Original Article

Pulmonary Function Test to Detect Early Pulmonary Involvement in Systemic Lupus Erythematous Patients. A SKIMS Experience.

Saba Bashir, Surjeet Singh, Fayaz Sofi

Abstract

Background

Autoimmune disease is a condition in which the immune system attacks tissues of the body. Systemic lupus erythematosus is a multisystem autoimmune disorder, which frequently occurs in females of childbearing age. It has protean clinical and laboratory manifestations, and a variable course and prognosis. Its clinical manifestations may be constitutional or specific depending upon the organ system involved. The pulmonary manifestations in SLE vary from patient to patient, but usually include cough with or without sputum, dyspnea, hemoptysis and chest pain. Early demonstration of lung involvement in SLE patients is difficult. The aim of present study is to reveal the early pulmonary involvement in systemic lupus erythematosus patients using pulmonary function test as a tool of pulmonary involvement assessment.

Methodology

This is a prospective observational study carried out by the Department of Clinical Pharmacology SKIMS in collaboration with the Department of Rheumatology SKIMS. Patients fulfilling the American College of Rheumatology Criteria were included in the study. All included patients were evaluated by complete history, gen. physical examination, systemic examination, basic lab. Investigations and some special investigations. Thereafter patients were subjected to pulmonary function test.

Results

After fulfilling inclusion criteria, a total of 50 patients were included in the study. Majority 24(48%) were in the age group of 26-41yrs, and proportion of females were more 47(94%) compared to males 3(6%). More patients were from rural area 42(84%) compared to urban 8(16%). Pulmonary function tests with abnormal or decreased lung volumes was observed in 26(52%) patients.

Conclusion

Periodic spirometry is a cost-effective option to detect the subclinical pulmonary changes in SLE.

JK-Practitioner2024;29(2-3):37-42

Introduction

The immune system is immensely powerful in terms of its ability to damage and kill foreign substances, and it has a capacity to recognize a myriad of molecular patterns in the microbial world. However, immune responses are not always beneficial. They can give rise to a wide range of inflammatory autoimmune diseases. Autoimmune disease is a condition in which the immune system attacks tissues of the body[1]. Systemic rheumatic diseases are autoimmune disorders that include systemic lupus erythematosus (SLE), scleroderma, mixed connective tissue disease, polymyositis and rheumatoid arthritis. Systemic lupus erythematosus is a connective tissue (collagen) disorder that occurs more frequently in women of childbearing age. Its worldwide incidence

Author Affiliations
Saba Bashir, MSc student; **Surjeet Singh**, Associate Professor;
Department of Clinical Pharmacology.
FayazSofi, Professor&Head: Department of Rheumatology.
SKIMS , Srinagar.

Correspondence
Dr.Surjeet Singh
Associate Prof. Department of Clinical Pharmacology SKIMS ,Srinagar.
Mob. No. 9797730444;
email: surjeet.singh@skims.ac.in

Indexed
EMBASE ,SCOPUS , IndMED ,ESBCO, Google Scholar besides other national and international databases

Cite this article as
Bashir S, Singh S, Sofi F.Pulmonary Function Test to Detect Early Pulmonary Involvement in Systemic Lupus Erythematous Patients. A SKIMS Experience.JK Pract2024;29(2-3):37-42

Full length article available at **Jkpractitioner.com** one month after publication

Keywords
Systemic lupus erythematosus (SLE); Pulmonary function tests (PFT)

Lupus auto-antibodies are present for 5-7 years before clinical onset of SLEoccurs4. With underlying genetic predisposition and in presence of various environmental triggers like smoking, exposure to UV-light, viral infections and specific medications e.g. sulfonamide antibiotics5-9, the balance of immune system shifts towards reacting against itself rather than self-tolerance. T and B lymphocytes become activated, leading to antibody production and eventual immune complex formation. These complexes circulate and deposit in critical tissues causing organ injuries10.

