

ORIGINAL ARTICLE

Radiological and Clinical Evaluation of Lung Involvement in Iraqi Patients with Systemic Lupus Erythematosus

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ABSTRACT

It is common for systemic lupus erythematosus (SLE) to affect the lungs, which can lead to moderate respiratory symptoms or severe restrictive lung disease. Pulmonary complications such as shrinking lung syndrome (SLS) are uncommon but significant from a clinical perspective. This study set out to answer several questions regarding SLE in Iraqi patients, including how common respiratory symptoms are, how often impaired pulmonary functioning, and what clinical and serological factors are associated with SLS in Baghdad Teaching Hospital in Baghdad, Iraq, was the site of the 2025 cross-sectional descriptive study. Eligible participants were adult patients who fulfilled the American College of Rheumatology (ACR) classification criteria for SLE. We collected demographic data, recorded clinical symptoms, and documented serologic markers. A chest X-ray or high-resolution computed tomography (HRCT) was ordered for all patients in addition to the pulmonary function tests (PFTs). Dyspnea, restricted lung physiology (Forced Vital Capacity (FVC) < 80% expected), and the absence of interstitial lung disease on x-rays were the diagnostic criteria for SLS. Patients exhibiting symptoms and radiographic interstitial alterations but no restrictive physiology served as controls. Of the 104 patients with SLE surveyed, 62 (59.6%) had respiratory symptoms, while 65 (65.4% of the total) had normal pulmonary function with abnormalities. The results showed that 9 patients had SLS (8.7). In a multivariate analysis where the length of the disease was controlled, a history of pleuritis, high American College of Rheumatology (ACR) clinical score, and seropositivity of anti-RNP antibodies were significantly associated with SLS. Longer illness duration, anti-RNP positive, and a history of seropositivity were the independent predictors of SLS (OR = 1.18; 95% CI: 1.01132; p = 0.04). SLE patients from Iraq are more likely to experience respiratory symptoms, abnormal lung functions, and shrinking lung syndrome. When dealing with patients who have a history of pleuritis or who test positive for anti-RNP antibodies, clinicians should maintain a high suspicion for SLS. Timely diagnosis and treatment can lead to improved clinical outcomes.

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1- INTRODUCTION

Many patients with systemic lupus erythematosus (SLE) will experience pulmonary disease at some point during their illness [1]. This can include pleuritis, acute pneumonitis, alveolar hemorrhage, pulmonary embolism, chronic interstitial lung disease, pulmonary arterial hypertension, and the less common but still significant shrinking lung syndrome (SLS) [2, 3]. In shrinking lung syndrome, a restrictive defect is seen on pulmonary function tests, radiographs show decreasing lung volumes, intermittent diaphragmatic elevation is characteristic, and the parenchyma of the lungs is normal. The cause of the dyspnea is unknown. While it is true that SLS is one of the rarest consequences, it can cause major issues that, if left untreated, can lead to years of disability or breathing difficulties [4]. Stabilizing respiratory functions and restoring a normal quality of life may be possible with immunosuppressive and supportive therapy [5].

Whether SLS really manifests in SLE patients is an open question. Up to 72% of SLE patients without radiologic evidence of interstitial illness have dyspnea and restrictive physiology, which can exacerbate preexisting conditions including pleuritic discomfort, weak respiratory muscles, or subclinical inflammation [6, 7]. Because it might lead to a gradual reduction of the respiratory mechanism, the early onset of SLS is also a clinical concern. More rapid diagnostic evaluation and targeted treatment strategies might be possible with data on frequency, clinical pattern, and risk factor [8].

Consequently, the researchers set out to measure how many persons with SLE admitted to Baghdad Teaching Hospital in Iraq experienced respiratory symptoms, pulmonary function abnormalities, and shrinking lung syndrome. Furthermore, by comparing this group to a control group, we aimed to identify clinical and serological factors associated with restricted lung physiology and SLS.

