Brief Report



# Spirometry Plays a Limited Role in Assessing Lung Disease in Children with Newly Diagnosed Rheumatic Conditions

Spyridon Prountzos , Kyveli Chiotopoulou , Katerina Kourtesi , Evdoxia Sapountzi , Dafni Moriki , Elpiniki Kartsiouni , Efthymia Alexopoulou , Konstantinos Douros , Lampros Fotis *

Posted Date: 1 November 2024

doi: 10.20944/preprints202411.0083.v1

Keywords: Lung; Pediatrics; Rheumatic Diseases; Spirometry; Tomography; X-ray Computed

 doi:10.20944/preprints202411.0083.v1



*Article*

# Spirometry Plays a Limited Role in Assessing Lung Disease in Children with Newly Diagnosed Rheumatic Conditions

**Spyridon Prountzos [1], Kyveli Chiotopoulou [2], Evdoxia Sapountzi [3], Katerina Kourtesi [2], Dafni Moriki [4], Elpiniki Kartsiouni [4], Euthymia Alexopoulou [1], Konstantinos Douros [4,†] and Lampros Fotis [2,*,†]**

[1] 2nd Department of Radiology, ATTIKON General Hospital, National and Kapodistrian University of Athens, Greece; spyttt@gmail.com; ealex64@hotmail.com

[2] Division of Pediatric Rheumatology, 3rd Department of Pediatrics, ATTIKON General Hospital, National and Kapodistrian University of Athens, Greece; kyvelich@yahoo.gr

[3] 2nd Department of Pediatrics, AHEPA General Hospital, Aristotle University of Thessaloniki, Greece; kourtesikaterina@yahoo.com; esapountzi@gmail.com

[4] Division of Pediatric Pulmonology and Allergology, 3rd Department of Pediatrics, ATTIKON General Hospital, National and Kapodistrian University of Athens, Greece; dafnimoriki@yahoo.gr; elpikartsiouni@gmail.com; costasdouros@gmail.com

* Correspondence: lafotis@med.uoa.gr; Tel.: +30 210 5832228

† The last two authors contributed equally to the development of this manuscript.

**Abstract: Introduction**: Lung involvement in pediatric rheumatic diseases significantly impacts morbidity and mortality. High-resolution computed tomography (HRCT) is a sensitive diagnostic tool for detecting lung involvement; however, it raises concerns regarding radiation exposure. Spirometry, a non-invasive and widely accessible test, is often used to assess pulmonary function, but its accuracy in identifying lung disease in children with newly diagnosed rheumatic conditions remains uncertain. This study evaluates the reliability of spirometry, using HRCT as the reference standard, in detecting early lung involvement in this population. Methods: At our institution, all patients suspected of having lung involvement—either due to respiratory symptoms or the high prevalence of respiratory involvement associated with their specific disease—underwent an HRCT scan and pulmonary assessment. A retrospective review of HRCT scans was conducted for 22 pediatric patients diagnosed with rheumatic disease between January 2021 and December 2023, all of whom exhibited pathological findings in their HRCT scans. HRCT scans were conducted with a paired end-inspiratory and forced-expiratory protocol using 1-mm collimation. Radiological findings, including parenchymal opacities, ground-glass opacities (GGOs), reticular patterns, honeycombing, parenchymal bands, bronchiectasis, peribronchial wall thickening, and air trapping were assessed. Spirometric values, including percent predicted values for Forced Expiratory Volume in 1 second (ppFEV1), Forced Vital Capacity (ppFVC), and the FEV1/FVC ratio, were collected for all patients who had an acceptable flow-volume curve. Results: Of the 22 patients enrolled, 17 (77.3%) had technically acceptable spirometry results. Using HRCT as the reference standard, spirometry yielded a sensitivity of 29.4%. Conclusion: Although spirometry demonstrated excellent positive predictive value, its low sensitivity indicates that it may miss early lung involvement in children with newly diagnosed rheumatic diseases. These findings reinforce HRCT as the preferred diagnostic tool in this population, despite concerns about radiation exposure, to ensure accurate detection and management of lung involvement.