Respiratory abnormality is a prevalent finding in patients with SLE11. Most common pulmonary presentations include pleuritis, acute pneumonitis, chronic pulmonary interstitial disease, diaphragmatic weakness and alveolar hemorrhage12,13. Pleural manifestations have been reported in 30-60% of SLE patients14. Respiratory disease in SLE may be due to direct involvement or as a consequence of disease affecting other organ system. Aim of conducting the present study was to reveal the early pulmonary involvement in systemic lupus erythematosus patients by performing pulmonary function test in such patients in our department.

Material and Methods

This prospective study was carried out by the Department of Clinical Pharmacology in collaboration with the Department of Rheumatology at Sher-i- Kashmir Institute of Medical Sciences for a period of four months (Sep. 2019 to Jan. 2020). Both inpatients and outpatients fulfilling the American College of Rheumatology Criteria for the classification of SLE were included in the study. Pregnant patients; patients below 10 years; presence of cardiac problems; or a hemoglobin conc. below 8 gms/dl; patients with chronic obstructive pulmonary disease, tuberculosis, recent surgery on thorax or abdomen, recent eye surgery were excluded from the study.All patients included in the study were evaluated by complete history; general physical examination; systemic examination; and basic laboratory investigations including CBC, blood urea, serum creatinine, LFT, ESR, urine examination, 24 hrs urinary proteins, rheumatoid factor, c-reactive protein. Furthermore special investigations including antinuclear antibodies, anti-Ro, anti-La, anti-phospholipids (IgM, IgG), anti-sm, anti-RNP, and anti-double stranded deoxy-ribonucleoproteins (dsDNA) were also done. There after, patients were subjected to pulmonary function test using Spirometer (Medikro Windows Spirometer). Spiro 2000 software version 1.8. (M8304-1.8-eng). Model_M9460. SN:M946000101419

Results

Total of 50 patients fulfilling the American Rheumatism Association Criteria for diagnosis of SLE were included in the study. Demographic profile of these patients is presented in table 1.

Table 1. Demographic profile of patients

Demography	Variables	No. of patients	Percentage
Age	11-26 yrs	12	24%
	26-41 yrs	24	48%
	>41 yrs	14	28%
Sex	Male	3	6%
	Female	47	94%
Area	Rural	42	84%
	Urban	8	16%

Most of the patients 24(48%) were in the age group of 26-41 years of age and proportion of females were more 47(94%) compared to females 3(6%). More patients were from rural areas 42(84%) compared to 8(16%) from urban areas.

Pulmonary function tests were performed in all 50 patients. Pattern of pulmonary function are represented in table 2.

Table 2. Pulmonary function profile of patients

Parameters	No. of patients	Percentage
Reduced VC	34	68%
Reduced FVC	15	30%
Reduced FEV1	26	52%

Normal pulmonary function pattern was seen in 24 (48%) patients whereas in 26 (52%) patients the pattern was abnormal. Table 3.

Table 3. Pattern of pulmonary function tests

Interpretation of PFT	Total no. of patients (50)	Percentage
Normal	24	48%
Moderate decrease	9	18%
Mild decrease	13	26%
Moderately severe decrease	3	6%
Severe decrease	1	2%

Out of 26 patients with abnormal pattern of pulmonary function, restrictive, obstructive and mixed patterns were observed in 14 (53.85%), 11 (42.31%), and 1 (3.85%) patients respectively. Table 4.

Table 4. Type of abnormal pulmonary function

PFT abnormality	No. of patients (out of 26)	Percentage
Restrictive	14	53.85%
Obstructive	11	42.31%
Mixed pattern	1	3.85%

HRCT was done in patients whose clinical, pulmonary and chest x-ray findings were suggestive of development of early and possibly reversible interstitial lung disease. Table 5

The clinical course of SLE is highly variable with broad range of clinical manifestations. Most common pulmonary symptom observed was cough followed by exertional dyspnea and chest pain. Table 6. Each patient had more than one signs and symptoms.

