Original Article

Pulmonary Complications in Systemic Lupus Erythematosus Patients : A Cross Sectional Observational Study in a Tertiary Care Set-up

Rupak Chatterjee[1], Debananda Gonjhu[2], Shatavisa Mukherjee[3], Netai Pramanik[4], Saswati Haldar[5], Sibes Kumar Das[6]

Abstract

Background : Studies suggest that pulmonary complication is a well prevalent manifestation of Systemic Lupus Erythematosus (SLE), with most common complications being pleuritis - with or without effusion followed by Interstitial Lung Disease (ILD) and infections. Many patients continue to harbour pulmonary complications, with no clinical features. The present study aims to explore the pulmonary complications in SLE patients.

Materials and Methods : A cross-sectional, observational study included adult admitted cases of SLE, who were interviewed for basic demographic information and detailed medical history. Physical examination, haematological, biochemical, microbiological and serological tests were conducted. Patients were made to undergo Spirometry and Chest X-ray in all cases; and pleural fluid study and High-resolution CT (HRCT) Scan of Thorax was done selectively as required. Pulmonary complications were assessed and type of involvement was noted.

Results : Out of the 50 patients, 32% had pulmonary complication, with most common being pleural effusion noted in 18% patients, followed by ILD in 10%. Pulmonary manifestation on clinical presentation were however positive in 20% patients. On Chest X-ray, abnormality was noted in 22% patients whereas, PFT and HRCT showed pulmonary manifestations in 30% and 32% patients. Radiological imaging – HRCT and PFT detected pulmonary involvement in a significant number of patients who were asymptomatic. PFT was found to have restrictive lung pattern in 15 patients, while HRCT Chest was abnormal in 16 cases.

Conclusion : As almost one-third of SLE patients have pulmonary complications, so all patients of SLE should routinely undergo screening so as to exclude pulmonary complication if any.

Key words : Systemic Lupus Erythematosus, Pulmonary Complications, High Resolution CT scan, Spirometry, Chest X-ray.

Systemic Lupus Erythematosus (SLE) is an autoimmune disease in which organs and cells undergo damage mediated by tissue-binding antibodies and immune complexes. The greatest prevalence of SLE is among women of child-bearing age. Among the ethnic groups, the greatest prevalence is noted in that of African-American and Afro-Caribbean people[1]. The pathogenesis of SLE includes genetic factors, epigenetic factors and environmental factors which cause abnormal immune response and development of autoantibody and immune complexes resulting in inflammation ultimately leading to tissue damage[1]. SLE can have a wide range of manifestations, involving virtually every organ or apparatus and its severity can vary from very mild disease without major organ involvement, to severe life-threatening conditions. Clinical manifestations may include cytopenia, fever, malar and other skin rashes, oral ulcers, polyarthralgia/non erosive arthritis, vasculitis, renal, neurological, cardiac and pleuro-pulmonary involvement[2].

Editor's Comment :

- Pulmonary complication is a well prevalent manifestation of Systemic Lupus Erythematosus (SLE), with most common complications being pleuritis - with or without effusion followed by Interstitial Lung Disease (ILD) and infections.
- Many patients continue to harbour pulmonary complications, with no clinical features.
- All patients of SLE should routinely undergo screening so as to exclude pulmonary complication if any.

Department of Tropical Medicine, Calcutta School of Tropical Medicine, Kolkata, West Bengal 700073
[1]MD, Senior Resident
[2]MD, Associate Professor
[3]M Pharm, PhD Scholar, Department of Clinical & Experimental Pharmacology and Corresponding Author
[4]MD, Former Professor
[5]MD, Professor, Department of Dermatology, Venereology and Leprology
[6]MD, Professor, Department of Chest and Respiratory Medicine, Medical College and Hospital, Kolkata, West Bengal 700073

Received on : 09/02/2023
Accepted on : 08/05/2023

How to cite this article : Pulmonary Complications in Systemic Lupus Erythematosus Patients : A Cross Sectional Observational Study in a Tertiary Care Set-up. Chatterjee R, Gonjhu D, Mukherjee S, Pramanik N, Haldar S, Das SK. *J Indian Med Assoc* 2025; **123(6):** 36-41.

