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Evaluation of Serum Amyloid A and some Biochemical markers in Iraqi patients with systemic lupus erythematosus

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ABSTRACT: An autoimmune condition called systemic lupus erythematosus (SLE) is caused by long-term inflammation. Amyloid A (AA) amyloidosis results in nephropathy and other internal symptoms, including death. The current study set out to look at the relationship between serum amyloid A (SAA) levels in circulation and SLE patients. **Methods:** Sixty SLE patients and 30 healthy with age range (19-55) years were involved in this study. A SLE patient was identified in the teaching hospital in Baghdad. In this study, laboratory indicators such as blood lipid, kidney function, test results, and total cholesterol (TC), triglyceride (TG), SAA, and ALB were assessed using an automated biochemical analyzer. **Results**: Patients with active SLE had serum amyloid A (SAA) values 5.83 mg/L [IQR: 2.08–10.87], 4.92 mg/L [IQR: 1.57–11.43], and 1.33 mg/L [IQR: 0.13–3.12], respectively, substantially upper than persons with inactive SLE or healthy control subjects ($P < 0.001$). ESR values in healthy control subjects, patients with inactive SLE, and patients with active SLE. **In conclusion**, the current study's findings offered more proof of SAA's potential involvement in SLE and suggested that it might be valuable biomarkers that could reveal more details about the disease's activity.

Keywords: serum amyloid A (SAA), Lipid profile, Kidney function, Albumin

1. INTRODUCTION

Nearly all organ systems can be impacted by the multisystemic, autoimmune disease known as systemic lupus erythematosus (SLE), which is a long-lasting, recurrent sickness. Even for experienced professionals, diagnosing it is challenging because it does not come with a distinctive presentation. Autoimmune Lymphoma (SLE) is distinguished by the existence of autoreactive B and T cells as well as the generation of a diverse array of autoantibodies, or auto Abs SLE has been linked to more than fifty genes)1). Given that women of childbearing age are nine times more likely than men to acquire SLE, sex also plays a role in disease vulnerability. SLE has been hypothesized to be induced or enhanced by environmental factors, such as exposure to ultraviolet light and infection, such as the Epstein-Barr virus (2). Of patients (SLE), 35-75% develops clinically apparent lupus nephritis (LN). About 60% of individuals who present when they are around 50 years old have renal involvement, while 80% of youngsters have renal in volvement at some point throughout their disease (3). A well-known precursor of amyloid A (AA), primary isoform of severe-phase SAA and through tissue deposition it leads to secondary amyloidosis. Another indicator of inflammation is acute-phase SAA (4,5). The chemotactic and cytokine-like characteristics of recombinant human SAA were determined through in vitro characterisation. Serum amyloid A (SAA), which is current in blood, can increase 1000 times in a 24-hour period during an inflammatory response.

2. MATERIAL AND METHOD

Sixty SLE patients were identified in the teaching hospital in Baghdad. Every patient must have content the American College of Rheumatology's 1997 diagnostic requirements (8). Individuals with liver hepatitis, RA, malignancies, pregnancy, viral illnesses, steatosis, cirrhosis, and other conditions that potentially impair SAR were not

included in the study. In this study, laboratory indicators such as blood lipid, kidney function, test results, and total cholesterol (TC), triglyceride (TG), SAA, and ALB were assessed using an automated biochemical analyzer.

3. Statistical analysis

The spss20.0 was used to create the database. Category variables were linked using the chi-squared test., which were displayed equally counts. Data having a common supply were plotted as mean ± SD and subjected to a Pupil's t-test comparison. Data with non-normal distribution were displayed using the interquartile range (IQR) plus median.