Antinuclear antibodies were positive in 46 (92%) of patients. Table 7.

Table 5. HRCT findings

The clinical course of SLE is highly variable with

Cases	HRCT features
Case no. 8	Bilateral patchy ground-glass opacities admixed with reticulation. Non-specific interstitial pneumonia.
Case no. 9	Bilateral prominent broncho-alveolar markings.
Case no. 11	Bilateral mild pleural effusion. No features of pulmonary embolism.
Case no. 17	Traction bronchiectasis/broncheolectasis. No honeycombing. Usually predominantly basal thus showing NSIP(non-specific interstitial) pattern, pleuro-pericardial effusion. No pulmonary thrombosis seen.
Case no. 22	Normal study.
Case no. 35	Organizing pneumonia, left linear lobe fibrotic area.
Case no 36	Emphysema
Case no. 37	Mild intralobular septal thickening with doubtful early honeycombing, signs of probable UIP (usual interstitial pneumonia) pattern.
Case no. 40	Shows signs of ILD with ground-glass appearance, dilated LA/LV

broad range of clinical manifestations. Most common pulmonary symptom observed was cough followed by exertional dyspnea and chest pain. Table 6. Each patient had more than one signs and symptoms

Table 6. More than one manifestation was observed in each patient.

Signs / Symptoms	No. of patients	Percentage
Alopecia	37	74%
Arthralgia	32	64%
Cough	34	68%
Cutaneous lupus	2	4%
Dry mouth	30	60%
Fever	14	28%
ILD	4	8%
Lupus carditis	1	2%
Lupus nephritis	9	18%
Lupus perinio	1	2%
Malar rash	34	68%
Muscle weakness	31	62%
Myalgia	1	2%
Nasal ulcer	15	30%
Neurolupus	1	2%
Optic neuritis	2	4%
Oral ulcers	36	72%
Photosensitivity	42	84%
Polymyositis	1	2%
Puffiness of face	21	42%
Pulmonary artry hypertension	1	2%
Renal tubular acidosis	3	6%
Raynaud's phenomenon	19	38%
Sjogren's syndrome	6	12%
Small vessel vasculitis	2	4%
Vascular headache	35	70%

Antinuclear antibodies were positive in 46 (92%) of

Discussion

SLE is an inflammatory multisystem autoimmune disease of unknown etiology with protean clinical and laboratory manifestations and a variable course and prognosis. Its clinical manifestations may be constitutional or specific depending upon the organ system involved. The skin and mucous membrane, joints, kidneys, brain, serous membranes, lungs, heart, and occasionally, the gastrointestinal tract maybe affected[15]. The most common initial manifestation of SLE is arthralgia, or arthritis[16] with frequency of 48% in patients followed for 10 years[17]. In some patients the disease may run in a relatively benign course. Other patients may manifest serious and life threatening complications of the disease with relapses and remissions[18].

Table 7. Types of antibodies

S. No.	Laboratory investigations	No. of cases	Percentage
1.	ACCP	3	6%
2.	ACLA Positive	2	4%
3.	ANA Hep2	46	92%
4.	Anemia	15	30%
5.	Anti La	7	14%
6.	Anti Ro	9	18%
7.	Anti-Smith Antibody	2	4%
8.	APLA Positive	9	18%
9.	CRP	7	14%
10.	dsDNA	12	24%
11.	Hyperproteinemia	3	6%
12.	Hypoalbuminemia	4	8%
13.	Hypothyroidism	16	32%
14.	LDH	8	16%
15.	Leucopenia	2	4%
16.	Low complement (C3)	12	24%
17.	Low C4	19	38%
18.	Lupus anticoagulant	6	12%
19.	Proteinuria	20	40%
20.	Rheumatoid factor	2	4%
21.	Thrombocytopenia	8	16%
22.	Vit. D deficiency	11	22%

Pulmonary abnormalities have been demonstrated in all collagen diseases. The early demonstration of lung involvement in SLE patients is difficult. The pulmonary manifestations in SLE vary from patient to patient but usually include cough with or without sputum, dyspnea, hemoptysis and chest pain[19]. Respiratory symptoms and abnormal lung function are relatively common in SLE. There have been many studies concerning pulmonary involvement in patients with SLE. Most of these studies relied upon the characteristics of PFT and HRCT for picking up abnormal lung function in this sector of the patients[20,21,22].

