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Pulmonary Affection of Juvenile Idiopathic Arthritis Using High Resolution Computed Tomography: The Egyptian Experience

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ABSTRACT

Background: Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease in pediatrics. Interstitial lung disease (ILD) is not uncommon among cases of JIA. However, it less frequently manifests clinically. High resolution computed tomography (HRCT) is the modality of choice for imaging of ILD. It commonly manifests initially as ground-glass opacity and evolves to septal thickening and pulmonary fibrosis. **Objective:** This study aimed to assess the pulmonary manifestations of patient with JIA and to correlate it with the findings on HRCT. Patients and methods: This cross-sectional study involved 30 JIA patients who were attending regularly at Rheumatology Clinic of Cairo University. Cases were assessed by complete history taking, general, articular, ophthalmological, chest examination and HRCT.

Results: Out of 30 patients, 14 were males (46.7%) and 16 were females (53.3%) with female to male ratio of 1.1: 1. Pulmonary manifestation was reported in 14/30 JIA patients (46.7%) who presented with chronic cough, 11 of them (36.7%) was associated with sputum expectoration, 8 patients (26.7%) had additional wheezes while 4 patients (13.3%) had associated crepitation. Only 11/30 patients (36.7%) showed HRCT findings suspecting ILD. The most common finding was ground glass appearance in 9/ 30 patients (30%) followed by air trapping in 8/30 (26.7%), then interlobular thickening in 5 patients (16.7%). Only one patient presented with pulmonary nodule (3.3%). Out of 11 patients with positive HRCT findings, 5 patients had pulmonary manifestations (45.5%). There was no statistically significant relation between any of the pulmonary manifestations when compared with HRCT findings. **Conclusion:** Pulmonary complications of JIA are not uncommon and increasing in incidence. They are not necessarily associated with other specific clinical systemic or articular manifestations but they may be related to some types of biological treatment. HRCT findings of pulmonary complications in JIA patients are more common than clinically overt pulmonary manifestations. So, the routine use of HRCT is indicated for cases of JIA for early identification and proper treatment of any pulmonary complications.

Keywords: Pulmonary manifestations, HRCT, Juvenile idiopathic arthritis.

INTRODUCTION

Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease of unknown aetiology in childhood [(1)]. It is a significant cause of both short and long-term disabilities. It is defined as arthritis of unknown etiology that begins before the 16th birthday and persists for at least 6 weeks, other known conditions are excluded [(2)]. Lung involvement in rheumatological diseases in children has been described with low frequency. Lung injury may be caused by the disease itself or by the biologic/non-biologic disease modifying anti-rheumatic drugs (DMARDs) [(3)].

JIA may be associated with pleural disease (pleurisy & pleural effusion), parenchymal affection (interstitial lung disease), vascular disease (pulmonary hypertension), airway obstruction (cricoarytenoid arthritis & bronchiolitis obliterans) and others (infection, drug toxicity & thoracic cage restriction etc...). Systemic JIA (SoJIA) is the subtype most frequently associated with pulmonary manifestations. It occurs in up to two thirds of the cases (according to some studies), however, it also occurs in other types of JIA [(4)].

Pulmonary complications manifest as different pathologies affecting pleura, parenchyma, air way, and pulmonary blood vessels and others. They may manifest clinically or may be discovered by investigations without overt clinical manifestations [(5)]. Pulmonary complications are usually seen on HRCT but respiratory symptoms are rarely observed. Routine use of high-resolution chest CT is recommended for early diagnosis and timely treatment of pulmonary complications in children with JIA [(6)]. Therefore, this study aimed to evaluate the pulmonary manifestations of patient with JIA and to correlate it with the findings on HRCT.

PATIENTS AND METHODS

This is a cross-sectional study, which involved 30 JIA patients who were already diagnosed clinically and laboratory. All patients were attending regularly to follow up at Rheumatology Clinic of Cairo University. The diagnosis of JIA was determined according to ILAR classification criteria [(2)].

Inclusion criteria: Patients of both sexes with age below 16 years old, weather had chest manifestation or not, weather in activity or in remission.

Exclusion criteria: Patients affected with other rheumatological diseases, above 16 years or has any other

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chronic pulmonary or cardiac diseases irrelative to the condition.

