LIVER FUNCTION PROFILES IN SAUDI NATIONALS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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SUMMARY: Liver function tests were investigated in Saudi patients suffering from systemic lupus erythematosus (SLE) and compared with the results obtained in a group of age and sex matched controls. The results showed that the mean for total protein and total bilirubin were not statistically different in the patient and the control group. However, albumin, A/G ratio and cholesterol were significantly lower, while globulins, serum glutamate oxaloacetate transaminase (SGOT), and alkaline phosphatase were significantly elevated. Hypoalbuminemia was the most frequent abnormality and was encountered in 65.6% of these patients. This paper present our findings and discusses the results in the light of the studies reported in literature.

Key Words: Systemic lupus erythematosus, liver function profiles.

INTRODUCTION

Systemic lupus erythematosus (SLE), an autoimmune disorder of unknown aetiology, presents with a varying severity depending upon host variables and different aetiological stimuli (1). It leads to a multi-system disorder any many affect vital tissues of the body in some individuals (2). At the molecular level the antibodies produced against different body cells and against the nuclear components (3, 4) are responsible for the multi-system derrangement.

The disease occurs at a significantly higher prevalence in the females compared to males. This preponderance of the disease has led to the suggestions that specific X-linked alleles together with some autosomal factors predispose to the development of SLE (5). Other suggestions of aetiological factors include exposure to sunlight, ultra-violet radiations, viral and genetic factors. In addition, prolonged administration of certain drugs, including hydrallazine and procainamidemay induce the development of SLE-like disease. Some studies report abnormalities of several laboratory variables that indicate liver involvement in SLE (6-11). However, the prevalence and extent of liver function test abnormalities differs significantly in reported studies on SLE patients.

In this study, we investigated the liver function tests abnormalities in Saudi patients with SLE and compared the results with age and sex matched controls in an attempt to determine the prevalence of liver involvement in SLE patients.

MATERIALS AND METHODS

Thirty-two male and female subjects who had been diagnosed as SLE patients using the criteria outlined by the American Rheumatism Association (12) and who were attending clinics at the Riyadh, Al-Kharj Hospital (RKH) were investigated. The patients were complemented with age and sex matched controls, who had volunteered to be included in this study. The patients group included 23 females (age range 13-65 years) and 9 males (age range 35-72 years).

Blood (10 ml) was collected by venipuncture from the patients prior to initiation of treatment, and the controls in plain tubes and left at room temperature to clot. Serum was separated by centrifugation for 5 minutes at 3000 RPM, and stored frozen until required for analysis.

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Figure 1: Distribution of total protein and albumin in SLE patients (P) and normal control (C). The bar (□) indicates the 'normal reference interval' for the parameters.

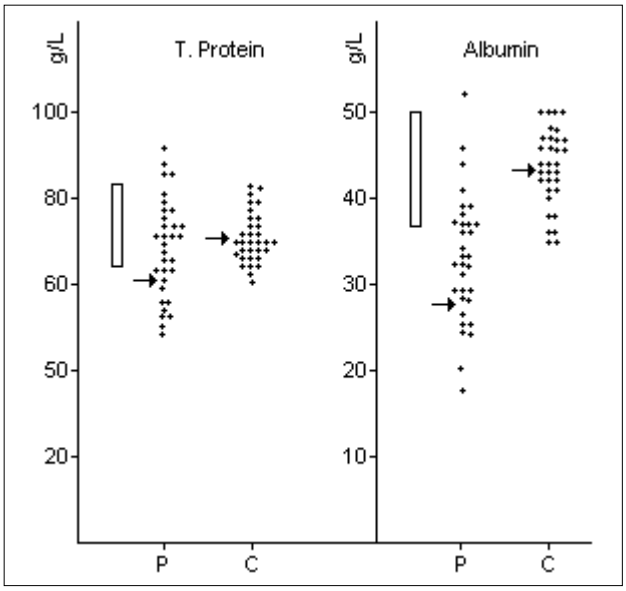
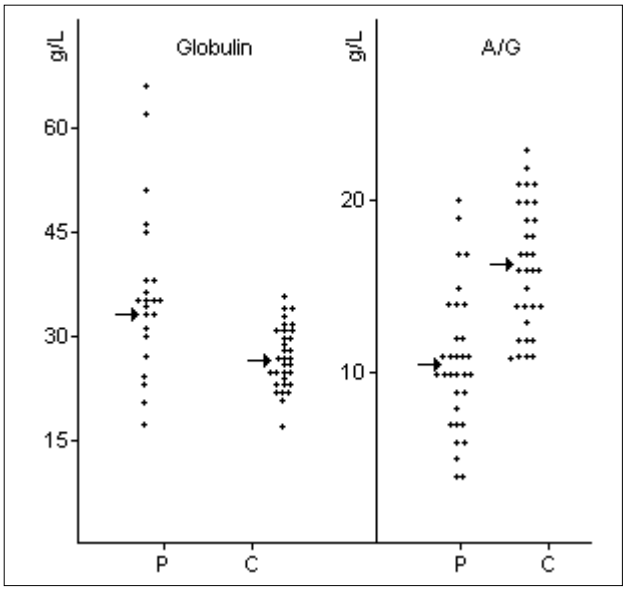


