Ultrasound Findings in Systemic Lupus Erythematosus Patients in Saudi Arabia

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Abstract: Systemic lupus erythematosus (SLE) is a systemic inflammatory disease, which can affect multiple organs including liver, kidney, blood vessels, heart, and lungs. Early detection of organ damage is essential to optimise treatment of SLE and reduce the risk of irreversible organ damage. The objective of this study was to examine the frequency of ultrasound-detectable pathology in SLE population to determine the potential utility of routine ultrasound screening for SLE patients. the study samples were for the Patients who presented to the rheumatology clinic in King Abdulaziz University during January, 2011 to September, 2011 with SLE but with no abdominal symptoms. Associations between blood and urine biochemical markers and ultrasound-detectable pathologies were examined. the study illustrated that seventy-five patients were included in the analysis, mean age 32.75 ± 11.97. Of the total, 92% were female and 30.7% of the total studied samples were of Saudi nationality. Evidence of an enlarged liver was detected in 43% of the population, 22% had an enlarged spleen, and 30% had evidence of kidney disease. Ascites was present in the majority (88%) of patients, gallstones were detected in 8% of patients and thickening of the gall bladder wall in a further 7%. Moreover, 5% had evidence of enlarged lymph nodes. No significant correlations were detected between blood biochemical analyses and ultrasound-detectable pathologies. the study concluded that the multi-organ pathology is a major cause of morbidity and mortality in SLE. Presence of ultrasound-detectable pathology is high in patients with SLE suggesting that this may be a useful screening tool for early detection of systemic multi-organ disease.
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1. Introduction

Systemic lupus erythematosus (SLE) is a heterogeneous, systemic autoimmune disease, which can affect any part of the body. SLE is a rare disease affecting approximately 0.05–0.1% of the populations, approximately 90% of whom are female. (O'Neill and Cervera, 2010) Although prognosis following SLE diagnosis has improved significantly over recent years due to both earlier recognition and improved management, with five year survival now more than 90%, morbidity and mortality is significantly higher in patients who develop multi-organ disease and particularly those with renal and cardiovascular involvement.(Jakes, et al., 2012) Early detection of major organ involvement would enable earlier and more effective treatment and should improve mortality rates further.

Abdominal manifestations of SLE have been long been known to be both common and a major contributor to SLE-associated mortality. Through clinical examination, hepatomegaly incidence has been estimated to occur in around 40% of patients with SLE and splenomegaly in 6% (Kofman, et al., 1955. and Runyon, et al., 1980.) whilst studies of liver function in SLE patients using biochemical analyses observed abnormalities in 23-79% of patients.(Runyon, et al., 1980 and Miller, et al.1984) Recently, a study using ultrasound found hepatic abnormalities in 54% of SLE patients compared to 14% of healthy controls. Acute pancreatitis, although much rarer, is also found in SLE patients at an incidence of approximately 0.4 to 1/1000, rising to 8/100 of patients with abdominal pain. (Reynolds, et al. 1982; Saab et al., 1998 and Nesher, et al. 2006.) Despite low prevalence, mortality from pancreatitis is high at 27% and early detection is, therefore, essential.(Nesher, et al. 2006)

The use of imaging modalities, particularly ultrasound, as a clinical tool for diagnosis, prognosis, disease monitoring and prediction of response to treatment is becoming increasingly widespread across the medical spectrum.(Spyridopoulos, et al. 2010; Caiulo, et al. 2011; Gargani, 2011; Jain and Samuels, 201; Kaeley, 2011; and Mohammadi, et al. 2013) Although ultrasound images are not as precise as those obtained through computerised axial technology (CAT) or magnetic resonance imaging (MRI), it is a rapid and relatively inexpensive technique with good sensitivity and specificity and therefore an extremely valuable tool in clinical practice. Moreover, although technically an invasive procedure, due to penetration of body tissue by ultrasonic waves, there are no known examples of tissue damage for conventional ultrasound imaging and no known biological hazards

when used within the diagnostic range from the abovementioned illustration the main hypothesis reach to believe that ultrasound may provide a useful tool for early detection of organ involvement for patients with SLE. The aim of this study was to examine the frequency of ultrasound-detectable pathologies of the liver, kidney, spleen, gall bladder and lymph nodes in patients with SLE.

