

Original Research Article

A study on diagnostic efficacy of pulmonary imaging tool in patients with rheumatoid arthritis

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ABSTRACT

Background: Pulmonary complication in Rheumatoid arthritis is major health concern in the field of rheumatology. So this study is to find out the sensitive imaging tool for detecting different types of pulmonary changes seen in RA.

Methods: This is a comparative, analytical, cross sectional, Institution- based, single centre study. We included all adult willing patients of Rheumatoid arthritis (age >18) and selected them based on 2010 ACR/EULAR criteria. Severity was assessed by number of joints involve in both upper and lower limb, along with ESR, CRP, Anti CCP level. Chest x ray, PFT and HRCT thorax were done in all RA patients.

Results: Out of 50 RA patients, pulmonary involvement was observed in 25 patients identified by Spirometry, CXR, HRCT. Pulmonary involvement is more common in age group <40 years. Most common form of pulmonary involvement is ILD followed by obstructive lung disease like chronic bronchitis, bronchiectasis etc. HRCT is the most common tool for detection of Pulmonary involvement in rheumatoid arthritis. HRCT abnormality, most are Restrictive on spirometry (FEV1/FVC) <80% of predicted value. And this relation is statistically significant as P value is 0.001 (<0.05) by Chi-Square test. Patients having more the disease duration, more the pulmonary involvement. This association is statically significant as p value is 0.001 (<0.05).

Conclusions: High resolution CT thorax is more sensitive modality for detection of pulmonary pathology in rheumatoid arthritis. Because of its high cost, availability of this imaging technique is beyond the lower socio-economic group where chest x ray may be useful.

Keywords: Chest-X-ray, High resolution CT, Pulmonary involvement, Restrictive pattern, Rheumatoid arthritis, Spirometry

INTRODUCTION

Rheumatoid arthritis (RA) is a long-term autoimmune disorder that primarily affects joints.¹ It typically results in warm, swollen, and painful joints.² Pain and stiffness often worsen following rest.³ Most commonly, the wrist and hands are involved, with the same joints typically involved on both sides of the body.⁴ The disease may also affect other parts of the body.⁵ This may result in a low red blood cell count, inflammation around the lungs, and inflammation around the heart.⁶

Rheumatoid arthritis (RA) affects approximately 0.5-1% of the adult population worldwide.⁷ The prevalence and incidence of RA varies based on geographic location, both globally and certain ethnic groups within a country.⁷ For example, the Native American Yakima, Pima, and Chippewa tribes of North America have reported prevalence rates in some studies of nearly 7%. In contrast, many population studies from Africa and Asia show lower prevalence rates in the ranges of 0.2-0.4%.⁷

Like many other autoimmune diseases, RA occurs more commonly in female than in males with a 2-3:1 ratio. Interestingly, studies of RA from some of the Latin American and African countries show an even greater predominance of disease in females compare to males, with ratio of 6-8:1.⁷ Given this preponderance of females, various theories have been proposed to explain the possible role of estrogens in enhancing the immune response. For example, some experimental studies have shown that estrogen can stimulate production of tumor necrosis factor alfa (TNF- α), a major cytokine in the pathogenesis of RA.⁷

The pulmonary involvement in RA can be due to various causes including infection, drug toxicity and specific manifestation of immune processes. Pulmonary involvement contributes significantly to morbidity and mortality of patients with RA and is the 2nd most common cause of it.⁸

Aim of this study was to find out the sensitive imaging tool for detecting different types of pulmonary changes seen in RA over the passage of time.

METHODS

The study has been conducted in the Rheumatology unit and department of General Medicine of Midnapore Medical College and Hospital situated in Paschim Medinipur district of West Bengal. The main catchment area is rural with few township and Municipal area covering Purba and Paschim Medinipur, Purulia districts of West Bengal as well as adjoining areas of Orissa and Jharkhand. The study involves the Department of General Medicine, Biochemistry, Pathology, Radiology and chest medicine for necessary laboratory tests and investigation data. This study was conducted for period of twelve months from February 2016 to January 2017.

There were 50 patients of rheumatoid arthritis were diagnosed according to the 2010 ACR/EULAR classification criteria for rheumatoid arthritis and clinically assessed by rheumatologist.

This is a comparative, analytical, cross sectional, Institution- based, single centre study. The study was approved by the Institutional Ethics Committee of the Hospital. Written and informed consent was taken from each of the study subjects. The subjects were selected randomly, only they had to satisfy the inclusion and exclusion criteria.

Inclusion criteria

- All adult patients(age>18 years),
- All patients who are willing to participate in the study.
- The subject to the study will be selected based on the 2010 ACR/EULAR classification criteria for rheumatoid arthritis.

Exclusion criteria

- Subject with respiratory illness.
- Subject with cardiac diseases.
- Subject with thoracic abnormality.
- Subject with vertebral abnormality.
- Subject with Methotrexate therapy.
- Subject with congenital anomaly.
- Subject with genetic disorder.
- Smoker.