SLE may affect all the components of the respiratory system, including upper airways, lung parenchyma, lung vasculature, pleura and respiratory muscles[23]. Pleuritis and pulmonary infections are the most prevalent pulmonary manifestations in SLE. Other associations include acute lupus pneumonitis, pulmonary hemorrhage, pulmonary vasculitis, pulmonary embolism and shrinking lung syndrome. The early detection of these diseases may help in preventing their fatal complications.

In the present study, we studied data of 50 patients with SLE who had attended rheumatology department, with a primary focus on pulmonary function test patterns in these patients. Here out of 50 cases proportion of female was more (94%) compared to males (6%), with a female to male ratio of 15.6:1. This result is almost similar to previous studies like Amin et.al. 2005[24] showing female to male ratio of 10.88:1,

and Sameul et.al. 2005[25] showing 83.3% female predominance, and Abbad et.al. 2000[26].

It was observed that majority of the patients (48%) were in the age group of 26-41 years of age, followed by age group >41 years of age (28%). Majority of female patients were of child bearing age group. Almost similar was observed by previous sudies[25,26,27,28].

In the present study higher prevalence was seen in rural population with rural to urban population ratio of 5.25:1. Reason could be lower education rate and low employment rate in rural population, along with higher pesticide exposure in them (suspected etiological factor)[29]. However in contrast to this, an increased trend of SLE prevalence in urban population was observed Barnabe C. et.al.[30].

In the present study, pulmonary function tests were performed in all the 50 patients despite presence or absence of pulmonary signs and symptoms. Normal pattern was observed in 24 (48%) patients whereas abnormal pattern was seen in 26 (52%) patients, out of which 14 (53.84%) patients show restrictive pattern. Samuel et.al[25] in their study show that 22 patients out of 36 patients (61.11%) with pulmonary manifestations had normal pattern of pulmonary function, whereas 14 patients (38.89%) (out of 36 patients with pulmonary manifestations) had abnormal (restrictive type) pattern. Reason could be because here, pulmonary function testing was performed only in those patients showing pulmonary signs and symptoms, i.e. 36 (51.4%) out of total 70 patients included in the study. Although few other studies show almost similar results as present study[23, 31, 32]

In the present study, out of 50 patients, 38 (76%) were having pulmonary symptoms and signs, and the rest 12 (24%) patients were asymptomatic. Out of 38 symptomatic patients, only 14 have abnormal pulmonary function test, whereas all the 12 asymptomatic patients show abnormal pulmonary function test. This may be because of subclinical respiratory involvement in patients with SLE as depicted by previous studies[32,38,39,40]also.

The most common symptom observed in present study was cough followed by exertional dyspnea and chest pain. Almost similar findings were observed in other studies[25,27,26,28,33], with Samiha Samuel[25] showing exertional dyspnea, productive cough and chest pain as commonest presenting symptoms. Any part of pulmonary system can be affected including airways, lung parenchyma, pulmonary vasculature, pleura and diaphragm[11,14,34,35,36,37]. The diagnosis of thoracic involvement in SLE has heretofore been made from clinical findings, chest radiographic features, pulmonary function tests, and lung biopsy[31]. Pulmonary complications of SLE are protean and include acute and chronic lupus pneumonitis, interstitial lung disease (ILD) or chronic interstitial pneumonitis (CIP), cavitatory pulmonary nodule, pulmonary hypertension, pulmonary vasculitis, pulmonary embolism, diaphragmatic dysfunction and shrinking lung syndrome, alveolar hemorrhages and opportunistic lung infections due to immunosuppressive therapy[32,38-45]. Antinuclear antibodies was positive in 92% of patients in present study, which is nearly similar to another study by Samuel S et al.[25] which show antinuclear antibodies to be positive in 95.7% of cases.

