RESEARCH BRIEF

Spirometric Evaluation in Juvenile Systemic Lupus Erythematosus

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Objective: Spirometric evaluation in juvenile systemic lupus erythematosus.

Methods: Forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), FEV1/FVC, forced expiratory flow between 25-75% of vital capacity ($FEF_{25-75\%}$) and peak expiratory flow rate (PEFR) of 21 patients with juvenile SLE (jSLE) were compared to controls.

Result: Reduced FVC and $FEF_{25-75\%}$ was found in 18 and 9 patients, respectively. All had normal FEV1/FVC. None had respiratory complaint. When compared to controls, patients had significantly reduced FVC [mean (SD):1.97 (0.56) *vs* 2.35 (0.60), *P*=0.002] and $FEF_{25-75\%}$ [2.19 (0.83) *vs* 2.63 (0.76), *P*=0.028] but similar FEV1/FVC [86.87(7.03) *vs* 86.72 (6.35), *P*=0.639].

Conclusion: jSLE patients had significant restrictive pattern and small airway involvement.

Keyword: *Pulmonary function tests, Spirometry, Systemic lupus erythematosus*.

Systemic lupus erythematosus (SLE) is a multisystem autoimmune disorder with a broad spectrum of clinical presentations, frequently involving dermatological, renal, neurological and hematological systems. Pulmonary morbidities, although less frequent, have been described in juvenile SLE (jSLE) patients [1].

Interstitial lung disease and small airway involvement have been documented in adult SLE (aSLE) [2-4]. Evaluation of pulmonary function abnormality is often overlooked in children, and there is limited data in jSLE. The present study was carried out to evaluate pulmonary function by spirometry in jSLE patients and compare with matched controls.

METHODS

This cross-sectional comparative study was carried out from May 2013 to May 2014 in the Institute of Post-Graduate Medical Education and Research, Kolkata, India, after obtaining clearance from the Institutional Ethics Committee. Written consent from parents and assent from older patients (age 12-18 yrs) were taken. All consecutive previously diagnosed SLE patients attending the pediatric and adult rheumatology clinic with disease onset before 16 years were included as cases. Same number of age-sex, height- and weight-matched controls were recruited from patients attending OPD with minor ailments and no rheumatic or respiratory disorders. Patients under 5 years of age were not included as they fail to understand the instruction for spirometry [5]. Patients with chronic respiratory diseases, concurrent congenital heart disease, congenital facial defects, and history of smoking or surgery in the head and neck region were excluded. We performed spirometry after recovery in those with infection, pleurisy or pleural effusion.

Laboratory investigations included hematological and serological investigations, examination of urine, chest *X*-ray, high resolution computed tomography (HRCT) thorax, echocardiography and ultrasonography of abdomen. SLEDAI (SLE Disease Activity Index) score was used to evaluate disease activity [6]. Spirometry was done using Windows-based digital spirometer (Spirowin version 2.0) after explanation and demonstration to the subject. The nose was manually closed by the examiner while they were asked to take maximal inspiration and then to blow into the mouthpiece as quickly, forcefully and maximally as possible. Forced vital capacity (FVC), Forced expiratory volume in 1 second (FEV1), FEV1/FVC ratio, Forced expiratory flow between 25-75% of vital capacity ($FEF_{25-75\%}$) and peak expiratory flow rate (PEFR) were noted. American Thoracic Society (ATS) criteria for acceptability and repeatability of spirometry were followed. Spirograms with satisfactory start and satisfactory exhalation were considered acceptable. The spirometric procedure was repeated until at least two acceptable spirograms showed FVC within 0.150 L of each other [7]. Maneuver with largest sum of FVC and FEV1 was used. Patients with unacceptable spirometry and/or inadequate effort were excluded. Global lung Initiative (GLI)-2012 equation for 'others/mixed' group

(Quanjer) was used for calculating lower limit of normal for FVC, FEV1 and $FEF_{25-75\%}$ [8].

GraphPad Prism version 5 (San Diego, CA: GraphPad Software Inc., 2007) was used for statistical analysis. Data were analyzed by Wilcoxon signed rank test with *P* value less than 0.05 considered significant.

RESULTS

Out of 31 jSLE patients initially enrolled, five were very sick and could not perform spirometry. Three young children failed to perform acceptable spirometry due to problem in comprehension, while two older children with sub-maximal effort did not meet repeatability criteria. Of the remaining 21 patients (age 9-18 years), 20 were females. Mean age, height and weight were 15.52 yrs, 148.0 cm and 41.81 kg, respectively. Mean duration of the disease was 2.6 years. Majority of patients (*n*=13) were in remission with SLEDAI score of zero. None had respiratory symptom at rest or with activities.

Reduced FVC and FEV1 were found in 18 (86%) patients. FEV1/FVC ratio was normal in all. $FEF_{25-75\%}$ was decreased in 9 (43%) patients. Eight patients had simultaneously decreased FVC, FEV1 and $FEF_{25-75\%}$. ***Table* I** shows the comparison of parameters between jSLE patients and controls. FVC, FEV1 and $FEF_{25-75\%}$ were significantly compromised in jSLE patients. But FEV1/FVC ratio and PEFR were similar to those of controls. ***Fig.* 1** compares median, maximum, minimum and inter-quartile range of FVC and FEV1, FEV1/FVC and $FEF_{25-75\%}$ of cases and controls.