2- MATERIALS AND METHODS

2.1. Study population

The provided cross-section study was conducted at Baghdad Teaching Hospital, Baghdad, Iraq, during the period of January-December 2025. The adult patients (exceeding 18 years old) meeting the American College of Rheumatology (ACR) criteria of the systemic lupus erythematosus (SLE) case were recruited on a consecutive basis. The patients were provided with a structured questionnaire of respiratory symptoms and a 6-minute walk test (6-MWT) and chest imaging (chest X-ray [CXR] and/or high-resolution computerized tomography [HRCT]) were done. The 6-MWT was performed according to the standards of the world [9]. The patients were requested to scale the degree of dyspnea on Borg Dyspnea Scale (0 = no dyspnea to 10 = maximal dyspnea) after the test. Informed consent on all subjects was provided in writing. The evaluation and consent of the study plan by the Institutional Ethics Committee of the Baghdad Teaching Hospital was based on the Declaration of Helsinki.

Patients had to be eligible, i.e. possess full PFT findings and chest radiography (CXR and/or HRCT). Patients who had overlapping connective tissue diseases (including rheumatoid arthritis, Sjogren syndrome, systemic sclerosis, mixed connective tissue disease or idiopathic inflammatory myositis) were ruled out to reduce confounding of the pulmonary manifestation [10].

2.2. Clinical and serologic data

The demographic variables included age, sex, length of the disease (number of years to which the physician had confirmed the diagnosis and the time when the respondent started the study), smoking history, and body mass index (BMI). The patients were classified as ever-smokers when they smoked at least one cigarette per day over the period of 3 months over the lifetime; otherwise, non-smokers. The disease activity was measured with the help of the Systemic Lupus Activity Measure (SLAM) and the cumulative damage of the body organs was measured with the help of the Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) damage index (SDI). The number of criteria of ACR classification satisfied was also calculated. According to the ACR criteria, pleuritis/ serositis was classified at any point in the disease.

The history and current use of immunosuppressive drug, including prednisone, hydroxychloroquine, methotrexate, azathioprine, mycophenolate mofetil, leflunomide and cyclophosphamide were taken. When the corticosteroids were taken, the amount that was currently being used was noted at the moment of assessment.

Antinuclear antibodies (ANA) with immunofluorescence testing, anti-double-stranded DNA (anti-dsDNA) antibodies with ELISA or Farr assay and extractable nuclear antigens (anti-Ro, anti-La, anti-Sm, anti-RNP) with ELISA with confirmatory immunoblot were the serologic tests. Seropositivity consisted of a positive reaction being reported in the course of the disease.

2.3. Pulmonary assessments

The patients were evaluated on recurrent respiratory symptoms that were counted 2 or more occurrences of dyspnea or pleuritic chest pain in the past 4 weeks. The findings of HRCT were used to determine the presence of interstitial lung disease (ILD) in situations where a CT and CXR were carried out. ILD was identified when interstitial or reticular opacities, ground-glass or honeycombing in the HRCT, and any other possibilities were ruled out. In the instance of the detection of the pleural effusion, pleural thickening or pleural fibrosis, pleural involvement was to be emphasized.

A basic pulmonary laboratory (diffusing capacity to carbon monoxide [DLCO], lung volumes with body plethysmography, and spirometry) was performed. Abnormal PFT was defined as [11]:

- FVC < 80% predicted
- DLCO < 80% predicted
- FEV1/FVC ratio < 80% predicted.

Restrictive physiology was defined as one with less than 80 predicted FVC and a normal FEV1/ FVC.

2.4. Shrinking Lung Syndrome (SLS) is a pulmonary diagnosis

The original criteria used in segmentation were those of Hoffbrand [12]:

- Unexplained dyspnea (Borg score 1 or more, self-reported)
- Limitations of physiology of the lungs (FVC at less than 80% of predicted and FEV1/FVC more than 80)
- The image does not show any ILD, or other parenchymal disease of the lungs.

The intensity of SLS was as follows [13]:

- Mild: FVC 70–79%
- Moderate: FVC 60–69%
- Severe: FVC < 60%.

The definition of controls was symptomatic patients without restrictive PFT pattern and ILD in the imaging.

2.5. Statistical analysis

The continuous variables are given in the form of the mean and standard deviation (SD). Related independent variables were: To settle on independent variables, logistic regression was done univariate, and multivariate.