Abnormal pulmonary function tests were recorded in 52% of SLE patients in our study, and majority among them (53.85%) show restrictive pattern. The interpretation of lung function in the context of connective tissue diseases can be complex, because of variety of compartments potentially involved in the same patient. The possible main mechanism leading to lung function impairment can be interstitial abnormalities. These are associated with restrictive pattern, with proportional reduction in forced vital capacity (FVC) and forced expiratory volume in one second (FEV1), and concomitant reduction in transfer coefficient for carbon monoxide (DLCO)[46] , latter being the most sensitive marker of interstitial lung disease (ILD) and is the first parameter to be reduced in early and limited stages of disease. However this parameter was not available with our instrument and we exclusively drew the results from other parameters, i.e. reduced total lung capacity (TLC) and normal FEV1/FVC ratio. Spirometry can be normal in mild disease or mixed obstructive-restrictive disorders[47].

High resolution computed tomography (HRCT) was advised in 9 (18%) of patients, all with abnormal pulmonary function tests, out of which 7 (14%) show abnormal HRCT features. Commonest HRCT abnormality was interstitial lung disease with pleural involvement. Patients were considered to have ILD if there were reticular and/or interstitial opacities with or without ground glass opacities and/or honeycombing, if all other differential diagnosis for such features were excluded[48]. Pleural involvement was considered by presence of pleural effusion, pleural thickening, or pleural fibrosis, when other causes for such features were excluded. Similar features were also observed in previous few studies[32,41].

Conclusion

Periodic spirometric evaluation might be a cost effective option to detect the subclinical pulmonary changes in settings where DLCO and HRCT cannot be carried out. Early detection of patients at risk of developing future pulmonary complications, by timely screening could guide the clinician for appropriate intervention at the outset.

Pleuropulmonary disease may occur in a well-established case of lupus or may be the first manifestation of SLE. The pulmonary function abnormalities are present in SLE patients even in asymptomatic cases, so that early recognition and introduction of the therapy will help in preventing the morbidity and mortality in such cases.

Moreover, more studies with increased sample size are needed to demonstrate the efficacy of pulmonary function test in diagnosing early pulmonary

involvement in SLE patients even in absence of clinical signs and symptoms.