Data were obtained through direct interviews with all patients and their legal guardians, as well as a study of medical records from rheumatology clinic of pediatric specialized hospital of Cairo University. Data from clinical settings were documented during the initial presentation. Clinical data that were gathered included demographics, symptoms, preceding illnesses, duration of disease, manifestations during activities and number of joints affected, pulmonary manifestation (e.g. cough, expectoration of sputum, hemoptysis and dyspnea) and medication therapy. All patients were subjected to through general examination with emphasis on articular examination (joint swelling, skin changes, muscle wasting, limping, joint tenderness & limitation of movement), chest examination (inspection of shape of the chest & auscultation of lung zones) and ophthalmological examination.High resolution computed tomography (HRCT) to all of the patients were done. Scanogram from lower neck to upper abdomen. During HRCT acquisition the patient must be at breath holding position. Patient moves at constant speed through the gantry. The table speed, rotation time and the total width of all simultaneously imaged sections determined whether the transverse slabs of the patient, which were exposed sequentially during data acquisition, are overlapping, contiguous or with interspaces. Volume acquisition through the lung with reconstruction of contiguous 1 mm slices. Axial, coronal, sagittal and minimal intensity projection (MINP) images will be reconstructed (Table 1).

Table (1): HRCT technique of the machine used in the study (Bright speed GE MS 8)

	Bright speed GE MS 8
Scout	Kv110 mA25 Holding breath
Scan type	Helical
Detector Row	8
Helical Thickness	1.25cm
Interval	10cm
Gantry tilt	0.0
FOV	351mm
Kv	110
mA	70
Total exposure time	16-20 sec
	Holding breath in full inspiration. Reconstruction type: STD (standard). Mediastinal window images are also taken.

Ethical considerations

Before being enrolled in the study, the patients or their legal guardians provided their informed consents. Throughout the study, the investigators were the only ones with access to coded data and the identity of the informants.

Cairo University Ethical Committee accepted the study protocol according to the Institutional Committee for the Protection of Human Subjects and following the 18th World Medical Assembly, Helsinki, Finland.

Statistical analysis

Data were coded and entered using the statistical package SPSS (Statistical Package for the Social Sciences) version 25 (IBM, Armonk, New York, United States). Data were summarized using mean, standard deviation, median, minimum and maximum in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data. Comparisons between quantitative variables were done using the non-parametric Mann-Whitney test (7).

For comparing categorical data, Chi square (2) test was performed. Exact test was used instead when the expected frequency is less than 5 (8). P-values $\leqslant 0.05$ were considered as statistically significant.

RESULTS

This cross-sectional study included 30 JIA patients who were already diagnosed clinically. They were recruited from Rheumatology Clinic, Specialized Pediatric Hospital, Cairo University. Out of 30 patients, 14 were males (46.7%) and 16 were females (53.3%) with female to male ratio of 1.1: 1. Age of patients ranged from 8 years to 14 years old with mean of 10.47 ± 1.94.

Age of diagnosis ranged from 1.5 to 13 years with a mean of 5.99 ± 2.68 years. The majority of female patients were of systemic type (68.8%) and the remaining were of oligoarticular type (31.2%) while in males, the distribution of the two types was the same: SoJIA 50% and oligoarticular type: 50%.

In the current study pulmonary manifestation was reported in 14 JIA patients (46.7%) who presented with chronic cough, 11 of them (36.7%) was associated with sputum expectoration, 8 patients (26.7%) had additional wheezes while 4 patients (13.3%) presented with cough associated with crepitations. None of the cases were presented with hemoptysis, dyspnea, chest pain, apnea or cyanosis as shown in figure (1).