4. Results

4.1 Features of the population under examination

The present study enrolled 60 patients with SLE were categorized into 2 groups, those who are active SLE (30 patients) and those who inactive SLE (30 patients). Table 1 displays the demographic details of both patients and healthy subjects. According to age, the mean age of patients with active SLE was 30.17 ± 8.38 years old, 29.86 ± 8.40 years old for patients with inactive SLE, and that of control subjects was 36.40 ± 11.16 ages and there was major change between dissimilar groups (P = 0.013). Regarding to gender, in overall, 20 (22.2%) male and 70 (77.8%) female were included. Patients with active SLE included 7 (23.3%) cases were male gender and 23 (76.7%) cases were female, patients with inactive SLE 5 (16.7%) cases were male gender and 25 (83.3%) cases were female, while control topics included 8 (26.7%) cases were male gender and 22 (73.3%) cases were female and non-significant change in the frequency dispersal of ills and healthy subjects allowing to gender (P = 0.638). Allowing to BMI, both groups of patients revealed a significant increase (p< 0.001) associated to control groups (28.78 ± 3.39 and 28.55 ± 3.43) vs (26.71 ± 2.86) respectively, whereas non-significant change (p>0.05) was found between patient groups themselves.

Table 1. - Characteristics of patients with SLE and healthy control

Characteristic	Active SLE (n=30) Mean ± SD	Inactive SLE (n=30) Mean ± SD	Healthy Control (n=30) Mean ± SD	*P*
Age (years)	30.17 ± 8.38^{A}	29.86 ± 8.40^{A}	36.40 ± 11.16^{B}	0.013
Sex				
Male	7 (23.3%)	5 (16.7%)	8 (26.7%)	0.638
Female	23 (76.7%)	25 (83.3%)	22 (73.3%)	
BMI kg/m2	28.78 ± 3.39^{A}	28.55 ± 3.43^{A}	26.71 ± 2.86^{B}	0.030
Duration of disease	5.93 ± 1.63	3.75 ± 1.25		> 0.001
Cho mg/dl	209.10 ± 20.38^{A}	202.0 ± 15.27^{A}	163.20 ± 18.67^{B}	> 0.001
TG mg/dl	200.96 ± 10.14^{A}	187.36 ± 11.29^{A}	110.43 ± 12.33^{B}	> 0.001
HDL mg/dl	34.63 ± 3.91^{A}	39.71 ± 1.95^{B}	42.96 ± 7.74^{C}	> 0.001
LDL mg/dl	112.42 ± 12.19^{A}	109.90 ± 11.74^{A}	97.83 ± 15.19^{B}	0.007
Urea mg/dl	57.76 ± 6.56^{A}	31.16 ± 4.01^{B}	23.36 ± 6.12^{C}	> 0.001
Creatinine mg/dl	1.86 ± 0.448^{A}	0.86 ± 0.156^{B}	0.75 ± 0.27^{B}	> 0.001
Total protein g/dl	6.49 ± 0.543^{A}	6.67 ± 0.502^{A}	7.17 ± 0.60^{B}	> 0.001
Albumin g/dl	3.04 ± 0.254^{A}	3.58 ± 0.514^{AB}	4.19 ± 0.46^{B}	0.017
ESR mm/h	56.36 ± 8.86^{A}	48.12 ± 5.32^{B}	5.13 ± 1.2^{C}	> 0.001

SAA mg/L	6.35 ± 2.64^{A}	5.27 ± 2.01^{B}	1.33 ± 0.43^{C}	> 0.001
Different latters signify to the significant differences at p< 0.05				

4.2 Measurements of inflammatory indicators

Values of erythrocyte sedimentation rate (ESR) in individuals with SLE who are either active or inactive, (56.36 ± 8.86 mm/h, 48.12 ± 5.32 mm/h) respectively, were higher than healthy control subjects (5.13 ± 1.2 mm/h, P < 0.001).