References

1. Betty Diamond, Peter E Lipsky (Editors). "Autoimmunity and Autoimmune Disease." In "Harrisons Principles of Internal Medicine". 20th edition, Vol. 2, United States, MacGraw Hill Education, 2018; 348: 2510
2. Siegel M, Lee SL. "The epidemiology of systemic lupus erythematosus". Semin Arthritis Rheum 1973; 3: 1-54
3. Pons-Estel GJ et.al. "Understanding the epidemiology and progression of systemic lupus erythematosus". Semin Arthritis Rheum 2008; 39: 257-268
4. Harley JB, James JA." Epstein-Bar virus infection may be an environmental risk factor for SLE in children and teenagers". Arthritis Rheum 1999; 42(8): 1782-1783
5. Tsokos GC, "Systemic Lupus Erythematosus". NEJM. 2011; 365: 2110-21
6. Christle M Bartels et.al. "Systemic Lupus Erythematosus (SLE)". Medscape, WebMD LLC, Mar 18, 2020, https://emedicine.mediscape.com/article/332244-overview#a3
7. Souyris M, Cenac C, Azar P, Daviaud D, Canivet A, Grunewald S, et.al. TLR7 escapes X chromosome inactivation in immune cells. Sci immunol. 2018; 3(19): [MEDLINE]
8. Nancy Walsh. "Estrogen and lupus: Exploring the Link-Unique relationship identified between SLE, estrogen and toll-like receptors". MedPage today, August 27, 2018, Jarjour W. "Sex bias in autoimmunity" OAR 2018. http://www.medpagetoday.com/meetingcoverage/oar/74787
9. Petri M, Allbritton J. "Antibiotic allergy in systemic lupus erythematosus: a case control study". J Rheumatol 1992; 19: 265-9
10. Cunha JS, Gilek-Seibert K. "Systemic Lupus Erythematosus: A review of clinical approach to diagnosis and update on current targeted therapies". R I MED J(2013) 2016 Dec 1; 99(12): 23-27
11. Gross M, Esterly JR, Earle RH. Pulmonary alterations in systemic lupus erythmatosus. Am Rev Resp Dis 1972; 105: 572-577
12. AM Segal, LH Calabrese, M Ahmad, RR Tubbs, CS White. "The pulmonary manifestations of systemic lupus erythematosus". Semin Arthritis Rheum, 1985; 14(3): 202-224
13. A Pines, N Kaplinsky, D Olchovsky, J Rozenman, O Frankl. "Pleuropulmonary manifestations of systemic lupus erythematosus: Clinical features of its subgroups", Chest 1985; 88(1): 129-135
14. Kamen DL, Strange C. Pulmonary manifestations of SLE, Clin Chest Med 2010; 31: 479-488
15. Daniel J Wallace, Micheal H Weisman. "Clinical features of SLE", Marc C Hochberg, Rheumatology 7thedition 2009(2): 135-1103
16. Cronin ME. Musculoskeletal manifestations of systemic lupus erythematosus. Rheum Dis North Am. 1988; 14(1): 99-116
17. Cervera R, Khamashta MA, Front J, Sebastiani GD, Gill A, Lavilla P et.al. Morbidity and mortality in systemic lupus erythematosus during a 10 year period: A comparison of early and late manifestations in a cohort of 1000 patients. Medicine (Baltimore) 2003; 82(5): 299-308
18. Fernando MM, Isenberg DA. How to monitor SLE in routine clinical practice. Annals of the Rheumatic Diseases, 2005; 64: 524-527
19. Dalcin PT, Barreto SS, Cunha RD, et.al. Lung clearance of Tc-DPTA in SLE. Braz J Med Bio Res 2002; 35(6): 663-8
20 .Ooi GC, Ngan H, Peh WC et.al. Systemic lupus erythematosus with respiratory symptoms: the value of HRCT. Clin Radiol 1997; 52: 775-781
21. Lilleby V, Aalokken TM, Johansen B et al. Pulmonary involvement in patients with childhood onset systemic lupus erythematosus. Clin Exp Rheumatol. 2006; 24(2): 203-208
22. 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
23. Karmn MY, Miranda LC, Tench CM et.al. Presentation and prognosis of the shrinking lung syndrome in SLE. Semin Arthritis Rheum 2002; 31(5): 289-98
24. Amin SN, Angadi SA, Mangat GK, Joshi VR, Haleankar AD, Salgaonkar DS et.al. Journal of Association of Physicians of India 1988; 36: 473-475
25. Samiha Samuel, Mona Mohsen, Rasha M, et.al. Pulmonary function tests in patients with SLE. Alex. J. Pediatr. 2005; 19(2): 277-281
26. Al-Abbad AJA, Cabral PA, Sanatanis et.al. Echocardiography and pulmonary function testing in childhood onset SLE. Lupus 2000; 10: 32-7
27. Manohar Joshi, Manisha Pendse, Gayatri Pendise. Study of pulmonary manifestations in systemic lupus erythematosus cases. MedPlus-International Medical Journal. Feb. 2017; 4(2): 254-257
28. Omer SB Alamoudi, Suzan M Attar. Pulmonary manifestations in systemic lupus erythematosus: Association with disease activity. Respirology 2015; 20: 474-480
29. Gergianaki I., Fanouriakis A., Adamichou C., Spyrou G., Mihalopoulos N. et.al. Is systemic lupus erythrmatosus different in urban versus rural living environment? Data from the Cretan Lupus Epidemiology and Surveillance Registry. Lupus 2019; 28(1): 104-113
30. Barnabe C, Josef L, Belisle P, Labrecque J et.al. Prevalence of systemic lupus erythematosus and systemic sclerosis in the First Nations population of Alberta, Canada. Arthritis Care Res (Hoboken) 2012; 64(1): 138-43
31. Felon HM, Doran M, Sant SM, Breatnach E. High resolution chest CT in systemic lupus erythematosus. AJR 1996; 166: 301-307
32. Kakati S, Doley B, Pal S, Deka UJ. Pulmonary manifestations in systemic lupus erythematosus (SLE) with special reference to HRCT. JAPI 2007; 55: 839-841