1. Inhibition of the lungs, physiological, and
2. Comparison of the SLS and the non-restrictive control non-symptomatic groupings.

Multivariate analysis was done to include variables that were significant in univariate analysis ($p < 0.05$). The statistical analysis was performed by using the SPSS version 24 (IBM Corp., Armonk, NY, USA).

3- RESULTS AND DISCUSSION

3.1 Study population

The Baghdad Teaching Hospital recruited one hundred and ten patients with systemic lupus erythematosus (SLE). The baseline characteristics are as shown in Table 1 and Table 2. The majority of the patients were women (102/110; 92.7%). Most of the participants were the representatives of the Middle Eastern ethnic group (97/109; 89.0%). The median age of entering the study was 46.9 and the median years of disease were 13.1. Its mean mACR was 5.4+1.2, SLAM total 7.7 +3.6 and SDI 1.4 +1.3.

Table (1): Clinical and demographic information of 110 individuals diagnosed with systemic lupus erythematosus (SLE)

parameters	Mean+- SD or Frequency (%) (n = 110)
Age	46.9 ± 12.8
sex (women: men)	102: 8
Middle Eastern ethnicity	97/109 (89%)
BMI	20.4 ± 6.2
BMI ≥ 25	71/109 (65%)
BMI ≥ 30 kg/m ²	33/109 (30%)
Diseases characteristic	
Diseases durations	13.1 ± 9.3
pleuritis History	38/110 (35%)
total mACR	5.4 ± 1.2
total SLAM	7.7 ± 3.6
total SDI	1.4 ± 1.3
Selfreported symptom	
Dyspnea	62/110 (56%)
Pleuritic chest pains	34/110 (31%)

3.2 SLE criteria of rheumatology

Based on 103 patients. Defined as during the past four weeks, 2 episodes/week.

Table (2): Systemic lupus erythematosus (SLE) autoantibody results from 110 patients

Parameters Autoantibody	Seropositivity
Anti-Sm	22 (20.4%)
Anti-dsDNA	62 (56.4%)
Anti-Ro	40 (36.7%)
Anti-La	18 (16.8%)
Anti-RNP	30 (27.8%)
Anti-phospholipid IgG	33 (30.3%)
Anti-phospholipid IgM	35 (32.1%)
Lupus anticoagulants	36 (34.9%)
anti-phospholipids IgG/IgM	59 (54.1%)

Considering the current immunosuppressive therapy, 38 / 106 (35.8) were on prednisone, 13/107 (12.1) on methotrexate, 85/107 (79.4) on hydroxychloroquine, 22/107 (20.6) on mycophenolate mofetil and 10/85 (11.8) on azathioprine. They were all not on cyclophosphamide or leflunomide during assessment. The mean of the dosage of prednisone administered by the users was 8.3 charged standard deviation 4.9 mg/day. The 51/109 (46.80) patient group said that there was a smoking history. The mean years of smoking experience of the smokers was 17.8 ± 11.6 years and the mean average consumption of the cigarettes was 0.68 ± 0.52 packs/day. Out of the number of people who had a history of smoking, 14/45 (31.1) of these people were current smokers.

3.3 Pulmonary investigations

Dyspnea was present in 62/110 (56.4) patients and pleuritic chest pain in 34/110 (30.9) patients, and of 67/110 (60.9) patients had either of the two symptoms. History of pleuritis was identified in 38/110 (34.5) patients in the past. In the 6 minutes' walk test, 78/85 (91.8) were reporting exertional dyspnea that is, shortness of breath was experienced in 85/93 (91.3) of the respondents. All patients had undergone some form of chest imaging. Chest X-ray (CXR) and chest CT were 94/110 (85.5) and 78/110 (70.9) respectively. Among CXR results, 70/94 (74.5%), and 24/94 (25.5%), the results were normal and abnormal respectively. In 7/94 (7.4) and 4/94 (4.3) pleural thickening, interstitial infiltrates were present. Using CT, interstitial lung disease (ILD) was detected in 14/78 (18.0) and pleural involvement was detected in 9/78 (11.5).