Figure 2: Distribution of globulin and A/G ratio in SLE patients (P) and normal control (C). The bar (□) indicates the 'normal reference interval' for the parameters.



The analysis of the parameters constituting the liver function test profile (Table 1) were carried out using the automated 'Parallel Analytical System' (American Monitor Corporation, Indianapolis, IN 66268). All analysis were done in duplicates. Both internal and external quality control systems were used for the quality control of the analysis. The globulin (G) level was calculated for each sample as the difference in the level of total protein and albumin (A) and the A/G ratio was calculated.

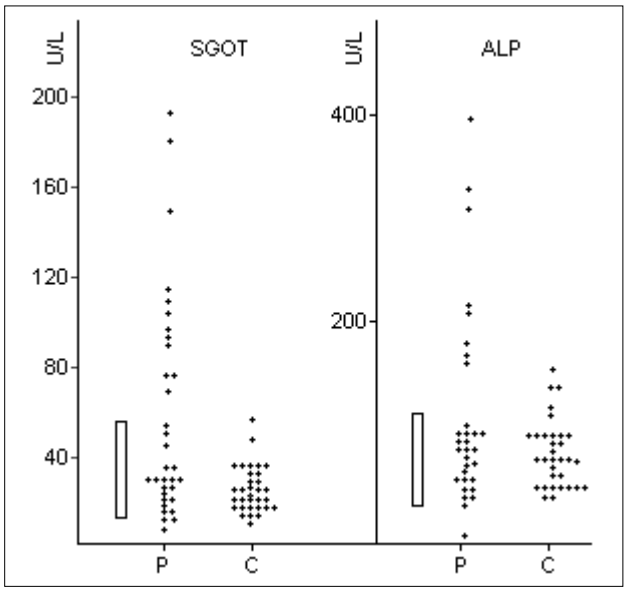
The results of the patients and controls were fed separately on the computer at King Saudi University Computer Center, Riyadh, and the mean and standard deviation were obtained using the Statistical Analysis System (SAS).

Table 1: The value of liver function test profiles in Saudi SLE patients an age and sex matched controls.

	SLE±SD		
Parameter	SLE patients	Control	p*
T. Bilirubin (μmol/l)	6.96±6.99	7.42±3.77	0.756
T. Protein (g/l)	61.81±22.44	71.39±5.39	0.035
Albumin (g/l)	28.32±12.21	44.21±4.96	0.0001*
Globulin (g/l)	31.74±15.92	27.24±4.47	0.181
A/G ratio	1.07±0.44	1.66±0.41	0.0001*
SGOT (U/l)	47.32±50.61	15.39±14.92	0.034*
ALP (U/l)	114.43±101.71	81.66±29.0	0.110
Cholesterol (mmol/l)	4.24±1.78	4.89±1.16	0.181
Triglyceride (mmol/l)	2.00±0.70	1.05±0.37	0.141

* P<0.05 was considered statistically significant.

