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Pulmonary Involvement in Systemic Lupus Erythematosus Children with Lupus Nephritis

Tarek Hamed Attia[1], Ezzat Kamel Amien[2], Hibah Shuayb Asrafeel[3]

[1]Professor of Pediatrics, Faculty of Medicine – Zagazig University, Zagazig, Sharkia, Egypt.

[2]Assistant Professor of Pediatrics, Faculty of Medicine – Zagazig University, Zagazig, Sharkia, Egypt.

[3]M.B.B.Ch, Department of Pediatrics, Faculty of Medicine – Omar Al Muktar University, Libya

Corresponding Author: Hibah Shuayb Asrafeel

Email: hebaasrafel@gmail.com

Abstract

Background: Systemic lupus erythematosus (SLE) is a complex autoimmune disorder of unknown etiology in which tissues and cells are damaged by pathogenic autoantibodies and immune complexes. The study aimed was to assess the role of spirometery in pulmonary involvement in children with lupus nephritis and the correlation of spirometric parameters with degree of renal affection.

Patient and Methods: This cross-sectional study was conducted in Nephrology unite at Zagazig University Hospital on 24 cases that diagnosed SLE patients during the period from Oct 2019- Mar 2020. Patients in the study had subjected to complete history taking, Laboratory investigations included hematological and examination of urine, kidney function test, Chest X-ray, ultrasonography of chest and Renal Biobsy, pulmonary function test (PFT), SLED score.

Results: Restrictive lung disease was prevalent in 54.2% of patients, mean value of FEV1 was (86.208 ± 23.268), forced vital capacity was (79.321± 23.79), FEV1/FVC was (108.14±11.731), MEF75 was (88.404±19.703). MEF50 was (93.358±25.616). MEF25 was (107.808±47.54), PEF was (84.4± 18.865) there was significant negative correlation between systemic lupus erythematous Disease score and Forced expiratory Volume in 1 sec, forced vital capacity and forced expiratory flow at 25% FVC There is significant negative correlation between grades of nephropathy by renal biopsy and forced expiratory flow at 25% FVC.

Conclusion: Present study showed that pulmonary diseases occur frequently in childhood onset Systemic lupus erythematosus. Serial PFT studies may be useful in assessing the presence of lung involvement in childhood onset SLE and monitoring of course and activity of the disease.

Keywords: Pulmonary function tests, Spirometry, Systemic lupus erythematosus.

1. Introduction

Systemic lupus erythematosus (SLE) is a chronic systemic disease involving multiple organs such as the kidneys, skin, and brain. Lung is another organ that can be affected. A number of pulmonary complications including pleurisy, pneumonitis, infectious pneumonia, pulmonary hemorrhage, pulmonary hypertension, and pneumothorax have been reported in patients with SLE. Pulmonary involvement is relatively frequent in adult

patients; it has infrequently been reported in children with SLE. However, pulmonary manifestations may be an initial and/or life-threatening complication of SLE in children [1] .

Adult SLE and childhood SLE have similar clinical features, but children are known to have a more severe disease course. SLE is the most common connective tissue disease affecting the lung, with a similar proportion between adults and children. In children with SLE, it has been reported that pulmonary involvement occurred in 7.6–75% of the patients (1–3). The types of pulmonary manifestations reported involve any portion of the pulmonary organ system including the pleura, diaphragm, parenchyma, and vasculature [2].

Symptomatic pleuro-pulmonary disease in SLE is well-described in both adults and children. There is considerable debate concerning the relative frequency, with some studies reporting a higher incidence in adults, and others similar proportions. The types of pulmonary manifestations reported are diverse, and may involve any portion of the pulmonary organ system including the pleura, diaphragm, parenchyma, and vasculature. The wide range of prevalence estimates found in the literature may be due to known racial and ethnic phenotypic variability, as well as different approaches taken to determine the presence of pulmonary involvement with cSLE [3].