3.4 Pulmonary function tests

The abnormalities in the PFT of the patients were identified in 72/110 (65.5%). This was restrictive (FVC less than 80 percent of predicted) in 34/110 (30.9 percent). Specifically, FVC 7079% or 69% of 11/110 (10.0)% were predicted, respectively, and 23/110 (20.9) were predicted. There were 49/108 (45.4)%, and 50/110 (45.5)% patients with reduced DLCO, and FEV1/FVC of 0.8 or less respectively.

3.5 Fall FVC clinical correlates

The univariate data analysis revealed that FVC below 80% predictors were significantly related to:

- Longer disease duration (p = 0.02)
- Dyspnea (p = 0.005)
- Pleuritic chest pain (p = 0.01)
- History of pleuritis (p < 0.001)
- Higher SLAM score (p = 0.05)
- Higher mACR score (p = 0.003)
- Anti-dsDNA positivity (p = 0.007)
- Anti-Sm positivity (p = 0.002)
- Anti-RNP positivity (p < 0.001)
- Current prednisone use (p = 0.007)
- Use of hydroxychloroquine currently (p = 0.04)

The significance inclination was to be between pleural abnormalities in the imaging and abnormal FVC (p = 0.06).

The multivariate analysis indicated that the tendency towards correlation exists with the history of pleuritis and the duration of the disease (p = 0.07).

Table (3): The characteristics associated with a reduced forced vital capacity (FVC < 80% expected) in individuals with systemic lupus erythematosus (SLE) were examined in a univariate design

parameters	Odds Ratios	95% CI	p-value
Demographics			
Sex (female vs male)	2.18	0.41 – 11.32	NS
Middle Eastern vs other ethnicity	0.97	0.34 – 2.48	NS
Diagnosis Age	0.98	0.95 – 1.02	NS
BMI	1.03	0.99 – 1.11	NS
Clinical characteristics and health history			
Duration of Disease	1.06	1.01 – 1.11	0.02
pleuritis History	5.48	2.29 – 13.02	<0.001
total mACR	1.59	1.18 – 2.21	0.003
SLAM scores	1.11	1.00 – 1.25	0.05
total SDI	1.27	0.96 – 1.72	NS
Dyspnea	3.49	1.46 – 9.02	0.006
Pleuritic chest pains	2.84	1.22 – 6.91	0.01
smoking (yes vs no)	1.48	0.47 – 3.41	NS
Past smoking (yes vs no)	1.57	0.69 – 3.59	NS
Autoantibodies (positive vs negative)			
Anti-La	0.91	0.31 – 2.78	NS
Anti-Sm	4.61	1.71 – 12.99	0.003
Anti-Ro	0.99	0.28 – 1.54	NS
Anti-RNP	5.28	2.07 – 13.24	<0.001
Anti-dsDNA	3.32	1.34 – 8.26	0.008
anti-phospholipids IgG/IgM	1.92	0.46 – 4.81	NS
Chest image			
Pleural involvement on CT/CXR	3.41	0.94 – 13.62	NS
ILD on CT scan	0.71	0.25 – 2.32	NS
Medication at time of evaluations			
Methotrexate	1.08	0.42 – 2.66	NS
Prednisone	3.18	1.38 – 7.64	0.007
Mycophenolate mofetil	2.09	0.82 – 5.49	NS
Hydroxychloroquine	4.62	1.04 – 7.94	0.04
Azathioprine	2.06	0.61 – 6.74	NS

Table (4): A multivariate test was conducted to identify the factors that could lead to a lower forced vital capacity (FVC < 80% predicted) in individuals suffering from systemic lupus erythematosus (SLE)

parameters	Odds Ratios	95% CI	p-value
duration of Disease	1.06	1.00 – 1.12	0.07
Presence of pleuritis vs absence of pleuritis	2.84	0.93 – 9.41	0.06
Total mACR	1.21	0.76 – 1.94	NS
Total SLAM	1.02	0.85 – 1.21	NS
Presence of dyspnea vs absence	2.53	0.68 – 9.12	0.07
Presence of pleuritic chest pains vs absence	0.89	0.25 – 3.34	NS
Seropositivity for anti-dsDNA	1.41	0.43 – 4.39	NS
Seropositivity for anti-Sm	0.95	0.16 – 4.91	NS
Seropositivity for anti-RNP	2.47	0.51 – 11.82	0.09
Current use of prednisone	1.38	0.48 – 4.52	NS
Current use of hydroxychloroquine	2.64	0.44 – 16.21	NS