According to study by Hannah, *et al*[3] in 2019 on pulmonary complications of SLE, pulmonary involvement was reported to be well prevalent and seen in 50 to 70% of SLE patients. In 4-5% of patients, it has been the presenting feature of SLE. Around 12% of patients was proposed to have evidence of permanent lung damage by 10 years postdiagnosis. Pulmonary complications are broad and include pleural disease, Interstitial Lung Disease (ILD), vasculitis, pulmonary hypertension, large airway disease and infection. This manifestation, when mild, may respond to treatment with Non-steroidal Anti-inflammatory Drugs (NSAIDs); when more severe, patients require a brief course of glucocorticoid therapy. Pulmonary infiltrates also occur as a manifestation of active SLE and are difficult to distinguish from infection on imaging studies. Life-threatening pulmonary manifestations include interstitial inflammation leading to fibrosis, shrinking lung syndrome, and intra-alveolar haemorrhage; all of these probably require early aggressive immuno-suppressive therapy as well as supportive care[1]. Some of the immuno-suppressive agents have also been linked to drug-induced lung injury[3].

Literature search suggests that pulmonary complication is a well prevalent manifestation of SLE, with most common complications being pleuritis- with or without effusion followed by ILD and infections. It is stated that HRCT Chest is more sensitive in diagnosing the complications than PFT and Chest X-ray. Nevertheless, many patients continue to harbour pulmonary complications, with no clinical features – ie, subclinical. Thus, the present study aims to assess the prevalence of pulmonary complications in SLE patients and further determine the proportion/type of each pulmonary manifestations occurring in the SLE patients.

Materials and Methods

A cross-sectional, observational study was conducted in the Inpatient and Outpatient Department of Tropical Medicine and Dermatology at School of Tropical Medicine, Kolkata over a period of one year. Permission for the conduct of the study was obtained from the Institutional Ethical Committee of the institute prior commencement (vide Approval No CREC-STM/573). Written informed consent was obtained from each individual prior participation. The study included patients over 18 years of age of both sexes fulfilling the SLICC 2012 classification criteria[4] of Systemic Lupus Erythematosus and admitted in Indoor and attending the designated Outdoor Departments. Patients with HIV, HBV or HCV co-infection; those with current or past malignancy within the past 5 years; those suffering from known pulmonary disorder that is not due to SLE; pregnant or lactating females and those unwilling to participate were excluded. A convenient sample size of 50 was selected for the study based on inclusion and exclusion criteria.

For each patient, basic demographic information and detailed medical history was noted. Physical examination in terms of general survey and systemic examination, haematological, biochemical, microbiological and serological tests were conducted. The preliminary assessment tried to determine whether patient has pulmonary manifestation of SLE. After clinical evaluation, patients were made to undergo Spirometry and Chest X-ray in all cases; and pleural fluid study and High-resolution CT (HRCT) Scan of thorax was done selectively as required. Pulmonary complications were assessed and type of involvement was noted.

Data were statistically analysed. Categorical data were presented as frequency and percentages, while continuous data were presented as mean ± Standard Deviation (SD). All statistical analysis for various measures were performed using various statistical software packages like Statistical Package for the Social Sciences (Windows version 21.0; SPSS Inc, Chicago, IL, USA) and Microsoft Excel.

Result

A total of 50 diagnosed patients of SLE were included in this study for analysis. The patients were diagnosed as SLE on fulfilling the SLICC criteria. The age distribution of the study population revealed that maximum number of patients belonged to the age group of 25 years to 35 years with 34 patients (68%) falling under this category. The mean age was 28.42 ± 5.6 years. There is a female preponderance with 96 % of the study population ie, 48 patients being female. Most of the patients (n=20) had a disease duration of 37 to 60 months followed by 14 patients with a disease duration of 13 to 36 months and 10 patients with disease duration of 61 to 84 months. The mean disease duration is 46 ± 24.37 months. (Table 1) Among the 50 patients included in our study,

Table 1 — *Patient Characteristics*

	No of patients (n=50)
Gender	
Female	48 (96%)
Male	2 (4%)
Age (in years)	
<25	11 (22%)
25-35	34 (68%)
>35	5 (10%)
SLE Disease Duration (in Months)	
<12	4 (8%)
13-36	14 (28%)
37-60	20 (40%)
61-84	10 (20%)
>84	2 (4%)
Presence of Nephritis	40 (80%)
Presence of musculoskeletal manifestations	35 (70%)
Presence of Skin, hair and mucous membrane manifestations	36 (72%)
Alopecia	16 (32%)
Oral ulcer	15 (30%)
Presence of Serositis (ascites/ pleural effusion/ pericardial effusion)	11 (22%)
Presence of Neuropsychiatric manifestation	2 (4%)
Presence of Haematological abnormality	
Anaemia	35 (70%)
Leukopenia	16 (32%)
Thrombocytopenia	12 (24%)