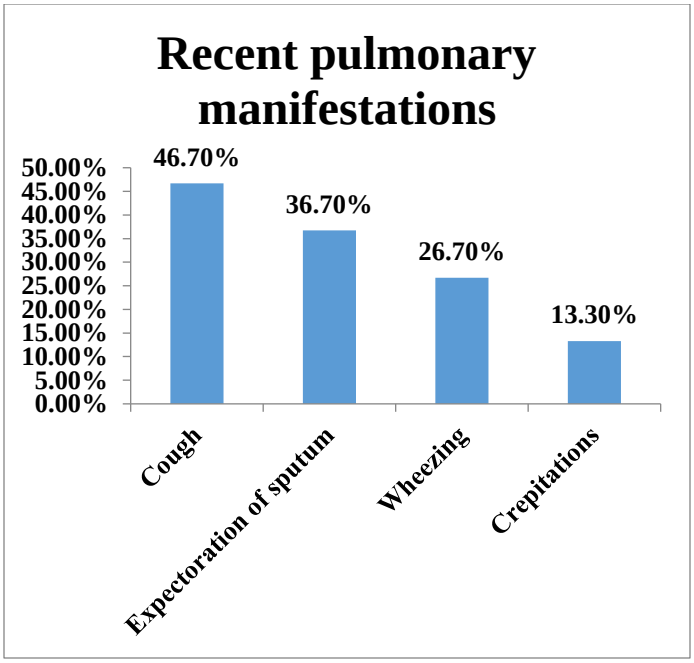

Figure (1): Recent pulmonary manifestations among studied patients.

Regarding clinical manifestations during the disease activity, it was found that 100% of patients developed joint manifestations during activities of JIA in the form of arthralgia & tenderness. While, 7 patients (23.3%) had systemic manifestations in the form of fever & malaise. and 9 patients (30%) developed pulmonary manifestations in the form of cough & expectoration of sputum as shown in figure (2).

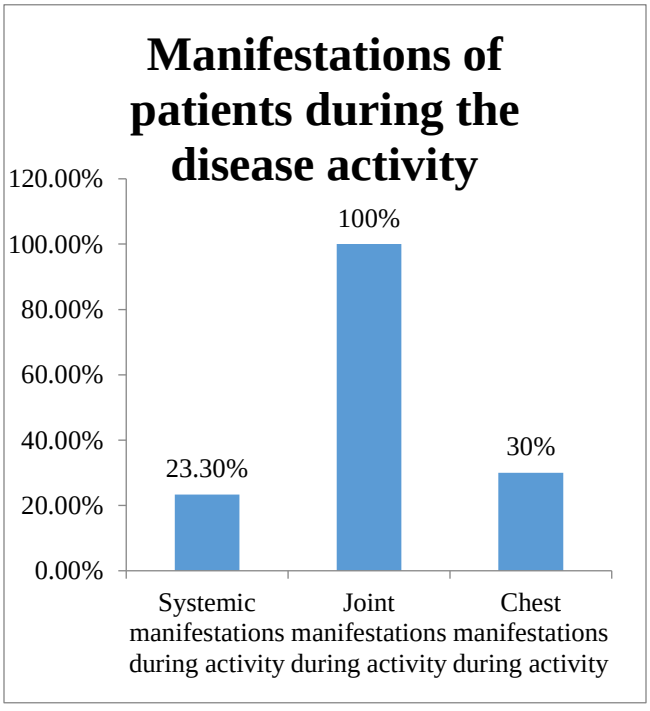

Figure 2: Manifestation of patients during the disease activities.

In this study out of 14 patients presenting with pulmonary manifestations at time of the study, 8 patients had arthralgia (57.14%), 8 patients had fever (57.14%), 8 patients had joint tenderness (57.14%), 7 patients had limitation of movement (50%), 6 patients had malaise (42.86%) and 6 patients had uveitis (42.86%). There was statistically significant relation between the fever, limitation of movements, malaise, joint tenderness and uveitis and presence of pulmonary manifestations at time of examination with P value < 0.001, 0.001, <0.003, 0.002 and 0.018 respectively. While, there was no statistically significant relation between pulmonary manifestations with number of affected joints with P value of 0.728 as shown in table (2).

Table (2): Relations of pulmonary manifestations at examination with other recent systemic and articular manifestations

	Pulmonary Manifestation at Examination				
	Yes N. = 14		**No N. = 16**		**P value**
	Count	**%**	**Count**	**%**	
Arthralgia	8	57.14%	8	50%	0.6956
Fever	8	57.14%	0	0%	< 0.001
Limitation of movement	7	50%	0	0%	0.001 *
Malaise	6	42.86 %	0	0%	0.003 *
Joint tenderness	8	57.14 %	1	6.25 %	0.002 *
Uveitis	6	42.86 %	1	6.25 %	0.018 *

P value less than 0.05 is considered statistically significant.