**Keywords:** Lung; Pediatrics; Rheumatic Diseases; Spirometry; Tomography; X-ray Computed;

## 1. Introduction

Rheumatic diseases are a group of autoimmune disorders that affect multiple organs, with the lungs being a common target. Individual or several components of the respiratory system, including

 doi:10.20944/preprints202411.0083.v1



the airways, vessels, parenchyma, pleura, and respiratory muscles, may be related to the illness itself or to the medications used. Lung involvement in rheumatic diseases is a major determinant of patient morbidity and mortality, while the pattern of lung disease is considerably heterogeneous in incidence, prevalence, and severity depending on the underlying rheumatic disease [1,2].

Systemic inflammatory diseases with the highest likelihood of pulmonary involvement are juvenile systemic lupus erythematosus (SLE), scleroderma (systemic sclerosis [SSc]), juvenile dermatomyositis (JDM), mixed connective tissue disease (MCTD), granulomatosis with polyangiitis and juvenile idiopathic arthritis (JIA) [3]. Interstitial lung disease (ILD) is usually the most frequent presentation of lung involvement in adult patients, while bronchiectasis, and obstructive airways disease may also occur. The incidence of pulmonary complications is lower in childhood, and some forms of diffuse lung disease are unique to infants and children [4]. Clinically significant pulmonary complications are relatively uncommon in childhood, and, if present, may require changes in disease management [5].

Recognition of pulmonary involvement depends on the methods used to detect the disease. Although various tests are available for assessing lung function, their sensitivity and specificity in detecting lung involvement in newly diagnosed patients are not always consistent with their efficacy in monitoring lung function throughout the course of inflammatory rheumatic disease [6].

**Children's Interstitial Lung Disease (chILD)** encompasses a diverse group of rare, chronic lung disorders affecting children and infants. These diseases are marked by a range of symptoms, such as persistent cough, shortness of breath, hypoxemia, and reduced exercise tolerance, which reflect underlying diffuse lung pathology {7]. Diagnostic imaging, particularly **high-resolution computed tomography (HRCT)**, is crucial in chILD, revealing characteristic patterns like hyperinflation, mosaic attenuation, air trapping, ground-glass opacities, consolidation, linear or reticular opacities, nodules, and cysts [8].

HRCT is the most effective tool for detecting lung disease, as it is highly sensitive in identifying morphological abnormalities. However, concerns about radiation exposure, particularly in children, necessitate careful use. In contrast, spirometry is a simpler, non-invasive method for assessing pulmonary function and is widely used for screening and monitoring lung function and involvement in patients with inflammatory rheumatic diseases. Despite its accessibility, the reliability of spirometry in detecting lung disease in children with newly diagnosed rheumatic conditions is uncertain [6].

In this study, we aimed to evaluate the diagnostic accuracy of spirometry in detecting lung involvement in a population of newly diagnosed children with rheumatic diseases, using HRCT as the gold standard

## 2. Materials and Methods

This retrospective study was conducted at the Unit of Pediatric Rheumatology and of Pediatric Pulmonology and Allergology, 3rd Department of Pediatrics, and the Pediatric Radiology Unit, 2nd Department of Radiology of University General Hospital “Attikon”, Athens, Greece, between January 2021 and December 2023.

In our institution, all patients suspected of having lung involvement—either due to the presence of respiratory-related symptoms or the high prevalence of respiratory involvement associated with the specific disease [9]—undergo a high-resolution computed tomography (HRCT) scan.