Table 2 — *Presenting symptom related to respiratory system in the study population*

No of Clinical Symptoms	No of patients	Presenting Pulmonary Symptoms	No of patients
1	1	Only Chest Pain	1
2	2	Chest Pain + Dyspnoea	2
3	5	Fever+ Cough+ Dyspnoea	1
>3	2	Chest Pain+ Fever+ Cough+ Dyspnoea	2
		Chest Pain + Fever + Dyspnoea	1
		Chest Pain + Cough + Dyspnoea	2
		Fever + Cough + Haemoptysis	1

Table 3 — *Clinical and Radiological Findings in SLE Patients*

	Abnormal findings	Findings	No of Patients
Clinical Examination	10 (20%)	Pleural effusion	6
		Pneumonia	4
		ILD	3
		Pulmonary hypertension	1
Radiological Examination			
Chest X Ray	11 (22%)	Pleural Effusion	8(2-Unilateral, 6-Bilateral)
		Opacification/ Infiltration	4
		Lymphadenopathy	1
HRCT Thorax	16 (32%)	Pleural effusion	9
		Pleural thickening	1
		LRTI	4
		ILD	5

12 were newly diagnosed cases. Remaining 38 patients were already diagnosed receiving treatment. All patients of the study were ANA positive. Anti-ds DNA were positive in 39 patients of our study.

Pulmonary Complications in SLE Patients :

Out of the 50 patients included in our study, total of 10 patients, ie, 20% had symptoms pertaining to pulmonary involvement. Of them, 8(16%) had Chest pain, 8 (16%) had Shortness of breath or dyspnoea, 6 (12%) had Cough, 5 (10%) had Fever and 1 patient had Haemoptysis as manifestation (Table 2).

Clinical examination of respiratory system revealed abnormality in 10 patients (20%). Radiological examination included Chest X-ray and HRCT thorax. Chest X-ray were abnormal in 11 subjects with most common abnormality being pleural effusion. HRCT thorax revealed abnormality in 16 cases (32%)(Table 3).

Pulmonary Function Test (PFT) done in all subjects of the study population showed abnormality in 15 patients (30%). PFT was of restrictive pattern in all the cases, with FEV1/FVC >0.7. Pleural fluid analysis was done in subjects with pleural effusion. Analysis of pleural fluid showed to be exudative in nature in all cases as per Light's criteria.

Sputum analysis in patients with Cough were done. Sputum CBNAAT was positive in one patient. In the four patients of Pneumonia, sputum Gram stain and culture revealed isolate in 2 cases (Streptococcus pneumonia – 1; Klebsiella pneumonia – 1).

Only 1 patient of our study had pulmonary arterial hypertension evidenced by loud P2 on clinical examination and verified by 2D Echocardiography.

So, a total of 16 patients (32%) of the study population had presence of pulmonary complications. Out of the 16 patients of our study population detected finally to have presence of pulmonary complication by clinical, microbiological and radiological assessment, 9 patients (18%) were found to have pleural effusion. Out of the 9 cases of pleural effusion, 2 had unilateral pleural effusion and rest 7 had bilateral fluid accumulation. Among the 9 patients of pleural effusion, 7 had only pleural effusion. Rest 2 patients had effusion co-existing with Pneumonia. In all the cases, the fluid was exudative in nature. Overall, the most common manifestation was pleural effusion

detected in 9 patients (18%) followed by ILD in 5 cases (10%) and Pneumonia in 4 patients (8%). Pulmonary tuberculosis, PAH and pleural thickening was detected in 1 patient each respectively. Out of the 5 ILD diagnosed cases, 2 had only ILD; 1 had ILD with PAH. In 1 patient with ILD, Pneumonia was also present and 1 had pulmonary TB with ILD. So, of the 16 patients diagnosed to have pulmonary involvement, 10 had only 1 pathology; rest 6 patients had more than one manifestation (Fig 1).