2. Methods

Patients and data extraction

Patients who presented to the rheumatology clinic in King Abdulaziz University during the period from January, 2011 to September, 2011 with SLE, but with no abdominal symptoms were enrolled into the study. Informed written consent of the patients was obtained before their inclusion in the study.

The following data were recorded:

1) Patient demographics, including age, sex and nationality

2) Urinary biochemical markers: urinary protein; urinary red blood cells; urinary white blood cells; urinary casts; 24 hour protein.

3) Blood biochemical markers: anti-nuclear antibody (ANA); antiDNA antibody (DNA); complement protein 3 (C3); complement protein 4 (C4); C-reactive Protein (CRP); erythrocyte sedimentation rate (ESR); vitamin D3 (VitD); haemoglobin; platelets; white blood cells; creatinine; alkaline phosphatase.

4) Ultrasound pathology: liver; spleen; kidney; gallbladder; presence of ascites; and lymph nodes.

Biochemical markers were coded as normal or positive/reduced, as applicable, for the purposes of analysis, except for haemoglobin, platelets, white blood cells, creatinine, alkaline phosphatise, CRP and ANA, which were analysed as actual levels. Ultrasound liver pathology was coded as normal, enlarged or shrunken, spleen as normal, enlarged or absent, kidney as normal or diseased, ascites as present or absent, gall bladder as normal, presence of gall stones, thickened wall or absent, and lymph nodes as normal or enlarged.

Statistical methods

Data was entered in excel and analysed using SPSSv19.0 for Windows (SPSS, Chicago, IL, USA). Demographic characteristics are presented for continuous variables as means and standard deviations and categorical variables as frequencies and percentages. Correlation between ultrasound features and blood/urine biochemical markers were examined using the chi-square test for categorical variables and student t-test and one-way ANOVA for binomial variables.

3.Results

Patient demographics

Seventy five patients were included in the analysis, mean age 32.75 ± 11.97 (Table 1). 92% of the patients were female and 30.7% were of Saudi nationality. Urinary markers were generally normal whilst most patients had raised C-reactive protein (CRP; 72%) and antiDNA (73%) and reduced complement 4 (C4; 69%) as expected for this study population (Table 2) Of the total, 58% of patients displayed abnormal ultrasound features in at least one organ.

Table 1. Patient characteristics

Demographic	N (%) or Mean ± SD
Age	32.75 ± 11.97
Gender	
Female	69/73 (94.5)
Male	4/73 (5.5)
Nationality	
Saudi	23/71 (32)
Non-Saudi	48/71 (68)

Evidence of an enlarged liver was detected in 43% of the population, 22% of the studied samples had an enlarged spleen and 30% of the studied samples had evidence of kidney disease (Table 3). Ascites was present in the majority (88%) of patients, gallstones were detected in 8% of patients and thickening of the gall bladder wall in a further 7%. Moreover, 5% of the studied samples had evidence of enlarged lymph nodes and 35% of patients showed normal ultra-sound detected pathology in all organs screened (liver, kidney, gallbladder, spleen, and lymph nodes). Also, 33% of the patients had one abnormal result, 16% of the studied samples had abnormal pathology in two organs and 9.4% of the patients had pathology in three or more organs. Screening was incomplete for 6.6% of patients. Presence of an enlarged liver was frequently associated with ultrasound-detectable enlargement of the spleen or evidence of kidney disease.

Relationship between biochemical analyses and ultrasound features

The relationships among blood and urine analyses were examined as well as, the presence of ultrasound detectable pathologies. The study illustrated that there is nNo significant relationships between biochemical analyses and either individual ultrasound pathologies or any ultrasound pathology (defined as abnormality in liver, kidney, spleen, gall bladder and/or lymph nodes) (Table 4). However, there was a trend towards higher 24 hour protein in patients with at least one ultrasound detectable pathology and towards patients with high urinary protein displaying one or more abdominal manifestations on ultrasound.

