The results obtained for the various analyses were separately fed on the computer at King Saud University Computer Center Riyadh, and using the Statistical Analysis System (SAS), the mean and standard deviation were calculated separately for the patients and the control groups. The statistical significance of the difference in the mean of any parameter in the patient and the control group was estimated using the Student's 't' test. $P<0.05$ was considered statistically significant.

RESULTS

The results (mean±SD) of serum creatinine, urea, uric acid and electrolytes in the SLE patients and the control group are presented in Table 2. The value of serum creatinine, urea and uric acid are significantly higher in the SLE patients compared to the values in the control group ($p<0.05$). The mean values of the electrolytes did not show any significant differences between the two groups.

Figures 1–4 compare the distribution of urea, creatinine, uric acid and electrolytes in the SLE patients and the control group. Eight (25%) of the SLE patients had significantly elevated uric acid level, while 6 (18.75%) had values lower than the normal range. Urea was elevated in 10 (31.25%) of the SLE patients. Five SLE patients (15.62%) had sodium level below the normal range, while potassium was elevated slightly in 5 (15.62%) patients.

The prevalence of one or more renal profile abnormalities are presented in Table 3. Only one patient had both

Figure 1: Distribution of urea and creatinine in SLE patients (P) and control group (C). The bar (I) represents the normal reference values.

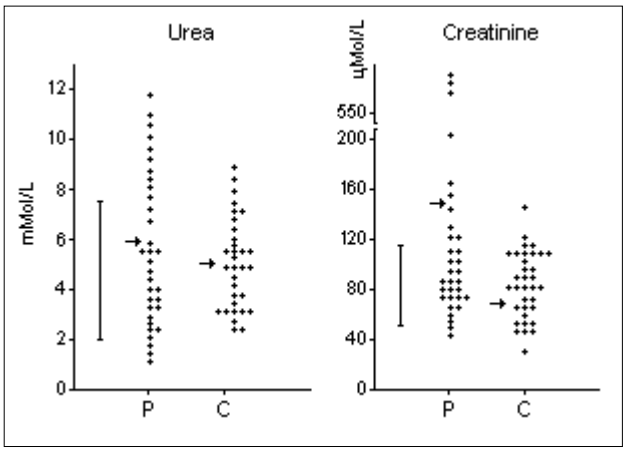


Table 2: Value of renal profile test and electrolytes in SLE patients and control group.

Parameters	Mean±SD		P value
	SLE Patients	Control	
Urea (mmol/l)	5.51±3.02	5.00±1.3	>0.05
Creatinine (µmol/l)	136.7±163.7	70.0±18.0	<0.05
Uric Acid (µmol/l)	348.9±168.5	269.3±82.3	<0.05
Na^+ (mmol/l)	137.5±4.5	138.8±2.7	>0.1
K^+ (mmol/l)	4.19±0.78	4.03±0.36	>0.3

Figure 2: Distribution of uric asid in SLE patients (P) and control group (C). The bar (I) represents the normal reference values.

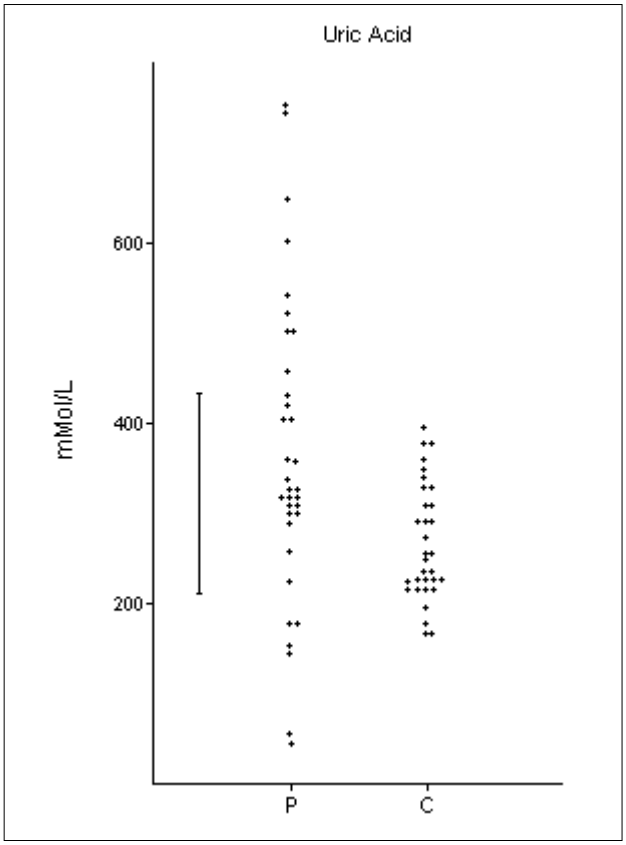


Table 3: Prevalence of renal profile abnormalities in SLE patients.

No. of renal profile abnormalities	Number	Prevalence (%)
0	17	51.5
1	8	24.24
2	7	21.2
3	1	3.03

urea and creatinine elevated, three had both creatinine and uric acid elevated, one had both urea and uric acid elevated. While 6 had one of the renal function profile abnormalities.