All patients fulfilled the commonly accepted classification criteria for their respective diagnoses. For SLE, the 2019 European League Against Rheumatism (EULAR)/American College of Rheumatology (ACR) classification criteria were used [10]. Systemic sclerosis (SSc) was diagnosed based on the Pediatric Rheumatology European Society (PRES)/ACR/EULAR provisional classification criteria [11]. Juvenile dermatomyositis (JDM) was classified according to the Peter and Bohan diagnostic criteria [12], and systemic juvenile idiopathic arthritis (JIA) was diagnosed using the 2019 Pediatric Rheumatology International Trials Organization (PRINTO) criteria [13]. Mixed connective tissue disease (MCTD) was diagnosed based on Kasukawa’s criteria [14], while granulomatosis with polyangiitis (GPA) was classified using the EULAR/PRINTO/PRES 2008 Ankara

 doi:10.20944/preprints202411.0083.v1



criteria [15]. For Behçet's disease, the pediatric Behçet's disease criteria were applied [16]. No formal classification criteria exist for microscopic polyangiitis, and the patient with unclassified vasculitis did not meet any of the available vasculitis criteria. Similarly, the patient with pulmonary hemosiderosis was diagnosed by exclusion, as no specific classification criteria exist for this condition.

All chest HRCT scans were conducted at our center between January 2021, and December 2023, and were reviewed retrospectively. All patients underwent chest CT examination using paired end-inspiratory and forced-expiratory scan protocol using 1-mm collimation and slice thickness reconstruction algorithm. Only patients with radiological findings were included in our study. Parenchymal opacities, ground-glass opacities (GGOs), reticular pattern, honeycombing, parenchymal bands, bronchiectasis, and peribronchial wall thickening were examined. Air trapping was assessed during expiratory scans.

The patients were treatment-naïve and had been diagnosed with rheumatic disease for the first time. Children with a significant combination of hyperinflation, mosaic attenuation, air trapping, ground-glass opacities, consolidation, linear or reticular opacities, nodules, or cysts were defined as having lung disease consistent with chILD.

Spirometry was performed in all patients, and the percent predicted values for Forced Expiratory Volume in 1 second (ppFEV1) and Forced Vital Capacity (ppFVC), along with the FEV1/FVC ratio, were recorded. Only patients with technically acceptable flow-volume curves were included in the analysis. Patients with reduced ppFEV1 and/or a reduced FEV1/FVC ratio were classified as having obstructive lung disease, while those with reduced ppFVC and a normal FEV1/FVC ratio were classified as having restrictive lung disease.

All symptoms associated with the respiratory tract were reviewed. Exclusion criteria were history of chronic lung or cardiac diseaseas, asthma, cystic fibrosis, immunodeficiency, congenital heart disease, bronchopulmonary dysplasia, pulmonary infection and recurrent aspiration.

The study protocol was approved by the Ethics Committee of Attikon University Hospital.

*Statistical analysis:* Our study focused exclusively on patients with definitive radiological findings. However, the absence of variability in the outcome variable hindered our ability to conduct a receiver operating characteristic analysis or derive a comprehensive set of accuracy metrics. As a result, we could only calculate sensitivity based on the available data on false negatives.

## 3. Results

Twenty-two pediatric patients diagnosed with various rheumatic diseases that exhibited one or more pathologic findings in their HRCT were included in the study. The demographic and clinical characteristics, the specific diagnoses and the radiological HRCT findings are detailed in Table 1. Twelve of the 22 patients (54.5%) had HRCT patterns consistent with chILD. Only 17 (77.3%) patients provided a technically acceptable spirometric flow-volume curve. Mean (sd) values for ppFVC, ppFEV1, and FEV1/FVC ratio were 90.71 (13.33), 95.06 (17.54), and 91.48 (8.63), respectively. Four (18.2%) patients had spirometic values suggestive of restrictive and one (4.5%) of obstructive lung disease.

Using HRCT scan findings as the reference standard the spirometry had a sensitivity of 29.4%.