TABLE I CHARACTERISTICS OF THE STUDY POPLATION (*N*=21)

	jSLE, Mean (SD)	*Control, Mean (SD)*
Age, y	15.52 (2.93)	15.76 (3.05)
Height, cm	148.0 (11.3)	148.3 (9.3)
Weight, kg	41.81 (8.75)	41.24 (7.99)
#FVC, L	1.96 (0.60)	2.35 (0.60)
*FEV1, L	1.681 (0.43)	2.02 (0.45)
FEV1/FVC, %	86.87 (7.03)	86.72 (6.35)
$FEF_{25\%-75\%}$, L/s	2.19 (0.83)	2.63 (0.76)
PEFR, L/s	3.56 (1.06)	3.58 (0.94)

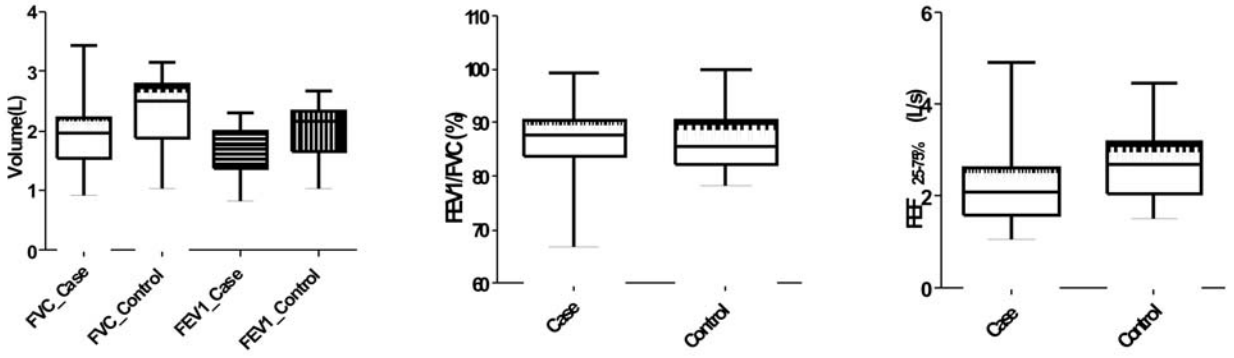
$^{*}P$ <0.001; $^{\#}P$=0.002, $^{\$}P$=0.029; jSLE: juvenile SLE patients.

DISCUSSION

This study, demonstrated significant restrictive pattern and small airway involvement in jSLE. Reduced FVC, FEV1 and $FEF_{25-75\%}$ but similar FEV1/FVC ratio indicate restrictive pattern and small airway involvement in jSLE patients. Small airway involvement was found in 43% of patients and 86% had possible subclinical restrictive disease that needs to be confirmed by Diffusing capacity for carbon monoxide (DLCO), High resolution computed tomography (HRCT) and measurement of Total lung capacity (TLC).

Due to lack of standardized data on spirometry, we compared cases with age-, sex-, height- and weight-matched controls. However, Quanjer's equation was also used for quantitative analysis. Exclusion of very sick children and those not fulfilling acceptability and repeatability criteria reduced the sample size in our study. HRCT could not be done in all children due to financial constraint. DLCO could also not been done due to unavailability of this facility in our institution.

Pulmonary manifestations in jSLE include pleuritis and pleural effusion, acute lupus pneumonitis, chronic interstitial lung disease (ILD), pulmonary hemorrhage, diaphragmatic dysfunction and pulmonary hypertension



(*a*) (*b*) (*c*)

***Fig.* 1** *Box and whisker plot comparing FVC and FEV1 (a), FEV1/FVC (b), and $FEF_{25-75\%}$ (c) of cases and controls.*

WHAT THIS STUDY ADDS?

- There is a significant restrictive pattern and small airway involvement on spirometry in jSLE patients.

[1,9,10]. ILD on HRCT has been documented in nearly one-third of aSLE with no clinical symptoms [2,3]. However, reports of ILD in pediatric population are scarce. ILD was found in 14% of jSLE patients in one study, while another showed abnormal HRCT in 8% but none had ILD [11,12]. Spirometry, an inexpensive and easily available screening tool, is especially suitable for early detection of restrictive pattern in pediatric rheumatologic diseases in a resource-limited infrastructure [13]. Abnormal spirometry and DLCO has been described in 20% to more than half of jSLE patients in different studies [11,14,15]. Progressive decline in $FEF_{25-75\%}$ indicating small airway disease in aSLE patients has been reported earlier [4]. It is possible that the jSLE patients would develop restrictive and/or obstructive lung disease at a later age.

Periodic spirometric evaluation might be a cost-effective option to detect the subclinical pulmonary changes in settings where DLCO or repeated 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. A longitudinal multi-center study is needed to establish the relation of pulmonary function with duration and disease activity.

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