Out of the 16 patients finally diagnosed with pulmonary involvement, 10 were clinically symptomatic. Chest X-ray revealed abnormality in 11 cases. PFT was found to have restrictive lung pattern in 15 patients. HRCT Chest was abnormal in 16 cases.

Discussion

The present cross-sectional, observational study revealed that 32 % of the included SLE patients had pulmonary complication, with most common complication being pleural effusion noted in 18% patients, followed by ILD in 10%. Infections was the next common manifestation- with Pneumonia seen in 4 cases and Pulmonary TB in 1 case. PAH was noted in only 1 patient. Pleural effusion was mostly bilateral and exudative in nature. From our study, we conclude that pulmonary manifestation on clinical presentation were positive in 20% patients. On Chest X-ray, abnormality was noted in 22% patients whereas, PFT and HRCT showed pulmonary manifestations in 30% and 32% patients. Thus, radiological imaging – HRCT and PFT detected pulmonary involvement in a significant number of patients who were asymptomatic. Out of the 16 patients finally diagnosed with pulmonary involvement, 10 were clinically symptomatic. Chest X-ray revealed abnormality in 11 cases. PFT was found to have restrictive lung pattern in 15 patients. HRCT Chest was abnormal in 16 cases.

Our study revealed 34 patients (68%) in the age group of 25 to 35 years with a mean age of 28.42 ± 5.59 years and a female preponderance of 48 patients (96%). This is in concurrence with similar studies as conducted by Teh, *et al* in 2018[5] for 4 years with 125 patients, which showed a mean age of 33.4 ± 14.2 years and a female predominance of 89.6 %. Another study by Skare, *et al*[6] in 2016 of 144 patients conducted and followed up for 5 years showed a mean

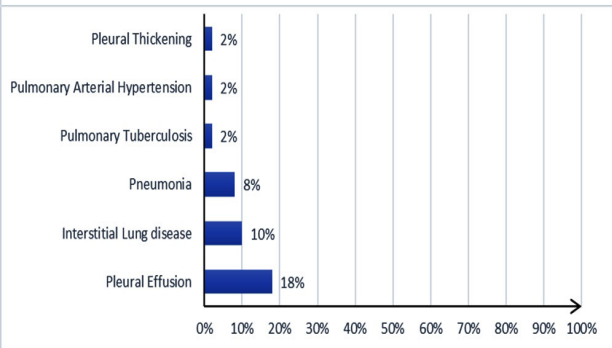

Fig 1 — *Pulmonary involvement in SLE Patients*

age of 39.15 ± 11.65 years with a female predominance of 93.8 %. Most studies on SLE have documented female preponderance and involvement of mainly female of reproductive age group[7]. While the gender predisposition was comparable in all the 3 studies, the higher mean age in both the reference studies can be attributed to a larger study population and longer study period. The reason for a significant female predominance is because of the genetic build-up of the present population which favours development of this autoimmune disease. Our study showed 20 patients (40%) who were admitted had lupus duration of 37 to 60 months. The mean disease duration was 46 ± 24.375 months.

The patients had various kinds of manifestations attributable to SLE. Nephritis was present in 40 patients (80%) of the study population with evidence of proteinuria on urine examination. In the study by Teh, *et al*[5], among 125 patients, Nephritis was present in 81 patients (64.8%). A case-control study by Jung, *et al*[8] in 2018 showed in a total population of 360 patients, 244 patients (67.8%) had Nephritis. In the same study 241 patients (66.9%) had Arthritis, which was quite in similarity to our findings (70%). The present study noted cutaneous manifestations in 72% study population, with the most common rash being erythematous, maculopapular and butterfly shaped rash on the face. While 16 patients (32%) had diffuse alopecia, 15 patients (30%) had chronic oral ulcer. This finding was in line with the study by Teh, *et al*[5], which showed the presence of mucocutaneous manifestations in 60 % of their population. The study by Skare, *et al*[6] showed that photosensitivity was present in 70.7%, malar erythema was present in 48.9% and oral ulcers were present in 45.6% of their study population of 144.