In this study out of 14 patients with pulmonary manifestations at the time of the study, 7 patients were receiving etanercept (50%), 4 patients were receiving adalimumab (28.57%), 2 patients were receiving both methotrexate and steroids (14.29%), 1 patient was receiving tocilizumab (9.1%) and no one was receiving methotrexate as a single therapy (0%).

There was no statistically significant relation between pulmonary manifestations at time of examination with any type of treatment. Only 11 out of 30 patients (36.7%) showed HRCT findings suspecting ILD, which were ground glass appearance (GGA), interlobular thickening, pulmonary nodules and air trapping. The most common finding was GGA that was found in 9/30 patients (30%) followed by air trapping that was found in 8/30 (26.7%), then interlobular thickening in 5 patients (16.7%). Only one patient presented with pulmonary nodule (3.3%). No patient had HRCT finding suspecting

pleural effusion and pulmonary hypertension or alveolar proteinosis as shown in table (3).

Table (3): HRCT findings suspecting ILD

HRCT finding	**Count (N= 30)**	**%**
Ground glass appearance	9	30.0%
Air trapping	8	26.7%
Interlobular thickening	5	16.7%
Pulmonary nodules	1	3.3%
Diminished attenuation	0	0%
Bronchiectasis or bronchiolectasis	0	0%
Pleural effusion	0	0%
Crazy paving appearance	0	0%
Pulmonary artery dilatation	0	0%
Pruning of peripheral pulmonary vascularity	0	0%

In current study some patients presented with one HRCT finding e.g. air trapping, while other presented with 2 or even 3 HRCT findings. Out of 11 patients (36.7%) with HRCT findings suspecting ILD, 2 (6.6%) patients with air trapping only, 3 (10%) patients presented with GGA and air trapping, 3 (10%) presented with GGA and interlobular thickening, 2 (6.6%) presented with GGA, interlobular thickening and air trapping and one (3.3%) presented with GGA, pulmonary nodules and air trapping. Eight patients with positive HRCT were of systemic onset JIA (SoJIA) type (72.72%), 3 patients (27.27%) were oligoarticular JIA. There was no statistically significant relation between numbers of affected joints when compared to HRCT findings with P value 0.299.

There was no statistically significant relation between recent articular or systemic manifestations of JIA as arthralgia, fever, limitation of movement or malaise when compared to HRCT findings. In our study, out of 11 patients with positive HRCT findings, 5 patients had pulmonary manifestations (45.5%) in the form of cough, cough and wheezing in 2 patients (18.2%) and cough and crepitations in 2 patients (18.2%).

While, out of the 19 with negative HRCT findings, 9 patients presented with cough (47.4%), one with only cough (5.3%), 6 with cough and wheezing (31.6%) and 2 with cough and crepitations (10.5%). There was no statistically significant relation between any of the pulmonary manifestations when compared with HRCT findings as shown in table (4).

Table (4): Relation between HRCT and pulmonary manifestations of studied JIA group

	HRCT				
	Positive N. = 11		**Negative** N. = 19		**P value**
	Count	%	Count	%	
Cough	5	45.5%	9	47.4%	1
Cough and wheezing	2	18.2%	6	31.6%	0.672
Cough and crepitation	2	18.2%	2	10.5%	0.611

P value less than 0.05 is considered statistically significant.

There was no significant relation between HRCT findings with neither number of activities nor rate of activities per year. There was no significant relation between HRCT findings with neither age nor sex with P value 0.442 and 0.510 respectively.

There was no statistically significant relation between HRCT findings with any of the manifestations affecting the patients during the activity, systemic, articular, chest manifestations. Out of the 11 patients with positive HRCT findings, 3 patients (27.3%) developed uveitis, out of the 19 patients with negative HRCT findings, 4 patients (21.1%) developed uveitis, and there is no statistically significant relation between HRCT findings and uveitis with p value of 1.

Out of 11 patients with positive HRCT findings, 6 patients were receiving etanercept (54.5%), 2 patients were receiving methotrexate (18.2%), 1 patient was receiving adalimumab (9.1%), 1 was receiving tocilizumab (9.1%), 1 patient was receiving combined treatment methotrexate and steroids (9.1%). There was no statistically significant relation between HRCT findings with any type of treatment.