Table 4 presents the results of bone profile analysis in the SLE patients and the control group. The mean value for alkaline phosphatase level was significantly elevated in the SLE patients compared to the controls ($p<0.05$).

Figure 3: Distribution of electrolytes (Na^+, K^+) in SLE patients (P) and control group (C). The bar (I) represents the normal reference values.

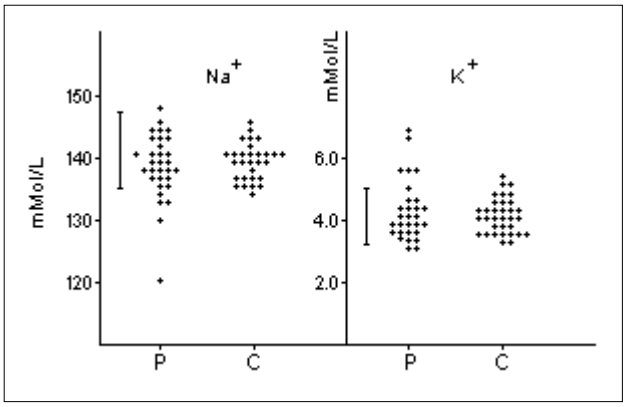
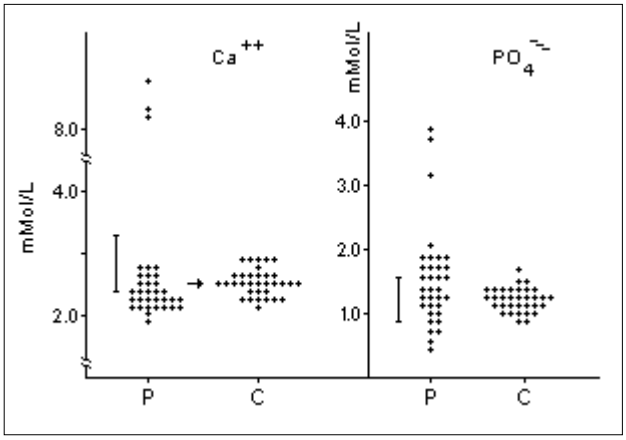


Figure 4: Distribution of Ca^{++} and PO_4^{---} in SLE patients (P) and control group (C). The bar (I) represents the normal reference values.



The mean for both calcium and phosphate were also elevated in the SLE patients though the difference was not statistically significant. Figure 4 presents the distribution of Ca^{++} and phosphate in the SLE patients and the control group. Calcium was significantly elevated in 3 (9.38%) of the patients and was lower than the normal range in 16 (50%) of the patients. Phosphate, on the other hand, was elevated in 11 (34.37%) patients while alkaline phosphatase was elevated in 8 (25%) of the SLE patients. The prevalence of one or more bone profile abnormalities in the SLE patients are presented in Table 5.

The mean and SD for the immunoglobulins and complements are presented in Table 6 and the distribution of these parameters in the patient and control group is shown in Figures 5 and 6. The mean for IgG and IgA were

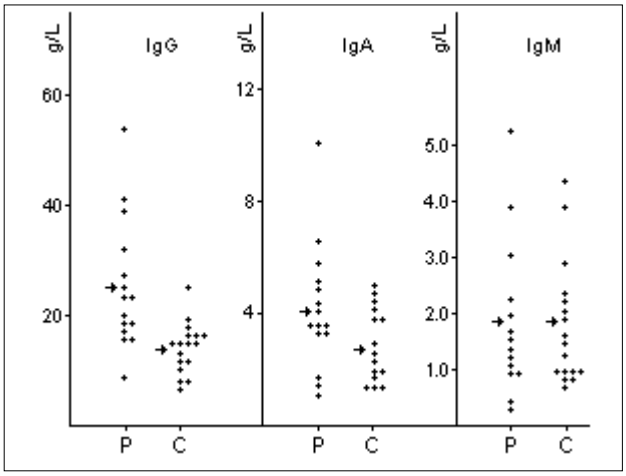
Table 4: Value of bone profile investigations in SLE patients and control group.

Parameters	Mean±SD		P value
	SLE patients	Control group	
Ca^{++} (mmol/l)	2.91±2.02	2.34±0.14	>0.10
PO_2 (mmol/l)	1.40±0.82	1.1±0.12	>0.059
Alkaline phosphatase (U/l)	119.4±101.9	81.7±29.0	>0.10

Table 5: Prevalence of bone profile abnormalities in SLE patients.

No. of bone profile abnormalities	Number	Prevalence (%)
0	22	66.7
1	8	24.24
2	2	6.06
3	1	3.03

Figure 5: Distribution of immunoglobulin IgG, IgA and IgM in SLE patient (P) and control group (C). The arrow points to the mean.



significantly higher in the SLE patient, though IgM did not show any significant difference compared to the values in the control group. The complement C3 was significantly reduced in majority of the patients and the mean was lower than in the control group ($p<0.05$). Complement C4 was also lower in several (33%) of the patients, and the difference in the mean compared to the mean in the control group was statistically significant.