Figure 3: Distribution of SGOT and alkaline phosphatase (ALP) in SLE patients (P) and normal control (C). The bar (□) indicates the 'normal reference interval' for the parameters.



The significance of the difference in the mean of each parameter in the patients and control group was obtained by applying the Student's t-test. p<0.05 was considered statistically significant.

Table 2: Number of liver function profile* abnormalities in SLE patients.

No. of abnormalities	No. of patients	Prevalence (%)
0	7	21.87
1	5	15.63
2	3	9.38
3	7	21.26
4	5	15.63
5	3	9.28
6	2	6.25

* Hyperglobulinemia is included in this calculation.

RESULTS

The mean and standard deviation for each of the parameters investigated in the SLE patients and the control group are presented in Table 1. The 't' test showed that the difference in the mean of albumin, globulin, A/G ratio, SGOT, alkaline phosphatase and cholesterol were statistically significant between the two groups.

The distribution of the total protein and albumin in the patients and control are presented in Figure 1. Four patients (i.e. 12.5%) had elevated protein level (i.e. >80 g/l) and in each case the elevation was due to high globulin level. Seven SLE patients (i.e. 21.875%) had hypoproteinemia (i.e. <60 g/l), while the rest had normal total protein. Hypoalbuminemia (i.e. albumin <35 g/l) was encountered in 21 patients (i.e. 65.6%).

The distribution of globulin level and A/G ratio in the SLE patients and the controls are presented in Figure 2. 53.12% had increased globulin level and A/G ratio less than 1.1 was encountered in 50% of the patients.

Figure 4: Distribution of cholesterol in SLE patients (P) and normal control (C). The bar (□) indicates the 'normal reference interval' for cholesterol.

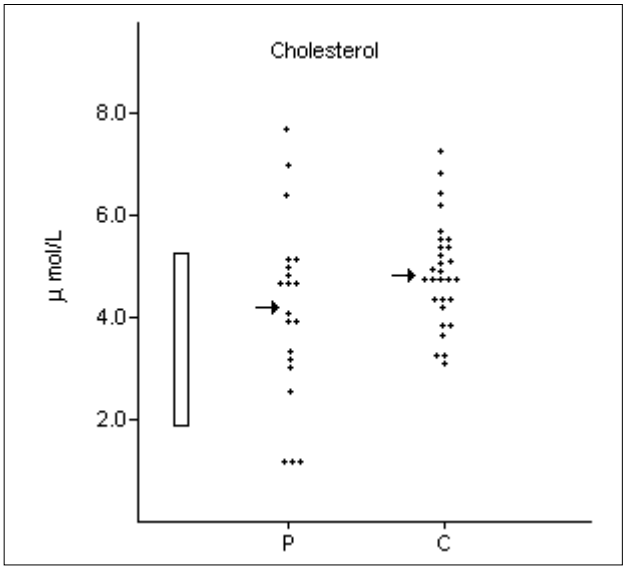
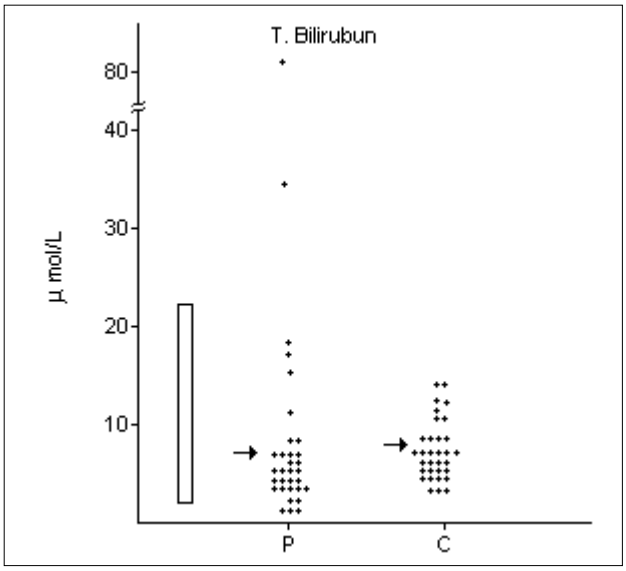


Figure 5: Distribution of total bilirubin in SLE patients (P) and normal control (C). The bar (□) indicates the 'normal reference interval' for bilirubin.