Table (5): Relation between HRCT finding and age, sex, number and rate of activities, clinical manifestation during activity and treatment of studied JIA patients

		HRCT				
		Positive (N = 11)		Negative (N = 19)		P value
		Count	%	Count	%	
Age of patients in years	**≤ 10 years**	8	72.7%	10	52.6%	0.442
	> 10 years	3	27.3%	9	47.4%	
Sex	**Male**	6	54.5%	8	42.1%	0.510
	Female	5	45.5%	11	57.9%	
Total no of activities	**≤10 activities**	6/11	54.5%	5/19	26.3%	0.238
	>10 activities	5/11	45.5%	14/19	73.7%	
Rate of activities per year	**1-3 activities /year**	11/11	100.0%	15/19	78.9%	0.268
	4-6 activities /year	0	0.0%	4/19	21.1%	
Clinical manifestations during activity	**Systemic Affection**	3	27.3%	4	21.1%	1
	Joint Manifestation	11	100.0%	19	100.0%	---
	Pulmonary Manifestation	3	27.3%	6	31.6%	1
Ophthalmological examination	**Uveitis**	3	27.3%	4	21.1%	1
Treatment	**Methotrexate**	2	18.2%	1	5.3%	0.537
	Etanercept	6	54.5%	7	36.8%	0.454
	Adalimumab	1	9.1%	8	42.1%	0.100
	Tocilizumab	1	9.1%	2	10.5%	1
	Combined (methotrexate and steroids)	1	9.1%	1	5.3%	1

P value less than 0.05 is considered statistically significant.

DISCUSSION

In the current study pulmonary manifestation was reported in 14 JIA patients (46.7%) who presented with chronic cough, 11 of them (36.7%) was associated with sputum expectoration and 8 patients (26.7%) had additional wheezes, while 4 patients (13.3%) presented with cough associated with crepitations. None of the cases presented with hemoptysis, dyspnea, chest pain, apnea or cyanosis. Similarly in **Islam *et al.*** [5] study**,** 4 patients had prolonged cough (100%), 2 patients (50%) presented with dyspnea, none of them manifested with chest pain**.**

Also, **Kimura *et al*** [9] has performed a retrospective chart review on 25 patients with severe fatal pulmonary complications of soJIA including pulmonary arterial hypertension, interstitial lung disease, alveolar proteiniosis and lipoic pneumonia. Among the 25 patients, 18 patients (72%) complained of dyspnea on exertion, 16 patients (64%) complained of shortness of breath, 11 patients (44%) complained of cough, 10 patients (40%) complained of clubbing and 5 patients (20%) complained of chest pain. One patient (4%) was diagnosed at autopsy and did not have any known prior pulmonary symptoms.

Although **Koo *et al.*** [10] reported that clinically evident pulmonary parenchymal disease in JIA is extremely uncommon and so mentioned **Rahman** [11], in his case report that was about 10 years old female with 7 years history of polyarticular RF positive JIA on methotrexate, leflunomide and prednisolone. Over the last one year, she developed pulmonary manifestations in the form of (cough and dyspnea). HRCT chest findings include reticulonodular opacities in all lobes of both lungs. She was diagnosed as JIA-induced ILD. However, **Domingues *et al.*** [4] mentioned that SoJIA is the subtype most frequently associated with airway manifestations. It may occur in up to two thirds of the cases, usually in a mildly symptomatic form and associated with pericarditis or other signs of disease activity.

In our study, only 11 out of 30 patients (36.7%) showed HRCT findings suspecting ILD, which are ground glass appearance (GGA), interlobular thickening, pulmonary nodules and air trapping. The most common finding was GGA, which was found in 9 out of 30 patients (30%) followed by air trapping in 8 patients (26.7%), then interlobular thickening in 5 patients (16.7%). Only one patient presented with pulmonary nodule (3.3%). No patient had HRCT finding suspecting pleural effusion and pulmonary hypertension or alveolar proteinosis.

In current study some patients presented with one HRCT finding e.g. air trapping, while other presented with 2 or even 3 HRCT findings. Out of 11 patients (36.7%) with HRCT findings suspecting ILD, 2 (6.6%) patients with air trapping only, 3 (10%) patients presented with

GGA and air trapping, 3 (10%) presented with GGA and interlobular thickening, 2 (6.6%) presented with GGA, interlobular thickening and air trapping and one (3.3%) presented with GGA, pulmonary nodules and air trapping. Eight patients with positive HRCT were of systemic onset JIA (SoJIA) type (72.72%), 3 patients (27.27%) were oligoarticular JIA.