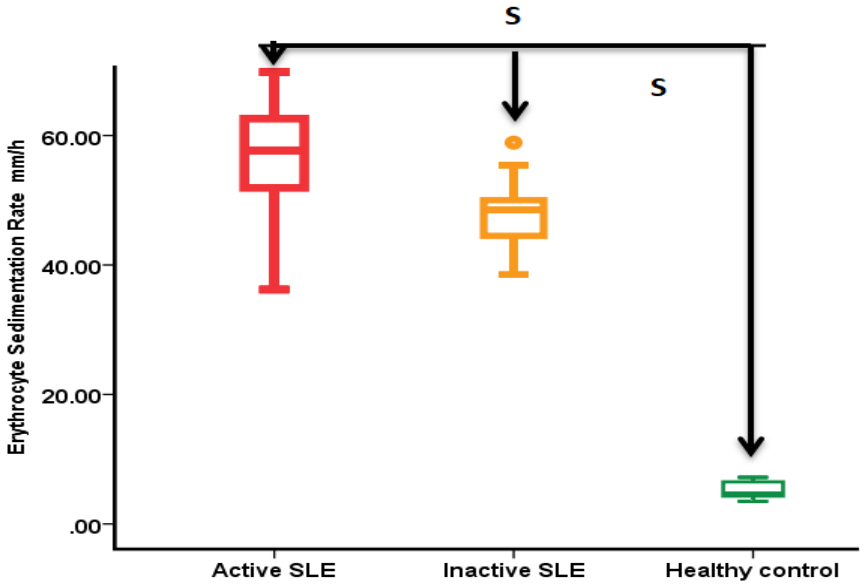

FIGURE 1. -. ESR levels between three groups.. NS: Not statistically significant, S: statistically significant P < 0.05

4.3 Measurements of serum Amyloid A (SAA)

Serum Amyloid A (SAA) concentrations in patients with active SLE were significantly greater than inactive SLE, or healthy control subjects (5.83 mg/L [IQR: 2.08–10.87], 4.92 mg/L [IQR: 1.57–11.43] and 1.33 mg/L [IQR: 0.13–3.12], respectively, P < 0.001).

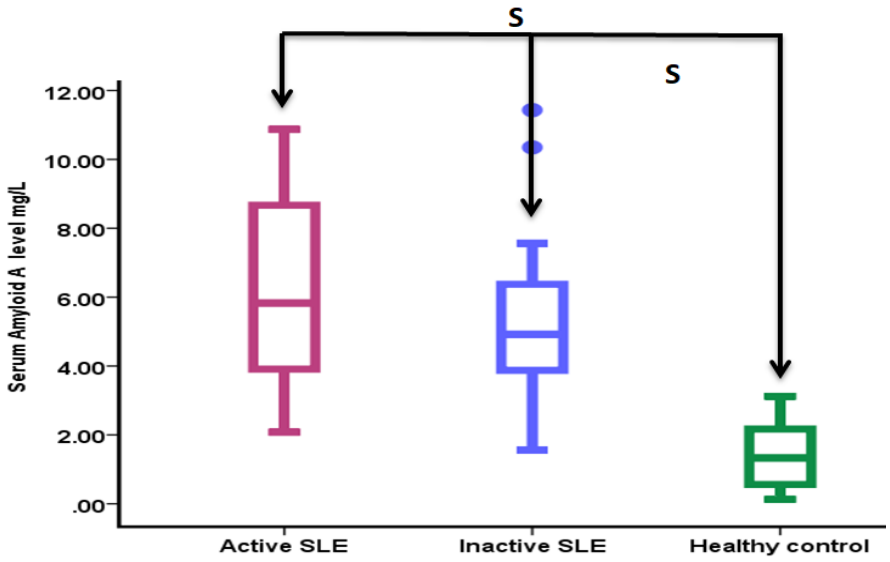

FIGURE 2. - Serum Amyloid A level in (active SLE, inactive SLE)patients and healthy control subjects. NS: Not statistically significant, S: statistically significant P < 0.05

4.4 Diagnostic accuracy of serum Amyloid A (SAA)

The diagnostic accuracy of utilizing SAA concentrations to differentiate between individuals with active SLE and healthy controls was investigated through the application of Receiver Operating Characteristic (ROC) analysis. An optimal SAA cut-off value of 3.58 mg/L resulted in an AUC value of 0.988 (95% sureness intermission [CI], 0.966-1.000, P < 0.001), sensitivity of 96.7%, specificity of 96.7%, PPV of 96.7%, and NPV of 96.7%.