**Table 1.** Demographic, clinical and radiological characteristics of enrolled patients.

| Variable | Categories | N (%) |
|---|---|---|
| Sex | Female | 18 (81.8%) |
| | Male | 4 (18.2%) |
| Age (in years) | | mean 13.05 (±3.169, min 3, max 16) |
| Cough | Yes | 6 (27.3%) |
| | No | 16 (72.7%) |
| Dyspnea | Yes | 3 (13.6%) |
| | No | 19 (87.4%) |
| Exercise intolerance | Yes | 9 (40.9%) |
| | No | 13 (59.1%) |

 doi:10.20944/preprints202411.0083.v1



| | | |
|---|---|---|
| Disease | Systemic lupus erythematosus | 4 (18.2%) |
| | Systemic sclerosis | 4 (18.2%) |
| | Juvenile dermatomyositis | 3 (13.6%) |
| | Systemic Juvenile Idiopathic Arthritis | 3 (13.6%) |
| | Mixed connective tissue disease | 3(13.6%) |
| | Microscopic polyangiitis | 1(4.5%) |
| | Granulomatosis with polyangiitis | 1(4.5%) |
| | Non-specific vasculitis | 1(4.5%) |
| | Behçet's disease | 1(4.5%) |
| | Idiopathic Pulmonary Hemosiderosis | 1(4.5%) |
| HRCT scan | Yes | 22 (100%) |
| | No | 0 (0%) |
| Parenchymal opacities | Yes | 7 (31.8%) |
| | No | 15 (68.2%) |
| Ground-glass opacities | Yes | 13 (59.1%) |
| | No | 9 (40.9%) |
| Reticular pattern | Yes | 10 (45.5%) |
| | No | 12 (54.5%) |
| Honeycombing | Yes | 1 (4.5%) |
| | No | 21 (95.5%) |
| Parenchymal bands | Yes | 12 (54.5%) |
| | No | 10 (45.5%) |
| Bronchiectatic changes | Yes | 9 (40.9%) |
| | No | 13 (59.1%) |
| Peribronchial wall thickening | Yes | 19 (61.4%) |
| | No | 3 (13.6%) |
| Mosaic attenuation | Yes | 11 (50.0%) |
| | No | 11 (50.0%) |

## 4. Discussion

The present study evaluated the diagnostic accuracy of spirometry in detecting lung involvement in children newly diagnosed with various rheumatic diseases, using HRCT as the gold standard. We evaluated pulmonary involvement in children with newly diagnosed rheumatic diseases who were suspected of having lung involvement. All participants underwent both chest HRCT scans and spirometry. HRCT was performed regardless of whether spirometry results were normal or abnormal. Overall, spirometry demonstrated poor sensitivity. While spirometry is a non-invasive and widely accessible tool, its utility in identifying lung abnormalities in this pediatric population may be limited when compared to HRCT.

Lung involvement is a recognized complication of systemic rheumatic diseases, although it is less common in pediatric patients compared to adults [2]. The diversity of rheumatic diseases in our cohort, including SLE, SSc, JDM, and others, reflects the heterogeneity of pulmonary manifestations associated with these conditions. ILD, ground-glass opacities (GGO), and bronchiectasis were frequently observed in HRCT, consistent with previous studies that identified these as common features of lung involvement in rheumatic diseases [17].

Spirometry is commonly employed in clinical practice for assessing lung function, given its simplicity and non-invasive nature. However, its diagnostic accuracy in pulmonary involvement in children with rheumatic diseases have remained a subject of debate. In this study, spirometry

 doi:10.20944/preprints202411.0083.v1



demonstrated a pour sensitivity. This suggests that it fails to detect a substantial number of cases with lung involvement. This aligns with previous reports highlighting spirometry's limitations in early detection of pulmonary abnormalities compared to HRCT [18, 19].

Earlier studies have reported varying results regarding spirometry's effectiveness in pediatric cohorts. In the study by Huang et al, 56.3% of children with newly diagnosed rheumatic disease had abnormal pulmonary function tests (PFTs), while only 16.7% showed abnormal HRCT findings. In the same study, half of the patients with abnormal HRCT results had normal PFTs [20]. Similarly, Lilleby et al. found that PFTs were abnormal in 37% of their patients with childhood-onset SLE, whereas only 8% had abnormal HRCT findings [21]. Consistently with our results, Veiga et al. showed that, in their cohort of patients with childhood-onset SLE, 70% had abnormal CT findings, which were minimal in 43% [22]. This study, along with our data, is aligned with studies in adult patients that have reported a high prevalence of chest CT abnormalities suggestive of lung involvement and ILD mostly in asymptomatic patients with rheumatic diseases who have normal PFTs [23].