33. Degado EA, Malleson PN, Pirie GE, Petty RE. Pulmonary manifestations of childhood onset systemic lupus erythematosus. Semin Arthritis Rheum 1990; 29: 285-93
34. Weinrib L, Sharma OP, Quismorio FP jr. A long term study of interstitial lung disease in systemic lupus erythematosus. Semin Arthritis Rheum 1990; 20(1): 48-56
35. Haupt HM, Moore GW, Hutchins GM. The lung in systemic lupus erythematosus. Analysis of the pathologic changes in 120 patients. Am J Med 1981; 71: 791-98
36. Orens JB, Martinez FJ, Lynch JR. Pleuropulmonary manifestations of systemic lupus erythematosus. Rheum Dis Clin North Am 1994; 20: 159-193
37. Quadrelli SA, Alvarez C, Arce SC, Paz L et.al. Pulmonary involvement of systemic lupus erythematosus: Analysis of 90 necropsies. 2009; 18: 1053-1060
38. Keane MP, Lynch JP. Pleuropulmonary manifestations of systemic lupus erythematosus. Thorax 2000; 55(2): 159-66
39. West JB (Editors). Pulmonary Pathophysiology. Baltimore: Lippincott Williams & Wilkins 2008
40. Peter HS, Paul FD. Pulmonary manifestations in systemic lupus erythematosus in adults. Online 2010. Available from: URL: http://www.upToDate.com. V19.3
41. Cheema GS, Quismoro FP. Interstitial lung disease in systemic lupus erythematosus. Curr Pulm Med 2000; 429-9
42. Bresford MW, Cleary AG, Sills JA, Couriel J, Davidson JE. Cardiopulmonary involvement in juvenile systemic lupus erythematosus. Lupus 2005; 14: 152-8
43. Ciftci E, Yalcmkaya F, Ekim M, IleriM et.al. Pulmonary involvement in childhood onset systemic lupus erythematosus: A report of five cases. Rheumatology 2004; 43: 587-91
44. Downey C, Leibrman G. systemic lupus erythematosus: Pleuropulmonary manifestations. Online 2010. Available from : URL: http://www.eradiology.bidmc.harvard.edu
45. Dubois EI TDL. Clinical manifestations of systemic lupus erythematosus: computer analysis of 520 cases. JAMA 1964; 190(2): 104-111
46. Wells AU, Hansell DM, Rubens MB, King AD et.al. Fibrosing alveolitis in systemic sclerosis: indices of lung function in relation to extent of disease on computed tomography. Arthritis Rheum 1997; 40: 1229-36
47. Aduen JF, Zisman DA, Mobin SI et.al. Retrospective study of pulmonary function tests in patients presenting with isolated reduction in single breath diffusion capacity: implications for the diagnosis of combined obstructive and restrictive disease. Mayo Clin Prac 2007; 82(1): 48-54
48. American thoracic society/European respiratory society international multidisciplinary consensus classification of idiopathic interstitial pneumonias. Am J Resp Crit Care Med 2002; 165: 277-304