In addition, an optimal SAA cut-off value of 2.5 mg/L could be used to distinguish inactive SLE from healthy control subjects with a sensitivity of 96.7%, specificity of 96.7%, PPV of 96.7%, and NPV of 96.7%. An optimal SSA cut-off value of 5.34 mg/L could be used to distinguish active SLE from inactive SLE with a sensitivity of 63.3%, specificity of 56.7%, PPV of 59.4%, NPV of 60.7%, and AUC of 0.613 (0.466-0.761), table (2).

Table 2. - Roc curve of serum Amyloid A (SAA)

Characteristic	**active SLE / Healthy control**	**Inactive SLE / control**	***active SLE / Inactive SLE***
Cutoff value (ng/mL)	> 2.40	> 2.5	> 5.34
P value	< 0.001	< 0.001	0.121
Sensitivity %	96.7 %	96.7 %	63.3 %
Specificity %	96.7%	96.7%	56.7 %
PPV %	96.7 %	96.7 %	59.4 %
NPV %	96.7%	96.7%	60.7%
AUC (95% CI)	0.988 (0.966- 1.000)	0.987 (0.961-1.000)	0.613 (0.466-0.761)

CI: Confidence interval, AUC: Area under curve.

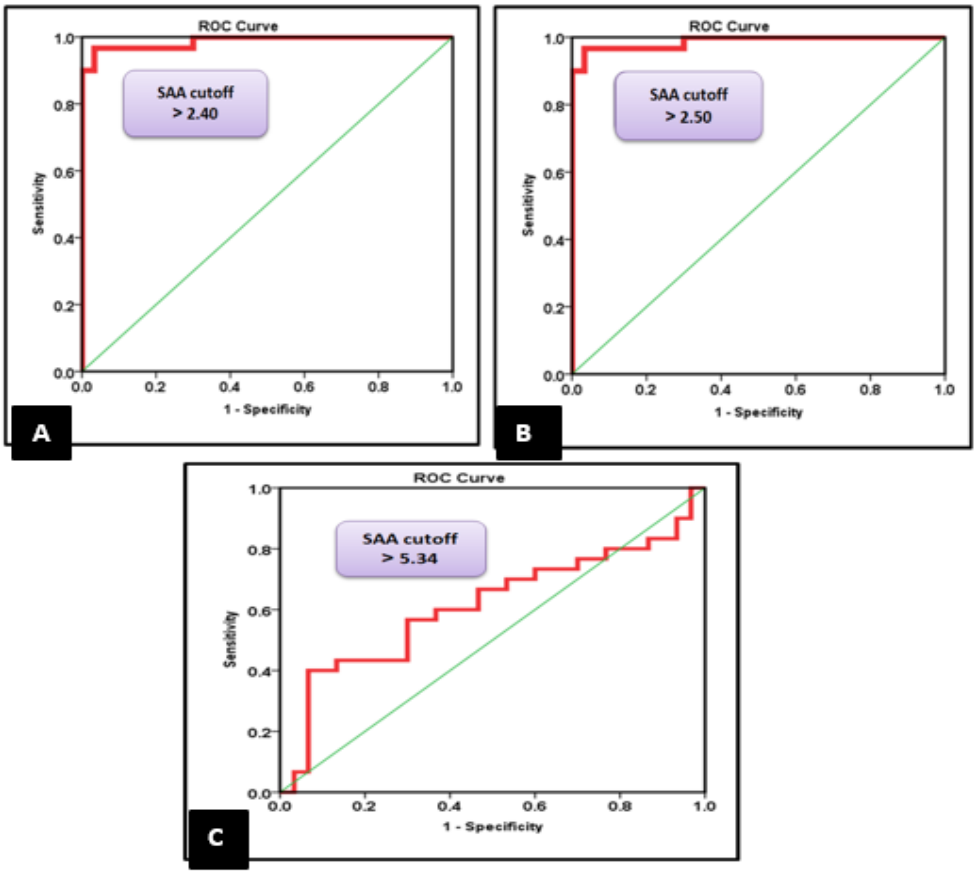

FIGURE 3. - (A) Receiver operating characteristic curve for SAA levels to detect active SLE from healthy control participants. (B) ROC for SAA levels to discriminate between participants with healthy controls and persons with inactive SLE. To distinguish among active and inactive SLE, use the receiver operating characteristic curve (C) for SAA levels

4.5 Correlation between serum Amyloid A levels and other parameters

The associations between serum levels of Amyloid A and other factors in patients with SLE were shown in tables (3). The present results show significant correlation between SAA and serum Creatinine in patients with active SLE. But the present results show non-significant correlation between SAA and all other parameters in both groups of patients.

Table 3. - Correlation between serum SAA level and inflammatory parameters.

Characteristic	SAA level			
	Active SLE		Inactive SLE	
	R	*P*	*R*	*P*
BMI	0.066	0.728	0.105	0.579
Cho	0.028	0.865	0.101	0.510
TG	0.026	0.823	0.015	0.936
HDL	0.123	0.517	0.219	0.245
LDL	0.012	0.950	0.203	0.283

Urea	0.324	0.080	0.187	0.322
Creatinine	0.406	0.026*	0.205	0.277
Total protein	0.036	0.852	0.044	0.816
Albumin	0.211	0.263	0.082	0.666
ESR	0.050	0.752	0.087	0.649

r: correlation coefficient.

5. Discussion

Long-term inflammation is the secondary cause of amyloid A (AA) amyloidosis, which results in nephropathy and other internal symptoms before dying (9). In certain rheumatic conditions, including (SLE), it is quite uncommon (10). Better levels of pro-inflammatory cytokines, containing TNF and Interleukins , cause over-transcription then the release of serum amyloid A (SAA), an severe stage reactant, during systemic infection. A series of pathological processes, such as protein