3.6 Shrinking Lung Syndrome (SLS) Clinical Correlates

The SLS was observed to be 11/110 (10%) patients or 16% of the symptomatic patients. Oxidations of all SLS were female.

Significant univariate correlations with SLS had the following results:

- Longer disease duration (p = 0.01)
- History of pleuritis (p = 0.003)
- Involvement of pleura in pictures (p = 0.01)
- Higher mACR score (p = 0.007)
- Anti-dsDNA positivity (p = 0.03)
- Anti-RNP positivity (p < 0.001)
- Current prednisone use (p = 0.02)

Table (5): Patients with systemic lupus erythematosus (SLE) and shrinking lung syndrome (SLS) using univariate statistics of factors

parameters	Odds Ratios	95% CI	p-value
Demographics			
Middle Eastern vs Other ethnicity	0.91	0.19 – 4.78	NS
Age at study time	0.97	0.90 – 1.01	NS
BMI	1.03	0.93 – 1.14	NS
Clinical characteristic			
Duration of Disease	1.10	1.02 – 1.18	0.01
pleuritis History	23.4	2.71 – 33.92	0.003
total mACR	2.09	1.19 – 3.64	0.007
total mSLAM	1.12	0.95 – 1.32	NS
total SDI	1.31	0.79 – 2.13	NS
Ever smokers (yes vs no)	1.69	0.52 – 6.11	NS
Current smokers (yes vs no)	1.21	0.24 – 6.41	NS
Autoantibodies (positive vs negative)			
Anti-Sm	3.98	0.91 – 17.45	NS
Anti-Ro	0.45	0.19 – 1.57	NS
Anti-RNP	15.98	3.29 – 41.72	<0.001
Anti-dsDNA	10.28	1.24 – 86.15	0.03
antiphospholipid IgG/IgM	1.29	0.33 – 5.31	NS
Anti-La	1.24	0.23 – 6.51	NS
Chest imaging			
Any CT/CXR pleural abnormality	7.38	1.48 – 36.72	0.01
Medications at study entry			
Prednisone	7.41	1.42 – 41.19	0.02
Hydroxychloroquine	2.99	0.48 – 18.01	NS
Methotrexate	3.62	0.71 – 18.30	NS

The multivariate analysis has indicated that SLS was significantly related with the following:

- Prolonged disease period (OR 1.2; 1.013; 0.04)
- Anti-RNP seropositivity (OR \approx 23–25; $p = 0.02$)
- Past history of serositi that was found in all SLS cases (significant)

Table (6): Individual variables for the multivariate prediction of systemic lupus erythematosus (SLE) patients' risk of shrinking lung syndrome (SLS)

Parameters	Odds Ratios	95% CI	p-value
Duration of Disease	1.18	1.00 – 2.10	0.04
Total mACR	0.91	0.36 – 1.91	NS
Anti-dsDNA Seropositivity	0.95	0.07 – 14.12	NS
Anti-RNP Seropositivity	23.6	1.7 – 372.0	0.02