All components of the respiratory system may be affected during the course of disease. The spectrum of pulmonary manifestations caused by SLE includes pleural disease, upper and lower airway dysfunction, primary pulmonary hypertension, pulmonary thromboembolism, acute reversible hypoxemia, diffuse interstitial lung disease, acute lupus pneumonitis, diffuse alveolar hemorrhage, and shrinking lung syndrome. Some patients may have more than one form of pleuropulmonary involvement during the course of their disease. The severity of these respiratory complications is highly variable and ranges from subclinical to potentially life-threatening conditions [4] .

The pleuropulmonary manifestation of Systemic Lupus Erythematous (SLE) are pleuritis, acute lupus pneumonitis, chronic interstitial lung disease with fibrosis, alveolar hemorrhage, respiratory muscle and diaphragmatic dysfunction, atelectasis, bronchiolitis obliterans, pulmonary vascular disease with pulmonary hypertension and pulmonary embolism. The pleura are the most common thoracic localization of SLE. Record studies with the use of imaging techniques like high resolution computed tomography (HRCT) chest suggest that not only pleural diseases are common but airway disease, lymphadenopathy and interstitial lung diseases are also common than previously thought [5].

This study aimed to assess the role of spirometry in detection of pulmonary involvement in children with lupus nephritis and to correlate spirometric parameters with degree of renal affection.

2. Patients and Methods

This cross-sectional comparative study was carried out from Oct 2019- Mar 2020 in pediatric nephrology unit at Zagazig University Hospital, after obtaining clearance from the Institutional Ethics Committee. Written informed consent was obtained from all childers' parents and the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University. The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Inclusion Criteria: Patient with pulmonary manifestation. All the patient meeting systemic lupus international collaborating clinic (SLICC 2012) for diagnosis of systemic lupus erythematous with lupus nephrties without evidence of other connective tissue diseases. Same number of age-sex, height- and weightmatched controls were recruited from patients attending OPD with minor ailments and no rheumatic or respiratory disorders.

Exclusion criteria: Patients under 5 years of age were not included as they fail to understand the instruction for spirometry. Resting tachycardia. Patient with concurrent congenital heart disease. Patient with history of surgery in the head and neck region was excluded.

Methods:

Patients in the study had subjected to Complete history taking including name, age, gender, Family history of SEL, Duration of SEL, SLE score, Laboratory investigations included hematological and serological investigations, examination of urine, kidney function test, Chest X-ray, ultrasonography of chest and Renal Biobsy, pulmonary function test, SLED score. Disease Activity was assessed at time of study enrollment and scored

according to systemic lupus erythematous Disease Activity index (SLEDAI) disease was consider active when index was 10 or more [6].

American Thoracic Society (ATS) criteria for acceptability and epeatability of spirometry were followed. 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 MEF75, MEF50, MEF25 and peak expiratory flow rate (PEFR) were noted.

FEF25-75% is the most sensitive measure of airflow in peripheral airways where primary airflow obstruction originates and it is reduced in early bronchial impairment, which is associated with small airway disease. maximal midexpiratory flow FEF25–75; the maximum rate of airflow measured between expired volumes of 25 and 75 per cent of the vital capacity during a forced expiration; represented graphically as the slope of the line connecting the points on the forced expiratory volume curve at 25 and 75 per cent of the forced vital capacity [7].

American Thoracic Society (ATS) criteria for acceptability and epeatability 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. Maneuver with largest sum of FVC and FEV1 was used. Patients with unacceptable spirometry and/or inadequate effort were excluded.

Statistical methods:

Analysis of the results was done via SPSS computer software version 18 (Statistical Package of Social Science) [8] employing mean and standard deviation as descriptive tools and student's T test, Chi square test and Pearson's correlation for comparisons. Results were considered significant at p value <0.05.