misfolding, protein fragmentation, and aggregation into highly organized amyloid fibrils, are facilitated by persistently elevated SAA levels (5). The current study's findings offered more support for SAA's potential roles in SLE and suggested that it might be a valuable biomarker that could reveal more details about the disease's activity (11). Serum amyloid A (SAA) is a indicator for a number of illnesses, such as infections, inflammatory responses, and cancers. SAA levels increase during inflammation by 10–100 times and can increase by up to 1000 times during severe inflammatory situations (12). The current study displayed serum levels of amyloid A (SAA) were noticeably greater in individuals with active SLE compere control participants or patients with inactive SLE. The diagnostic accuracy of utilizing SAA concentrations to differentiate between individuals with active SLE and healthy controls was investigated through the application of Receiver Operating Characteristic (ROC) analysis. According to a study conducted in 2022, SAR had a bad prognosis for SLE and a strong prognostic value for active and plain active SLE. Elevated surface area ratio (SAR) could serve as a viable indicator to forecast the course and outcome of SLE patients in China (13). According to Dakua S. et al., there was a noteworthy rise in blood levels of VLDL-C, triglycerides, and cholesterol, nonetheless, a drop in HDL-C in SLE patients in contrast to controls. Dyslipidemia has been linked to this pattern (14). The patients with SLE must been stated to have proinflammatory HDLs. Additionally, they are distinguished by elevated levels of the prooxidant SAA and lower amounts of protective proteins such APOA1. These HDL proinflammatory characteristics include their ability to increase LDL oxidation, which results in the formation of immunological complexes, the activation of immune cells such monocytes, and the generation of anti-oxLDL antibodies (15). As mentioned earlier, proinflammatory HDL have higher SAA levels, which are also seen in rheumatoid arthritis patients' joints, atherosclerotic lesions in blood arteries, and several solid tumor types (16).For both short- and long-term therapy planning, it is critical to assess disease activity in SLE patients in a timely, sensitive, and targeted manner. Previous research has demonstrated an association between the severity of SLE and inflammatory variables, such as complement C3, complement C4, tumor-necrosis factor-α (TNF-α), cruel platelet volume and neutrophil to lymphocyte ratio [17–19]. These earlier investigations' results confirm that inflammatory cytokines are crucial to the pathophysiology and etiology of SLE (20-21).