The distribution of alkaline phosphatase and SGOT in the SLE patients and the control group are presented in Figure 3. SGOT was elevated in 12 (37.5%) and alkaline phosphatase in 8 (i.e. 25%) of the SLE patients.

The distribution of total bilirubin is presented in Figure 4. Only 2 (i.e. 6.25%) patients had significantly elevated serum bilirubin while all others had the values in the 'normal range'.

Cholesterol distribution is presented in Figure 5. Three patients (i.e. 9.4%) had hypocholesterolemia and three (i.e. 9.4%) had hypercholesterolemia.

The number of SLE patients with one or more liver function profile abnormalities are presented in Table 2.

DISCUSSION

Systemic lupus erythematosus is often accompanied by a number of biochemical, hematological and immunological abnormalities. Though several of these abnormalities are non-specific (13).

It is generally agreed that liver involvement is relatively common is SLE patients.

However, the severity of liver involvement and the extent of liver function test abnormalities varies from one patient to another. Kofman and co-workers (6) reported hypoalbuminemia in 80% and hyperglobulinemia in 88% of 25 cases of SLE. The elevation of SGOT and SGPT were reported in 30% of SLE patients (7) and Gibson and

Myers (9) reported abnormal liver function tests in 55% of 81 SLE patients. However, Miller and co-workers (8) noted insignificant liver enzyme elevation in 23% of 260 patients with SLE, but no other serious hepatic involvement. Similarly, Gibson and co-workers (9) found no serious liver disease in SLE. Runyon *et al.* (11), on the other hand, found severe liver disorders including cirrhosis, chronic active hepatitis and granulomatous hepatitis in a large proportion of SLE patients. Bonafede *et al.* (14) fonud a single liver enzyme defects in 24% and two enzyme defects in 12% of 100 SLE patients investigated for the determination of hepatitis B surface antigen markers and suggested that the liver involvement was mild in their patients. Among the liver function test abnormalities hypoalbuminemia (i.e. albumin <35 g/l) was one of the most frequently reported findings in SLE and was encountered in almost 30-50% of the SLE cases, though the rest of the patients have normal albumin level (15-18). The hypoalbuminemia could be due either to decreased production of albumin caused by liver abnormalities of malnutrition, or may result from excessive albumin loss in the urine caused by renal disease. Renal function studies on SLE patients have shown that over half the patients have renal function abnormalities resulting in glomerular damage (19).

In this study, 7 of the 32 patients (21.87%) had no liver function abnormalities. Twelve (37.5%) had no liver enzyme abnormality and 5 (15.62%) had two liver enzyme abnormalities. Other liver function abnormalities ranging from 2-6 abnormal tests were encountered in almost 62.5% of the SLE patients. Two of these patients had severe liver disease indicated by significantly high plasma bilirubin, SGOT and alkaline phosphatase. Hypoalbuminemia was the most common abnormality and could have resulted from either liver damage, renal damage or both. Globulins were raised in (53.12%) of the patients investigated in this study. Serum electrophoresis revealed that the major elevation was in the d-globulins and ESR was elevated in all patients (Warsy *et al.* in preparation). The A/G ratio was decreased in several of the patients, in some due to decreased albumin level, while in others due to elevated globulin level. In numerous other studies hyperglobulinemia has been encountered. Dubois and Tuffanelli (19) found hyperglobulinemia in 32% of 398 SLE patients and Harvey *et al.* (20) found hyperglobulinemia in 58% of his SLE patients. The immunoglobulins and the immune complexes play an important role in the pathogenesis of SLE and elevation of immunoglobulins is a frequent finding.

In conclusion, this study has revealed that liver derangement is a common finding in SLE patients and determination of liver function tests in SLE patients during the study of disease prognosis are informative. Furthermore, drugs that further aggravate liver disorders should be avoid.

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