Islam *et al.* [5] has identified 4 patients of JIA with pulmonary lung manifestations, one of them was soJIA, 2 polyarticular and one with Enthesitis-related JIA. HRCT findings of the 4 patients revealed consolidation in 1 patients (25%), pneumonitis in 2 patient (50%) and pleural thickening in 1 patient. **García-Peña *et al.*** [12] mentioned that pleural and pericardial effusions are common findings that may affect around 60% of patients. Lung involvement in JIA commonly manifests as ground-glass opacity and evolves to septal thickening and pulmonary fibrosis. Lipoid pneumonia is less common, it manifests in HRCT as multiple pulmonary nodules, mainly in the centrilobular region. Rate of the patients with HRCT positive findings varies among the studies and findings of HRCT varies as well. This may be due to non-specificity of these findings, which may be early ILD or any other milder acute condition in many of cases [13].

In our study, out of 11 patients with HRCT findings suggestive of ILD, 9 patients had pulmonary manifestations at time of HRCT in the form of cough in 5 patients (45.5%), cough and wheezes in 2 patients (18.2%) and cough and crepitations in 2 patients (18.2%). None of the patients manifested with dyspnea or chest pain. While, out of the 19 with negative HRCT findings, 9 patients presented with cough (47.4%); one with only cough (5.3%), 6 with cough and wheeze (31.6%) and 2 with cough and crepitations (10.5%). There was no statistically significant relation between any of the pulmonary manifestations when compared to HRCT findings. Lack of the strong significant relation between the clinical pulmonary manifestations and the HRCT findings in our study and in the mentioned studies may be clarified by **Doyle *et al.*** [14] who mentioned that the prevalence of clinically evident interstitial lung disease in patients with rheumatoid arthritis is approximately 10%. An additional 33% of undiagnosed patients have interstitial lung abnormalities that can be detected with HRCT.

In our study, out of 14 JIA patients who had pulmonary manifestations at the time of the study, 8 patients had arthralgia (57.14%), 8 patients had fever (57.14%), 8 patients had Joint tenderness (57.14%), 7 patients had limitation of movement (50%), 6 patients had malaise (42.86%) and 6 patients had uveitis (42.86%).

Similarly, **Kimura *et al.*** [9] found that at time of diagnosis of the pulmonary diseases in JIA patients, 23 patients out of 25 (92%) complained of systemic manifestations, 15 patients (60%) had fever, 7 patients (28%) had rash, 6 patients (24%) had serositis, 6 patients (24%) had lymphadenopathy,11 patients (44%) had hepatomegaly, 12 patients (48%) had splenomegaly 15 patients (60%) had macrophage activation syndrome and one patient (4%) had thrombotic thrombocytopenic purpura. Co-existence of the pulmonary and systemic or articular manifestations together may raise the suspicion that the pulmonary complications of JIA are induced by the pathogenesis of the disease itself, as these manifestations appear and increase during activity [4].

In our study, out of the 14 patients who had pulmonary manifestations at the time of the study, 7 patients were receiving etanercept (50%), 4 patients were receiving adalimumab (28.57%), 2 patients were receiving both methotrexate and steroids (14.29%), and 1 patient was receiving tocilizumab (9.1%). No one was receiving methotrexate as a single therapy (0%).

Kimura *et al.* [9] reported that the most common used treatment among patients under study at time of development of pulmonary symptoms was corticosteroids, used by 24 patients (96%), followed by methotrexate used by 13 patients (52%), followed by IL-1 inhibitors; anakinra was used by 10 patients (40%), canakinumab used by 1 patient (4%) and rilonacept used by 1 patient (4%). TNF inhibitors were used by 3 patients (12%), 2 patients (8%) used adalimumab and one patient (4%) used etanercept. Tocolizumab was used by 2 patients (8%), cyclosporine was used by 7 patients (28%). Etoposide, gold and thalidomide, each was used by one patient. Only 4 patients were one single treatment, others were on combined treatment.

In our study, out of 11 patients who had HRCT findings, 6 patients were receiving etanercept (54.54%), 2 patients were receiving methotrexate (18.18%), 1 patient was receiving adalimumab (9.1%), 1 was receiving tocilizumab, (9.1%) and 1 patient was receiving combined treatment methotrexate and steroids (9.1%).