Ten patients presented with symptoms pertaining to

respiratory system in our study which constituted 20% of the study population. A study by Kakati, *et al*[9] found 23.68% of the study subjects to have sign/symptom indicating pulmonary involvement. Out of the 10 patients having symptoms of respiratory manifestations, 9 had Chest pain, 8 had Shortness of breath/dyspnoea, cough was present in 6 cases and Fever in 5 cases. Only 1 patient gave history of haemoptysis. So, the most common symptom observed was Chest pain followed by Dyspnoea and Cough. Similar findings were reported by Samuel, *et al*[10], Al Abbad, *et al* [11] and Omer, *et al*[7] in their study. Samuel, *et al*[10] observed exertional dyspnoea, productive Cough and Chest pain as commonest presenting symptom. Delgado, *et al*[12] also observed similar symptoms in their study. A study conducted by Ghosh, *et al*[13] found the commonest respiratory symptom to be dyspnoea.

Clinical examination of the patients with detailed respiratory system examination found the commonest clinical manifestation to be pleural effusion. By clinical examination alone, 6 patients were diagnosed to have pleural effusion. 4 patients were clinically diagnosed to have LRTI /Pneumonia. Features of ILD was found in 2 patients on clinical examination. A single centre cross-sectional observational study by Ghosh, *et al*[13] in a Tertiary Care Hospital of same study region also reported the commonest respiratory manifestation to be pleural effusion. Chest X-ray revealed abnormality in 11 patients (22% of the study population), PFT revealed abnormality in 15 patients (30%) and HRCT Chest revealed abnormality in 16 patients (32%) of the study population. So, HRCT was found to be more sensitive than Chest X-ray in diagnosing the pulmonary complications. Studies conducted by Ghosh, *et al*[13], Kakati, *et al*[9], Sant, *et al*[14] also noted similar findings. In the study by Ghosh, *et al*[13], among the finally diagnosed ILD cases diagnosed by HRCT Chest, 50% had normal Chest X-rays. Kakati, *et al*[9] found HRCT abnormalities in 55% cases while PFT and Chest X-rays were abnormal only in 29% and 18% cases respectively.

In our study, a total of 16 patients, ie, 32% -about 1/3rd of the study population was finally diagnosed to have pulmonary complication. Two large studies also showed similar prevalence of pulmonary involvement. A 10-year study conducted retrospectively in Arab involving 180 patients showed 33% patients to have pulmonary involvement[7]. Data from Spanish Rheumatology Society which included data of 3215 SLE patients noted 31% patients to have at least 1 pleuro-pulmonary manifestation most common of them being pleural disease[15]. Higher prevalence rated of up to 50% was also noted in some studies. According to Hannah, *et al*[3], pulmonary complications may be seen in 50-70% of SLE cases and around 12% of patients will have evidence of permanent lung damage by 10 years postdiagnosis[3]. In 16 patients diagnosed to have pulmonary involvement, 10 had only 1 pathology; rest 6 patients had more than one manifestation. The commonest pulmonary complication found in our study was pleural effusion seen in 9 cases (18%), followed by ILD in 5 patients (10%). Pleura-pulmonary infections was the next common manifestation. Pneumonia was diagnosed in 4 cases; Pulmonary TB was diagnosed in 1 patient. 1 patient with ILD was also found to have PAH. Studies by Ghosh, *et al*[13], Mittoo, *et al*[16] also found the commonest manifestation to be pleural effusion. Among the 16 patients diagnosed with pulmonary complication, all were females. This fact may be explained by the fact that females largely outnumber male SLE cases.

Analysis of pleural fluid revealed it to be exudative in nature in all cases. Of the 9 pleural effusion cases, 7 cases had bilateral involvement. Ghosh, *et al*[13] also noted pleural effusion to be bilateral in 80% of the cases. The second most common manifestation was ILD seen in 5 patients, which means 10% of the study population. Ghosh, *et al*[13] also noted same prevalence – 10% of study subjects had ILD. All the patients who were diagnosed to have ILD had disease duration for more than 60 months. A large-scale study conducted in China found a significant association between ILD and duration of disease[17]. The present study noted that HRCT and PFT were superior to routine Chest X-ray in diagnosis of pulmonary complications.

Our study had a few limitations which need a bit of attention. Firstly, the sample size was small to extrapolate and relate the findings of the study to a much larger population. Secondly, time duration of the study was small to consider any other major factors which may have influenced the results of the study. Thirdly, the observational design of the study did not allow for comparison of variables. Fourthly, whether injection cyclophosphamide had any role on development of ILD in the patients who were already

treated with the same as per protocol could not be clearly ascertained. Further prospective studies with larger sample size and longer duration among the Indian population might have a better understanding of the subject. This study thus sparks the need for conduct of future studies with improved study design to determine risk factors for development of pulmonary complications in SLE for an improved Quality of Life in these patients.