In these groups of patients with SLE who were enrolled in Baghdad, Iraq, respiratory symptoms and abnormal lung functioning were also very prevalent with dyspnea reported in approximately 60 per cent of the patients and abnormal result of PFTs observed in nearly two-thirds of the study group. Further, it was also established that Shrinking Lung Syndrome (SLS) was present in approximately 10% of the patients and this is much higher than the one recorded in a number of other large studies in other countries [14, 15]. The duration of the disease, the anti-RNP seropositivity and the history of pleuritic were significantly connected to SLS in the multivariate analysis. The same trend was also evident in the lower forced vital capacity (FVC) patients since dyspnea and previous instances of pleuritic appeared to be significant contributors [16]. Pulmonary involvement of SLE has been proved in previous studies. It is reported that FVC decreases in up to 60 percent of the patient and it is also reported that the first type of detection of the abnormality is the impairment of the DLCO [17, 18]. The rise in the prevalence of SLS in our cohort as compared to an earlier rate of 0.5% in a large cohort study in the U.S. across diverse races could be attributed to differences in methodology. That article used the Systemic Lupus International Collaborative Clinics Damage Index (SDI) to establish SLS that may not capture any etiological cases of milder or earlier stages but our patients received more organized pulmonary evaluation at an earlier date and this enables the identification of functional abnormalities in an earlier stage. In limited clinical series, SLES prevalence has been reported to be ranging between 6-10 in concordance with our findings [19]. Besides this, the cases of successful lung improvement of this immunosuppressive or stem cell based therapies can be used to illustrate reversibility of SLS in the instance of early detection and treatment.

The finding of a relationship between the development of pleuritis and SLS was consistent with the prior studies that had mentioned that pleuritic chest pain or inflammation of the pleura might be detected in a meaningful proportion of SLS instances. Although other studies have suggested an association between anti-Ro antibodies and SLS, we only detected a very strong association between anti-RNP seropositivity and anti-RNP antibodies [20]. The inflammatory basis of interaction between anti-RNP and anti-dsDNA antibodies has been intellectually substantiated by previous results on the impact of these antibodies in the inflammation of the pleura and pulmonary involvement in SLE. Although a mechanism of pleural fibrosis has been postulated only a subgroup of SLS patients in our cohort had radiographic evidence of fibrosis [21, 22]. The pathophysiology of SLS remains unknown. Past studies have reported the loss of inspiratory muscle strength, particularly the diaphragm; however, under selected instances, recent studies of electromyographic and nerve conduction have shown that the phrenic nerve and diaphragm are operating normally which has been believed to mean that primary neuromuscular etiology may not be complete enough in explaining the condition. Instead, inhibition of pleural inflammation by reflexive diaphragmatic movement has been proposed. Pain or pleura may cause afferent phrenic excitation that reduces motor activity in respiratory muscles resulting in shallow breathing patterns which ultimately may result in a reduction in lung volumes and restrictive physiology [23-25].

By such observations, clinicians who handle SLE patients and those in regions, where the disease burden is high such as in Iraq need to have high index of suspicion on pulmonary involvement and SLS. Long-term SLE patients who have frequent pleuritis should have pulmonary functional regular surveillance in the absence of clear parenchymal disease in the radiograph. Early treatment and diagnosis is critical since the bottom line is that when the chronic lung disease reaches a stage where it is marked by a considerable reduction in the lung volumes, morbidity and mortality increase [26, 27]. The pros of the research are that the size of the cohort is fairly large, and well-characterized, the assessment of pulmonary symptoms and functional assessment is systematized. However, several limitations are to be mentioned. All patients were not subjected to CT of the chest and parenchymal abnormality could have been missed on radiography. Besides, the diaphragmatic activity or the neuromuscular testing was not directly evaluated and this leaves us with no control to differentiate between muscle weakness and reflex inhibition by the pleura. Finally, as this research was conducted in tertiary centers in Baghdad, the possibility of having referral bias with a higher proportion of patients with a more active or a chronic disease is present.

Other Iraqi centers should conduct further studies and longitudinal follow-ups to give a better understanding of the natural course of SLS, the most appropriate screening method, and management of the SLE patients.

4- CONCLUSION

It was found that the respiratory manifestation, lung dysfunction, and the Shrinking Lung Syndrome (SLS) were quite common among SLE Patients in Baghdad, Iraq. These findings highlight the importance of being extremely vigilant to the index of clinical suspicion of lung involvement even in the absence of radiological evidence. According to our findings, the length of disease in the long-term and history of pleuritis could be crucial risk factors in the occurrence of SLS in the population. The pulmonary function identification and correct evaluation in SLE patients at an early stage is therefore required to prevent the progressive disablement of the respiratory functions as also to ensure the clinical outcome is positive.

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