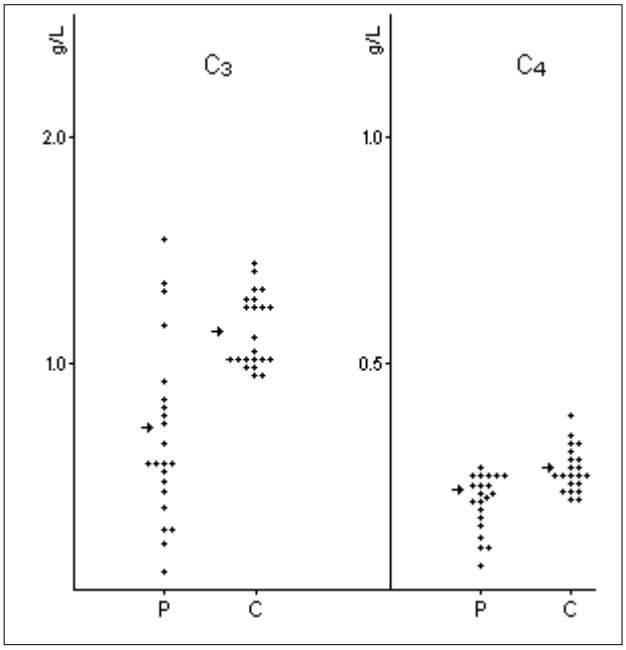
DISCUSSION

Renal involvement is one of the most frequent and serious derangement encountered in SLE patients. In several studies it is shown that renal dysfunction may occur in over half of the SLE patients during the first year of clinical diagnoses. As the disease progresses, the prevalence of renal involvement increases. However, severe renal disease occurs in only 15–20% of all SLE patients. In addition, renal involvement shows considerable ethnic variation in SLE patients, where some studies in black patients have reported a higher prevalence of renal disease compared to whites (8). In many patients

Table 6: Value of immunoglobulins and complements in the SLE patients and control group.

Parameters	Mean±SD		P value
	SLE Patients	Control	
IgG (g/L)	25.05±11.59	12.66±4.03	0.001
IgA (g/L)	4.20±3.20	2.54±1.23	0.001
IgM (g/L)	1.79±1.47	1.72±1.18	0.894
C3 (g/L)	0.68±0.39	1.10±0.24	0.0002
C4 (g/L)	0.19±0.06	0.26±0.05	0.0002

Figure 6: Distribution of C3 and C4 in SLE patients (P) control group (C). The arrow points to the mean.



renal injury i.e. glomerulonephritis, may occur, while in others only impairment of concentrating ability is observed (9, 10). Often the kidneys are severely involved and renal failure may develop (11). Since the primary function of the kidneys is to excrete non-protein nitrogenous substances and to maintain homeostasis of several ions, including Na^+, K^+, Cl^-, calcium phosphate, chronic renal failure is often associated with several biochemical abnormalities including azotemia, hyperkalemia, hypocalcaemia and phosphate retention (12).

This study has shown that 51.5% of the Saudi SLE patients had no biochemical abnormality which would indicate renal involvement. However, 48.5% had one or more renal profile abnormalities. This is consistent with the reports in literature on SLE patients (2, 4). However, the extent of renal involvement varied from patient to patients. Some of the patients had only slight abnormality as judged from the levels of the renal profile parameters, while others had severely elevated urea, creatinine and uric acid levels.

In the bone profile tests 33.3% of the SLE patients had one or more bone profile abnormalities. Among these 24.24% had only single abnormal test. The rets had two or more abnormal tests. In three of these patients Ca^{++} and phosphate were significantly elevated in blood plasma. This could either be due to excessive bone mobilization by elevation in parathyroid hormone, or decrease in calcitonin, which inhibits bone mobilization. In one of these young females (13 years), alkaline phosphatase was also elevated. This may have been either of bone or liver origin. However, liver function tests did not show any significant abnormalities in this patient. Elevation of alkaline phosphatase was also encountered in 8 SLE patients, however, the source of the alkaline phosphatase i.e. liver or bone origin was not determined.

The elevation of IgG is frequently reported abnormality in SLE due to the autoimmune aetiology of the disease (13,14). However, in this study IgM was not elevated, though IgA showed significant elevation. Low level of complement C3 and C4 is also a commonly reported abnormality (15). Total serum complement level is decreased in active cases of SLE, largely due to the action of immune complexes, cytotoxic antibodies and due to decreased synthesis (16). In the present study 18/22 SLE patients had lower C3 level. Complement C4 was also reduced in several (21/27) patients. This reduction in the complement level is believed to result from the renal dysfunction (17).

These results show very clearly that SLE is a very heterogeneous syndrome, which presents itself as diverse clinical manifestations and tissue involvements. None of these profile abnormalities could, on its own, be sufficient for conclusive diagnosis of SLE. However, along with clinical manifestations, these tests can be of value particularly in investigation of disease prognosis and in evaluation of drug response

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