A prior study evaluating a stepwise diagnostic screening approach, combining PFTs, chest radiography, and pulmonary HRCT, for detecting ILD in adult patients with immune-related diseases showed that HRCT had the highest sensitivity (100%) but lower specificity compared to PFTs and chest X-ray [24]. Like the current pediatric study, GGOs was the most common HRCT finding among these adult patients. The combination of PFTs such as diffusing capacity of the lung for carbon monoxide (DLCO) <80% and chest X-ray increased sensitivity and specificity, suggesting that patients with reduced DLCO or suspicious chest X-ray findings should undergo HRCT to confirm ILD and exclude other pulmonary conditions [24]. This suggests that HRCT despite involving radiation exposure, offers an accurate diagnostic tool for detecting ILD and other pulmonary abnormalities.

Both PFTs and HRCT are useful in providing a comprehensive assessment of lung involvement in rheumatic disease. While PFTs are favored for their non-invasiveness and ease of repeated measurements, HRCT is often reserved for cases where PFTs indicate significant abnormalities or where clinical suspicion of ILD is high [1]. HRCT is highly sensitive for detecting ILD, even at early or asymptomatic stages but its specificity can be lower, especially when it comes to distinguishing between different types of lung abnormalities. PFTs, particularly measures like DLCO have moderate sensitivity. They may miss early or mild ILD, especially in cases where structural changes precede functional impairment. PFTs are generally more specific than sensitive. A reduced DLCO may suggest ILD, but normal PFT results do not rule out the presence of early ILD. Due to being non-invasive and easily repeatable, PFTs are often preferred for initial assessments and ongoing monitoring, especially in cases where clinical suspicion of ILD is low [25].

While HRCT is more sensitive, its use in children is limited due to radiation exposure risks and the subclinical nature of lung disease in asymptomatic patients. Lung involvement in rheumatic diseases can be heterogeneous and may not always correlate with clinical symptoms or PFTs result [6]. Nevertheless, chest CT scan is considered the gold standard method for defining structural abnormalities [26]. Recent advances in CT technology have enabled faster scan times with super low-dose options, achieving dose-length (DLPs) as low as 7.66 mGy*cm per scan [27]. However, in pediatric populations, the concern about long-term radiation effects remains, especially for repeated scans. Despite these concerns, HRCT is still recommended for screening in high-risk pediatric patients [20]. The findings of the current study of prevalent lung involvement in asymptomatic pediatric patients, emphasize the subclinical nature of pulmonary manifestations in these diseases suggesting HRCT's potential role in identifying early structural changes before functional impairment becomes apparent and highlighting its potential role in early diagnosis and intervention. The ability of HRCT to detect subtle lung changes could guide clinicians toward more aggressive or protective treatment regimens, particularly in diseases known for their pulmonary toxicity, such as SSc and JDM.

Detecting ILD in pediatric rheumatic patients presents challenges distinct from those in adults. In adults, HRCT and PFTs are widely recognized as crucial tools for screening and monitoring ILD, with HRCT being highly sensitive in detecting early structural abnormalities, even before functional

 doi:10.20944/preprints202411.0083.v1



impairments manifest, as indicated by reduced pulmonary function parameters like FVC and DLCO [28]. The guidelines published by the American College of Rheumatology and the American College of Chest Physicians for people with systemic autoimmune rheumatic disease at increased risk of developing ILD, conditionally recommended HRCT and PFTs over PFTs alone for systemic autoimmune rheumatic diseases at high risk for ILD [28]. Our findings revealed that for children with rheumatic diseases that exhibited abnormalities on HRCT, spirometry identified definite pathology in only a minority of patients. This means that spirometry may overlook early or subtle lung involvement, which could delay appropriate interventions. This is underscored by the fact that a significant proportion of our patients exhibited no respiratory symptoms, yet HRCT identified abnormal findings in all cases. Thus, relying solely on spirometry could result in underdiagnosis of lung involvement, especially in asymptomatic individuals.