Arakawa [15] concluded that HRCT features of methotrexate-induced pulmonary injury in treatment of rheumatological diseases were variable and included diffuse and patchy bilateral ground-glass opacity with or without reticulation and centrilobular nodules. He reported that 8 patients with known rheumatological diseases on methotrexate treatment were complicated by pulmonary injury, 3 of them had patchy ground glass opacities with reticulations, 4 without reticulation and one patient with diffuse centrilobular ill-defined nodules.

LIMITATIONS

It was relatively small sample sized, which may limit the generalizability of the findings. Additionally, the study's cross-sectional design prevents the establishment of causality between the observed factors and outcomes. The absence of long-term follow-up limited the ability to assess the persistence or evolution of the observed clinical features. Finally, the study's findings may be influenced by

the specific population and healthcare setting, which may not be representative of broader or more diverse populations.

CONCLUSION

Pulmonary complications of JIA are not uncommon and increasing in incidence. They are not necessarily associated with other specific clinical systemic or articular manifestations but they may be related to some types of biological treatment. HRCT findings of pulmonary complications in JIA patients were more common than clinically overt pulmonary manifestations. So, the routine use of HRCT is indicated for cases of JIA for early identification and proper treatment of any pulmonary complications.

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REFERENCES

1. **Barut K, Adrovic A, Şahin S *et al.* (2017):** Juvenile idiopathic arthritis. Balkan medical journal, 34 (2): 90.
2. **Kim K, Kim D (2010).** Juvenile idiopathic arthritis: Diagnosis and differential diagnosis. Korean journal of pediatrics, 53(11):931-5.
3. **Quezada A, Ramos S, Garcia M *et al.* (2012):** Lung involvement in rheumatologic diseases in children. Allergol Immunopathol (Madr), 40 (2): 88-91
4. **Domingues V, Rodrigues M, Diniz C *et al.* (2011):** The respiratory tract and juvenile rheumatic diseases. Revista brasileira de reumatologia, 51 (1): 88-96.
5. **Islam M, Gomes K, Haque M *et al.* (2017):** Pulmonary Manifestations in Paediatric Rheumatic Diseases (PRDs): Experience in Tertiary Care Hospital. Bangladesh Journal of Child Health, 41 (2): 96-100
6. **Hu Y, Lu M, Teng L *et al.* (2014):** Risk factors for pleural lung disease in children with juvenile idiopathic arthritis. Zhongguo dang dai er ke za zhi= Chinese journal of contemporary pediatrics, 16 (8): 783-6.
7. **Chan Y (2003a):** Biostatistics102: Quantitative Data – Parametric & Non-parametric Tests. Singapore Med J., 44 (8): 391-396.
8. **Chan Y (2003b):** Biostatistics 103: Qualitative Data –Tests of Independence. Singapore Med J., 44 (10): 498-503.
9. **Kimura Y, Weiss J, Haroldson K *et al.* (2013):** Pulmonary hypertension and other potentially fatal pulmonary complications in systemic juvenile idiopathic arthritis. Arthritis care & research, 65 (5): 745-52.
10. **Koo C, Choi S, Ahn J *et al.* (2013):** A Case of Lung Involvement Associated with Juvenile Idiopathic Arthritis. Journal of Rheumatic Diseases, 20 (5): 332-5
11. **Rahman M (2018):** A ten years old girl presented with jia induced ild. Respirology, 23: 300.

García-Peña P, Boixadera H, Barber I *et al.* (2011): Thoracic findings of systemic diseases at high-resolution CT in children. Radiographics, 31 (2): 465-82.

12. **Marchiori E, Zanetti G, Hochhegger B (2016):** Interlobular septal thickening. Jornal Brasileiro de Pneumologia, 42 (2): 161.
13. **Doyle T, Dellaripa P, Batra K *et al.* (2014):** Functional Impact of a Spectrum of Interstitial Lung Abnormalities in Rheumatoid Arthritis. CHEST, 146 (1): 41–50.
14. **Arakawa H, Yamasaki M, Kurihara Y *et al.* (2003):** Methotrexate-induced pulmonary injury: serial CT findings. Journal of thoracic imaging, 18 (4): 231-6.