3. Results

Table (1), showed that females represented 70.8% of patients. They aged from 6 to 15 years with mean 11.333 years. BMI ranged from 15.306 to 32.653 kg/m2 with mean 21.066 kg/m2SLED score ranged from 3 to 33 with mean 16.58. Patients had lupus since 1 to 36 months with mean 16.792 month

Table (2), showed that FEV1 ranged from 31.7 to 124.9 with mean 86.208. FVC ranged from 28.3 to 140.6 with mean 79.321. FEV1/FVC ranged from 75.36 to 117.1 with mean 108.14. MEF75 ranged from 49.4 to 127.4 with mean 88.404. MEF50 ranged from 52.1 to 142 with mean 93.358. MEF25 ranged from 18.9 to 199.2 with mean 107.808. PEF ranged from 45.1 to 117.9 with mean 84.4

Figure (1), showed that there was negative correlation between grades of nephropathy by renal biopsy and all of FVC/ FEV1/FVC, MEF25, MEF50 and PEF

Figure (2), showed that there was statistically significant negative correlation between SLED score and FEV1, FVC and MEF25.

Table (1): Distribution of the studied patients according to demographic characteristics, disease severity and duration and anthropometric measures:

	N=24	%
Gender:		
Male	7	29.2
Female	17	70.8
Age (years):		
Mean ± SD	1	1.333±.632
Range		6 - 15

BMI (kg/m^2): Mean ± SD Range	 2 1	 1.066 ± 5.115 5.306 – 32.653
SLED score: Mean ± SD Range		 16.58 ± 9.03 4 - 33
Disease duration (months): Mean ± SD Range	 1	 6.792 ± 11.088 1 – 36

Table (2) Distribution of the studied patients according to spirometric measures:

Parameter	Value
FEV1: Mean ± SD Range	 86.208 ± 23.268 31.7 - 124.9
FVC: Mean ± SD Range	 79.321 ± 23.79 28.3 – 140.6
FEV1/FVC: Mean ± SD Range	 108.14 ± 11.731 75.36 – 117.1
MEF75: Mean ± SD Range	 88.404 ± 19.703 49.4 - 127.4
MEF50: Mean ± SD Range	 93.358 ± 25.616 52.1 – 142
MEF25: Mean ± SD Range	 107.808 ± 47.54 18.9 – 199.2
PEF: Mean ± SD Range	 84.4 ± 18.865 45.1 – 117.9

Table (3): Relation between activity by SLED score and spirometer

	Active	Not	t	P
FEV1	**78.61±12.54**	**100.36±33.58**	**2.452**	**0.015***
FVC	**73.75±15.11**	**95.30±31.25**	**2.314**	**0.024***
FEV1_FVC	**107.88±10.25**	**107.38±10.39**	**0.118**	**0.907**
MEF75	**89.97±18.16**	**85.70±25.92**	**0.476**	**0.639**
MEF50	**89.94±24.64**	**89.62±29.2**	**0.028**	**0.978**
MEF25	**93.45±30.58**	**130.78±43.81**	**2.265**	**0.036***
PEF	**84.25±17.62**	**83.76±24.85**	**0.057**	**0.955**

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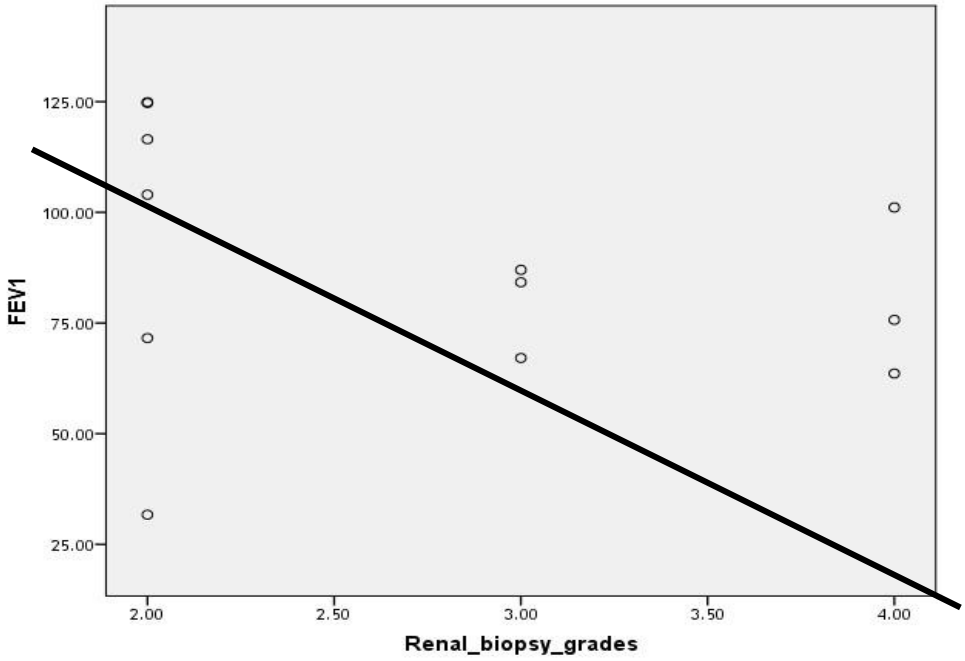