When assessing pediatric rheumatic patients, the choice between HRCT and PFTs should be carefully considered. HRCT's sensitivity for detecting early or asymptomatic structural changes contrasts with the safer, more easily repeatable PFTs, which may be challenging for younger children to perform reliably [25]. Similar issues may arise with HRCT, although sedation can be administered when necessary to facilitate the process. Clinical context, the specific rheumatic disease, and the presence of symptoms or other ILD risk factors should guide the decision. This study supports using HRCT as a complementary tool to PFTs in children with rheumatic diseases to facilitate early detection and intervention, potentially reducing long-term morbidity.

Certain limitations of this study include a small sample size which limits generalizability and the inclusion of various rheumatic diseases, each with distinct rates of lung involvement. Also, patients were not subjected to additional PFTs such as DLCO or plethysmography, which could have provided more comprehensive assessments of lung function. Future studies should include larger, more homogeneous cohorts, and a broader range of diagnostic tests to better understand PFTs sensitivity and specificity in comparison with spirometry or HRCT. Such research could further refine the balance between HRCT's diagnostic sensitivity and its safe application in younger populations.

## 5. Conclusions

The present study underscores the critical role of HRCT in identifying subclinical pulmonary involvement in pediatric patients newly diagnosed with rheumatic diseases, findings not always apparent through symptoms or spirometry alone. Given the heterogeneous nature of lung disease in these conditions and the associated risks, this study supports HRCT's inclusion in initial evaluations. Further research to refine diagnostic and monitoring strategies, could be pivotal in enhancing long-term respiratory outcomes for this vulnerable population.

**Author Contributions:** Conceptualization, SP, EA, KD and LF.; methodology, SP, KD, LF.; formal analysis, KD; writing—original draft preparation, SP, KC, ES, KK, DM, EK; writing—review and editing, EA, KD, LF; supervision, KC, KK, LF. All authors have read and agreed to the published version of the manuscript.

**Funding:** This research received no external funding.

**Institutional Review Board Statement:** The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of ATTIKON General Hospital, NKUA EBD494, date 02/07/2024.

**Informed Consent Statement:** Patient consent was not mandated according to current practice for retrospective studies in our institution when only a secondary review of imaging data and retrospective clinical data is undertaken.

**Data Availability Statement:** The clinical data supporting the findings of this study are available from the corresponding author upon reasonable requests via email: lafotis@med.uoa.gr.

**Conflicts of Interest:** The authors declare no conflicts of interest.

## References

1. Ha, Y.J.; Lee, Y.J.; Kang, E.H. Lung involvements in rheumatic diseases: update on the epidemiology, pathogenesis, clinical features, and treatment. *Biomed Res Int* **2018**, *2018*, 6930297. doi: 10.1155/2018/6930297