Table 2. Blood and urine analysis

Blood and urine analysis	N (%) or Mean ± SD
Urinary protein	
Normal	37/59 (62)
Positive	22/59 (38)
Urinary red blood cells	
Normal	45/59 (76)
Positive	14/59 (24)
Urinary white blood cells	
Normal	48/59 (81)
Positive	11/59 (19)
Urinary casts	
Normal	55/58 (95)
Positive	3/58 (5)
White blood cells	6.4 ± 3.0
Haemoglobin	10.8 ± 2.0
Platelets	272.9 ± 111.0
Creatinine	77.15 ± 59.3
Alkaline phosphatase	74.21 ± 36.2
24 hr protein	1.47 ± 1.64
ESR	49.3 ± 80.0
CRP	
Normal	18/64 (28)
High	456/64 (72)
ANA	843.19 ± 473.0
DNA	634.7 ± 571.0
Normal	11/41 (27)
High	30/41 (73)
C3	
Normal	47/60 (78)
Reduced	12/60 (20)
C4	
Normal	18/61 (30)
Reduced	42/61 (69)
VitD	30.2 ± 15.4

ANA, Anti-nuclear antibody; DNA, antiDNA antibody; C3, complement protein 3; C4, complement protein 4; CRP, C-reactive Protein; ESR, erythrocyte sedimentation rate; VitD, vitamin D3

Table 3. Ultrasound features

Ultrasound feature	N (%) or Mean ± SD
Liver	
Normal	42/74 (57)
Enlarged	32/74 (43)
Spleen	
Normal	57/72 (78)
Enlarged	16/73 (22)
Kidney	
Normal	52/74 (70)
Medical Disease	2/74 (30)
Ascites	
Present	623/73 (88)
None	9/73 (12)
Gallbladder	
Normal	62/73 (85)
Gallstones	6/73 (8)
Thick wall	5/73 (7)
Absent	0/73 (0)
Lymph nodes	
Normal	56/59 (95)
Enlarged	3/59 (5)

4. Discussion

This study set out to examine the frequency of ultrasound-detectable organ pathology in SLE patients and relevance to disease. As demonstrated in previous studies of SLE, a high frequency of abdominal manifestations were observed by ultrasound in the cohort.(Kofman, et al., 1955; Runyon, et al., 1980; Miller, et al. 1984; Reynolds, et al. 1982; Saab et al., 1998; and Nesher, et al. 2006) Patients most commonly showed liver, kidney and spleen abnormalities, with those displaying liver pathology also frequently showing pathology in either the kidney or the spleen. Less commonly abnormalities were detected in the gall bladder and the lymph nodes. This may reflect both reduced prevalence of these pathologies within the population and reduced sensitivity of ultrasound to detect abnormalities at these locations.

A large number of patients also displayed abnormal blood and urine tests, as may be expected for this population. However, no significant correlations were observed between biochemical analyses and ultrasound abnormalities, although trends were identified. The lack of significant correlations may reflect both the relatively low number of patients in the study and incomplete biochemical data for a number of patients in the study. Further study, with complete biochemical assessment in a larger study population may allow the preliminary findings of this study to be verified to significance.

The high frequency of ultra-sound detectable pathology in the SLE population highlights the potential of ultrasound as a diagnostic tool. Early detection of such pathology enables earlier intervention and therefore significantly reduces mortality and morbidity risks associated with organ disease. This study supports further exploration of the potential to introduce ultrasound as a routine screening tool in SLE clinics.

Conclusions

Multi-organ pathology is a major cause of morbidity and mortality in SLE. Presence of ultrasound-detectable pathology is high in patients with SLE suggesting that this may be a useful screening tool for early detection of systemic multi-organ disease. Further studies must be done for wider acceptability of ultrasonic as a routine screening tool for SLE.

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