The autoimmune disease recognized as systemic lupus erythematosus (SLE) is categorized by a reduction in immunity to autoantigen, such as the nuclear antigen, and by the creation of autoantibodies and other immune complexes that cause organ damage and tissue inflammation. SLE is a result of a complex interaction between hereditary and ecological causes; over 90% of cases involve females (22).Neonatal septicemia, diabetic renal disease, rheumatoid arthritis, and other conditions have been linked to SAA, a new inflammatory factor, according to recent research (18-20). Increased SAA levels were linked to rheumatoid arthritis patients' disease activity, according to Hwang et al. (23) superior measure of illness activity compared to C-reactive protein (CRP). SAA has been linked to the growth of atherosclerosis and has been identified as a critical biomarker in pro-inflammatory and pro-atherogenic disease action. Women with polycystic ovarian syndrome (PCOS) had a considerably greater level of SAA than controls in another study. Serum SAA levels were considerably higher in patients with young idiopathic arthritis related to healthy controls in a case-control study conducted by Dev et al. (24). Furthermore, lung infections in SLE patients have been linked to elevated SAA levels (25). The results of the current investigation demonstrated that SAA values were considerably greater in patients with active SLE than in individuals with inactive SLE, which is consistent with these earlier findings. The SLE patient, the level of SAA was independently correlated with illness activity. Increased peripheral CD4+ lymphocyte percentage, ESR, and CRP have all been found to be strongly correlated with elevated SAA values in patients with acute rejection following lung transplantation, juvenile idiopathic arthritis, and polycystic ovarian syndrome (PCOS) (25,26). As the target organ of immune-mediated injury, the liver can induce immunological tolerance, which can lead to a reduction in albumin synthesis in SLE. Moreover, the buildup of immune complexes may develop in lupus nephropathy, which worsens renal

protein loss. In fact, SLE patients frequently exhibit hypoalbuminemia. Anti-dsDNA is often detected in both serum and inflammatory lesions in glomerulonephritis, and is considered a crucial indicator in assessing the disease activity of SLE (27). The idea that anti-dsDNA is pathogenetically significant has been reinforced by the observation that elevated circulating antibody levels are typically linked to renal involvement and active SLE.(27).

Numerous studies have demonstrated that laboratory indicators, including as age, sex, race, economic status, and organ damage, might be used to assess treatment effect, recurrence, activity, and treatment outcome in addition to serving as key reference values for SLE diagnosis. Previous studies found that men had a worse prognosis than women, that Caucasians had a better prognosis than Blacks, and that patient with better family economic circumstances and higher educational attainment had a better prognosis than patients with lower family economic conditions and lower educational attainment (28).

Consequently, immune cells are implicated in immunological alternations, particularly T and B lymphocytes that are stimulated to create distinct immune components. Among these elements are autoantibodies that, according to the postulated hypothesis of molecular mimicry, respond with self-antigens in addition to non-self-antigens(29).

6. Conclusion

The purpose of this study was to examine the relationship between serum amyloid A (SAA) levels and systemic lupus erythematosus (SLE) activity. In SLE patients, there was a significant correlation found between SAA levels and disease activity, with SAA levels being strongly linked to active SLE.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest

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