2. Richardson, A.E.; Warrier, K.; Vyas, H. Respiratory complications of the rheumatological diseases in childhood. *Arch Dis Child* **2016**, *101*, 752–758. doi: 10.1136/archdischild-2014-306049
3. Dell, S.D.; Schneider, R.; Yeung, R. Pulmonary involvement in the systemic inflammatory diseases of childhood. In *Kendig's Disorders of the Respiratory Tract in Children,* 9th ed.; Wilmott, R.W., Deterding, R., Li, A., Ratjen, F., Sly, P., Zar, H.J., Bush, A., Eds.; Elsevier, Amsterdam, Netherlands, 2019; pp. 850–875.e7.
4. Griese, M. Chronic interstitial lung disease in children. *Eur Respir Rev* **2018**, *27*, 170100. doi: 10.1183/16000617.0100-2017
5. Dell, S.; Cernelc-Kohan, M.; Hagood, J.S. Diffuse and interstitial lung disease and childhood rheumatologic disorders. *Curr Opin Rheumatol* **2012**, *24*, 530–540. doi: 10.1097/BOR.0b013e328356813e
6. Hoffmann, T.; Oelzner, P.; Teichgräber, U.; Franz, M.; Gaßler, N.; Kroegel, C.; Wolf, G.; Pfeil, A. Diagnosing lung involvement in inflammatory rheumatic diseases-Where do we currently stand?. *Front Med (Lausanne)* **2023**, *9*, 1101448. doi: 10.3389/fmed.2022.1101448
7. Deterding, R. R.. Infants and young children with children's interstitial lung disease. *Pediatric Allergy, Immunology, and Pulmonology*, 2010; 23(1), 25–31. https://doi.org/10.1089/ped.2010.0011
8. Guillerman RP. Imaging of Childhood Interstitial Lung Disease. *Pediatr Allergy Immunol Pulmonol*. 2010 Mar;23(1):43-68. doi: 10.1089/ped.2010.0010.
9. Buckley, M.M.; Rabinovich, C.E. Pulmonary manifestations of rheumatic diseases in children. Pediatr Clin North Am. Pediatr Clin North Am . **2021** Feb;68(1):147-166. doi: 10.1016/j.pcl.2020.09.005.
10. Aringer M, Costenbader K, Daikh D, et al. 2019 European League against rheumatism/American college of Rheumatology classification criteria for systemic lupus erythematosus. *Arthritis Rheumatol* **2019**; 71(9): 1400–1412. doi: 10.1002/art.40930.
11. *Zulian F, Woo P, Athreya BH, Laxer RM, Medsger TA, Jr, Lehman TJ, et al. The Pediatric Rheumatology European Society/American College of Rheumatology/ European League against Rheumatism provisional classification criteria for juvenile systemic sclerosis. Arthritis Rheum.* ***2007;****57:203–212. doi: 10.1002/art.22551*
12. *Bohan A, Peter JB. Polymyositis and dermatomyositis. N Engl J Med.* ***1975;****292:344–347. doi: 10.1056/NEJM197502132920706.*
13. Martini A, Ravelli A, Avcin T, et al. Toward new classification criteria for juvenile idiopathic arthritis: first steps, pediatric rheumatology international trials organization international consensus. *J Rheumatol.* **2019**; 46(2): 190-197
14. *Kasukawa R, Tojo T, Miyawaki S. Preliminary diagnostic criteria for classification of mixed connective tissue disease. In: Kasukawa R, Sharp G, editors. Mixed connective tissue disease and antinuclear antibodies. Amsterdam: Elsevier;* ***1987****. pp. 41–47.*
15. Ruperto N, Ozen S, Pistorio A, et al. EULAR/PRINTO/PRES criteria for Henoch-Schonlein purpura, childhood polyarteritis nodosa, childhood Wegener granulomatosis and childhood Takayasu arteritis: Ankara 2008. Part I: overall methodology and clinical characterisation. *Ann Rheum Dis* . **2010**;69:790–797.
16. *Koné-Paut I, Shahram F, Darce-Bello M, Cantarini L, Cimaz R, Gattorno M, et al. Consensus classification criteria for paediatric Behcet's disease from a prospectiveobservational cohort: PEDBD. Ann RheumDis.* ***2016****;75:958–964. doi: 10.1136/annrheumdis-2015-208491.*
17. Hallowell, R.W.; Horton, M.R. Interstitial lung disease in patients with rheumatoid arthritis: Spontaneous and drug induced. *Drugs* **2014**, *74*, 443–450. doi: 10.1007/s40265-014-0190-z
18. Cooper, P.; MacLean, J. . High-resolution computed tomography (HRCT) should not be considered as a routine assessment method in cystic fibrosis lung disease. *Paediatric Respiratory Reviews*. 2006; 7(3), 197–201. https://doi.org/10.1016/j.prrv.2006.04.005
19. Maglione, M.; Bush, A.; Montella, S.; Mollica, C.; Manna, A.; Esposito, A.; Santamaria, F. Progression of lung disease in primary ciliary dyskinesia: Is spirometry less accurate than CT? *Pediatric Pulmonology;* 2012; 47(5), 498-504. https://doi.org/10.1002/ppul.21569
20. Huang, H.; Hu, Y.; Wu, Y.; Ding, F.; Xu, X.; Jin, Y.; Jin, Y.; Bao, Y. Lung involvement in children with newly diagnosed rheumatic diseases: characteristics and associations. *Pediatr Rheumatol Online J* **2022**, *20*. doi: 10.1186/s12969-022-00731-5
21. Lilleby, V.; Aaløkken, T.M.; Johansen, B.; Førre, Ø. Pulmonary involvement in patients with childhood-onset systemic lupus erythematosus. *Clin Exp Rheumatol* **2006**, *24*, 203–208. doi: 10.1177/0961203316629554
22. Veiga, C.S.; Coutinho, D.S.; Nakaie, C.M.; Campos, L.M.; Suzuki, L.; Cunha, M.T.; Leone, C.; Silva, C.A.; Rodrigues, J.C. Subclinical pulmonary abnormalities in childhood-onset systemic lupus erythematosus patients. *Lupus* **2016**, *25*, 645–651. doi: 10.1177/0961203316629554
23. Oman Medical Journal-Archive n.d. Available online: https://www.omjournal.org/articleDetails.aspx?coType=1&aId=192 (accessed on 28 April 2024).
24. Hoffmann, T.; Oelzner, P.; Franz, M.; Teichgräber, U.; Renz, D.; Förster, M.; Böttcher, J.; Kroegel, C.; Schulze, P.C.; Wolf, G.; Pfeil, A. Assessing the diagnostic value of a potential screening tool for detecting early interstitial lung disease at the onset of inflammatory rheumatic diseases. *Arthritis Res Ther* **2022**, *24*, 107. doi: 10.1186/s13075-022-02786-x