Conclusion

As almost one-third of SLE patients have pulmonary complications, so all patients of SLE should routinely undergo screening so as to exclude pulmonary complication if any.

Source of Funding : Nil

Conflict of Interest : None Declared

References

1 Jameson JL, Kasper DL, Longo DL, Fauci AS, Hauser SL, Loscalzo J — Harrison's Principles of Internal Medicine. 20th edition. The United States of America: Cenveo Publisher Services; 2018. Chapter 349, Systemic Lupus Erythematosus; 2515-25.

2 Zucchi D, Elefante E, Calabresi E, Signorini V, Bortoluzzi A, Tani C — One year in review 2019: systemic lupus erythematosus. *Clin Exp Rheumatol* 2019; **37(5):** 715-22.

3 Hannah JR, D'Cruz DP — Pulmonary Complications of Systemic Lupus Erythematosus. *Semin Respir Crit Care Med* 2019; **40(2):** 227-34.

4 Petri M, Orbai AM, Alarcón GS, Gordon C, Merrill JT, Fortin PR, *et al* — Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. *Arthritis Rheum* 2012; **64(8):** 2677-86.

5 Teh CL, Wan SA, Ling GR — Severe infections in systemic lupus erythematosus: disease pattern and predictors of infection-related mortality. *Clin Rheumatol* 2018; **37(8):** 2081-6.

6 Skare TL, Dagostini JS, Zanardi PI, Nisihara RM — Infections and systemic lupus erythematosus. *Einstein (Sao Paulo)* 2016; **14(1):** 47-51.

7 Alamoudi OS, Attar SM — Pulmonary manifestations in systemic lupus erythematosus: association with disease activity. *Respirology* 2015; **20(3):** 474-80.

8 Jung JY, Yoon D, Choi Y, Kim HA, Suh CH — Associated clinical factors for serious infections in patients with systemic lupus erythematosus. *Sci Rep* 2019; **9(1):** 9704.

9 Kakati S, Doley B, Pal S, Deka UJ — Pulmonary manifestations in Systemic Lupus Erythematosus (SLE) with special reference to HR CT. *J Assoc Physicians India* 2007; **55:** 839-41.

10 Samuel S, Mohsen M, Gamal El-Din RM, Hosny H — Pulmonary function Tests in patients with SLE. *Alexandria Journal of Pediatrics* 2005; **19(2):** 277-81.

11 Al-Abbad AJ, Cabral DA, Sanatani S, Sandor GG, Seear M, Petty RE, *et al* — Echocardiography and pulmonary function testing in childhood onset systemic lupus erythematosus. *Lupus* 2001; **10(1):** 32-7.

12 Delgado EA, Malleson PN, Pirie GE, Petty RE — The pulmonary manifestations of childhood onset systemic lupus erythematosus. *Semin Arthritis Rheum* 1990; **19(5):** 285-93.

13 Ghosh A, Das T, Ghosh A, Karmakar P, Pal J — Evaluation of respiratory manifestations in systemic lupus erythematosus with special reference to pulmonary interstitial involvement. *J Indian Med Assoc* 2012; **110(2):** 109-11.

14 Sant SM, Doran M, Fenelon HM, Breatnach ES — Pleuropulmonary abnormalities in patients with systemic lupus erythematosus: assessment with high resolution computed tomography, chest radiography and pulmonary function tests. *Clin Exp Rheumatol* 1997; **15(5):** 507-13.

15 Narváez J, Borrell H, Sánchez-Alonso F, Rúa-Figueroa I, López-Longo FJ, Galindo-Izquierdo M, *et al* — RELESSER Study Group. Primary respiratory disease in patients with systemic lupus erythematosus: data from the Spanish rheumatology society lupus registry (RELESSER) cohort. *Arthritis Res Ther* 2018; **20(1):** 280.

16 Mittoo S, Fell CD — Pulmonary manifestations of Systemic Lupus Erythematosus. *Semin Respir Crit Care Med* 2014; **35(2):** 249-54.

17 Chen Y, Wang Y, Chen X, Liang H, Yang X — Association of Interstitial Lung Disease with Clinical Characteristics of Chinese Patients with Systemic Lupus Erythematosus. *Arch Rheumatol* 2020; **35(2):** 239-46.