Fig. (1) Correlation between FEV1 and renal biopsy grades Significant negative correlation between FEV1 and renal biopsy grades .

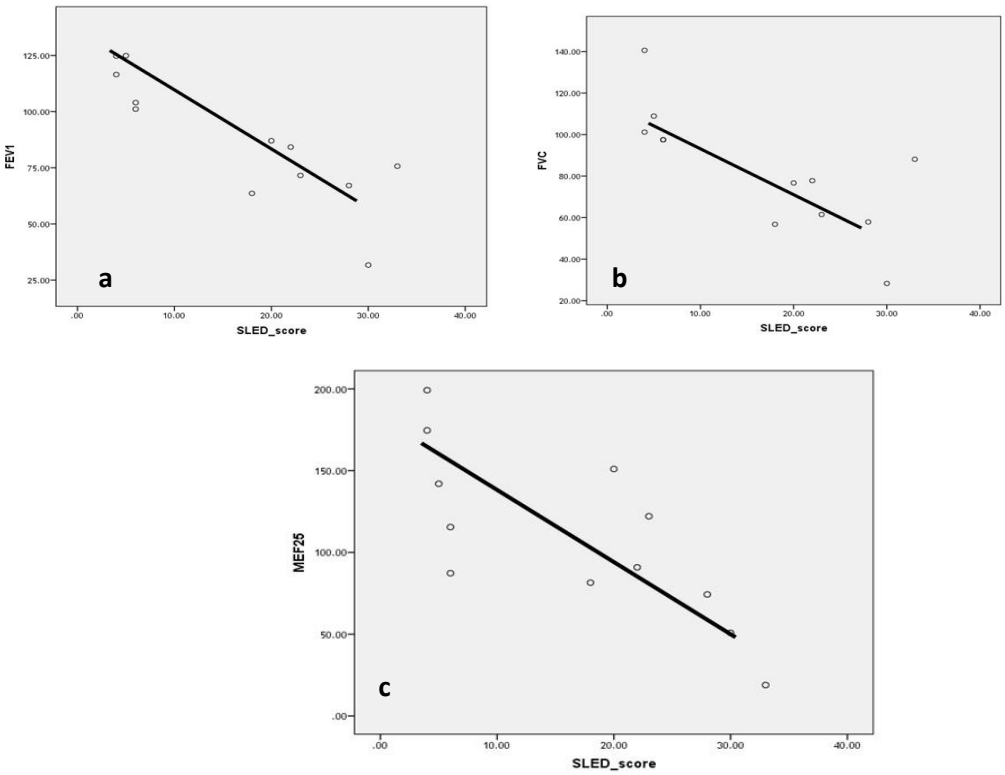

Figure. (2) Correlation between SLED and FEV1(a), FVC (b) , MEF25 (c)

4. Discussion

Lupus nephritis is one of the most serious manifestations of SLE, posing a considerable risk of morbidity and mortality. Early diagnosis and treatment with immunosuppressive agents is important for the better outcome of lupus nephritis. Thus, patients at risk of lupus nephritis should be identified as early as possible in the course of SLE [9].