 doi:10.20944/preprints202411.0083.v1




25. Wells, A., Denton, C. Interstitial lung disease in connective tissue disease—mechanisms and management. *Nat Rev Rheumatol* **2014**, **10**, 728–739. https://doi.org/10.1038/nrrheum.2014.149
26. Zulian, F.; Balzarin, M.; Birolo C. Recent advances in the management of juvenile systemic sclerosis. *Expert Rev Clin Immunol* **2017**, *13*, 361–369. doi: 10.1080/1744666X.2017.1243467.
27. Alexopoulou, E.; Prountzos, S.; Raissaki, M.; Mazioti, A.; Caro-Dominguez, P.; Hirsch, F.W.; Lovrenski, J.; Ciet, P. Imaging of acute complications of community-acquired pneumonia in the paediatric population-from chest radiography to MRI. *Children (Basel)* **2024**, *11*, 122. doi: 10.3390/children11010122
28. Johnson SR, Bernstein EJ, Bolster MB, Chung JH, Danoff SK, George MD, Khanna D, Guyatt G, Mirza RD, Aggarwal R, Allen A Jr, Assassi S, Buckley L, Chami HA, Corwin DS, Dellaripa PF, Domsic RT, Doyle TJ, Falardeau CM, Frech TM, Gibbons FK, Hinchcliff M, Johnson C, Kanne JP, Kim JS, Lim SY, Matson S, McMahan ZH, Merck SJ, Nesbitt K, Scholand MB, Shapiro L, Sharkey CD, Summer R, Varga J, Warrier A, Agarwal SK, Antin-Ozerkis D, Bemiss B, Chowdhary V, Dematte D'Amico JE, Hallowell R, Hinze AM, Injean PA, Jiwrajka N, Joerns EK, Lee JS, Makol A, McDermott GC, Natalini JG, Oldham JM, Saygin D, Lakin KS, Singh N, Solomon JJ, Sparks JA, Turgunbaev M, Vaseer S, Turner A, Uhl S, Ivlev I. 2023 American College of Rheumatology (ACR)/American College of Chest Physicians (CHEST) Guideline for the Screening and Monitoring of Interstitial Lung Disease in People with Systemic Autoimmune Rheumatic Diseases. Arthritis Rheumatol. **2024**;76 :1201-1213. doi: 10.1002/art.42860