The aim of the current study was to assess the role of spirometery in detection of pulmonary involvement in children with lupus nephritis and to correlate spirometric parameters with degree of renal affection.

The current study showed that females represented 70.8% of patients and males were (29.2%) with a mean age of 11.333 ± 2.632 years, the mean BMI was 21.066 ± 5.115 kg/m2, the mean SLED score was 16.58 ± 9.03, while the mean Disease duration was 16.792 ± 11.088 (months)

In agreement with our study, Mina et al., [10], reported that the mean age was 15.5 ± 2.7 years; (77%) were females and males were (23%) and mean disease duration was 18.24 ± 0.69 (months).

In agreement with our study, Lotfy et al., [1], who reported that the mean age was 14.8±3.037 years; (85%) were females and males were (15%) and mean, but different in mean disease duration where it was 4.9 ± 1.944 (years).

Current results showed BMI (kg/m2) was (21.066 ± 5.115) similar to the results of Singh et al. [11] who recorded BMI (kg/m2) of (21.17±3.43) and Disease duration was 13.6 ± 8.1 (months), but contrast with SELD score where it was 8.1 ± 7.4, while in current study it was 12.208 ± 8.236.

Current results showed that Restrictive lung disease was prevalent in 54.2% of patients, which in agreement with Borrell et al., [12] who found that Restrictive lung disease was presented in 52.3% of patients. On the other hand Veiga et al., [13] reported that twenty (50%) patients exhibited some type of respiratory disturbance: nine (22.5%) restrictive, eight (20%) obstructive, and 3 (7.5%) mixed, while Mohammad, et al. [14] reported that pulmonary function tests in all studied patients revealed that the majority of the patients (80%) presented with restrictive lung diseases.

Current study showed that the mean value of FEV1 was (86.208 ± 23.268), FVC was (79.321±23.79), FEV1/FVC was (108.14 ± 11.731), MEF75 was (88.404 ± 19.703). MEF50 was (93.358 ±25.616). MEF25 was (107.808. ± 47.54), PEF was (84.4± 18.865).

Lotfy et al., [1], who found that mean value of FEV1 was (96.9 ± 17.7), FVC was (89.175± 19.5), PEF25–PEF50 (99.250 ± 23.5).

The current study showed that FEV1, FVC and MEF25 were significantly lower in active group than not active group between studied groups. Which in agreement with the study of Abd El-Khalik et al., [15] reported that higher SLEDAI tended to be associated with lower PFTs, reported a similar results to our study.

While in contrast to our results, the study of Mohammad et al., [14], who found that there was no significant correlation between activity of SLE according to SLED score and respiratory functions, also, study of Abdulla et al., [16], who concluded that there was no correlation between altered PFTs and disease duration, activity and/or immunological findings.

There was a statistical negative correlation between grades of nephropathy by SLED score and FEV1, FVC and MEF25 which in agreement with the study of Deerojanawong et al., [17] who reported that there was negative correlation between SLED score and respiratory functions. While in contrast to our results, the study of Al-Abbad et al. [18], who reported a that their was no significant correlation between SLED score and respiratory functions.

Our results showed there was statistically significant negative correlation between grades of nephropathy by renal biopsy and FEV1.

Sharma et al., [19] reported that pulmonary function abnormalities are common among ESRD patients. Comparison of pre and posthemodialysis parameters showed significant improvements.

Lotfy et al., [1] reported that occult pulmonary disease occurs frequently in childhood-onset SLE, and that PFT abnormalities were found in 95% of these children.

5. Conclusion:

Present study showed that pulmonary diseases occur frequently in childhood onset Systemic lupus erythematosus. Serial PFT studies may be useful in assessing the presence of lung involvement in childhood onset SLE and monitoring of course and activity of the disease

Recommendations:

Further studies with a larger number of sample size with a long period follow-up are recommended to emphasize our conclusion and shed more light on the role of Spirometric Parameters in Systemic Erythematosus Children with Lupus Nephritis.

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