In each case a full history was taken and a complete clinical examination done. Severity was assessed by number of joints involve in both upper and lower limb, along with ESR, CRP, Anti CCP level. Special enquiry was made regarding previous history of respiratory diseases including pneumonia, pleurisy, pulmonary tuberculosis and other chest illness. A record was made regarding smoking history. All patient underwent routine investigation including Hb,CBC, ECG , ESR, Urea and Creatinine. Titers of rheumatoid factor (RF) were determined by laser nephelometry. A titer 40IU was considered to indicate sero-positivity. Antinuclear antibodies (ANAs) were detected by indirect immunofluorescence with the HEP2 cell line. Pulmonary function tests were performed on all RA patients.

All cases were subjected to Chest X-Ray both AP and lateral view. X-Ray of both palm and sole including wrist joint s elbow, knee joints also taken. High-resolution CT Scan examinations were performed with a Somatom Plus S CT unit (Siemens, Erlangen, Germany). Scans were obtained with 1-mm-thick sections at 10-mm intervals, extending from the lung apices to below the costophrenic angles.

Data collected during study was entered in Microsoft Excel spread sheet, analyzed statistically using appropriate biomedical software like SPSS for Windows 20.0 statistical package program. The quantitative data of the groups were compared using ANOVA (Analysis of Variance) and the qualitative data were compared using Chi-square tests. A P value of <0.05 was considered statistically significant.

RESULTS

Table 1 comprises baseline features of study patients mainly 72% patient belongs to female and percentage of normal chest X-ray, high resolution CT, spirometry is 86, 74, 66.66 respectively. Majority patients (66%) have RA less than three years with high DAS 28 score. But mean FEV1 and FVC ratio is more or less 96.

Table 2 shows maximum RA patients between the age group of 20-40 years (78%) and only 22% patients are above 40 years. Peak incidence of RA is observed in this (20 to 40) age group in our study.

Table 1: Baseline characteristics of study patients (n=50).

Parameters	Value
Age (in years, N50, Mean±SD)	35.01±5.01
Sex (M:F)	28%:72%
Disease duration(<3yrs:>3yrs)	66%:34%
ESR (Mean±SD)	26.7±18.3
CRP (Mean±SD)	18.7±13.82
DAS 28 (Mean±SD)	5.04±1.33
FEV1/FVC (Mean±SD)	96.46±10.94
CXR (Normal:Abnormal)	86%:14%
HRCT Normal:Abnormal)	74%:26%
Spirometry (normal:rest:obst)	66.66%:25%:8.34%

Table 2: Age distribution of RA patients (n=50).

Age distribution	No.	%
20-40	39	78
>40	11	22

Table 3: Sex distribution of the patients (n=50).

Sex Distribution	No.	%
Male	14	28
Female	36	72

Table 3 shows 72% of the patients are female and 28% are male. That means RA is more common in female compare to male.

Table 4: Association of age with sex of the patients (n=50).

Age Groups	Male		Female	
	No.	%	No.	%
20-40	10	20	29	58
>40	4	08	7	14

Table 4 shows most RA patients is between age group of 20-40 in both male and female belongs to 20% and 58% respectively. Whereas if RA occurs in elderly age group, there percentage of occurrence in both sexes is little closed to each other.

Table 5: Distribution of patients (n=50) according to disease duration.

Disease duration (yrs)	No.	%
<3	33	66
>3	17	34

Table 5 shows majority of the RA patients having disease durations between 0-3 years (66%) followed by disease durations >3 years in 34%.

Figure 1 shows that patients having high DAS28 score (>5.1) higher the pulmonary involvements. But lung

involvement is more in male (87%) compare to female 11 out of 13 (84.6%). That means more active the disease process higher is the pulmonary involvement male compare to female. DAS28 score is calculated by total swollen and tender joints count out of 28 joints, along with ESR, CRP.

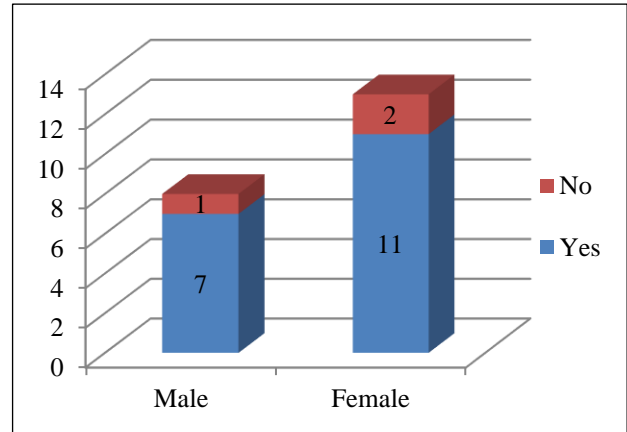


Figure 1: Pulmonary involvement is more in male sex than in female.

Table 6: Chest X ray findings (n=50).

Chest X Ray	No of patients (n)	Percentage (%)
Normal	43	86
B/L Lower zone haziness	4	8
Hyperinflation	2	4
Prominent pulmonary vasculature	1	2

Table 6 shows majority of C-X-R are normal (86%). C-X-R abnormality observed in 14% of patients. Most common CXR finding is B/L lower zone haziness followed by hyperinflation. Only 2% patients have prominent pulmonary vascularities.

Table 7: Spirometric changes (FEV1/FVC) in RA patients (n=50).

Spirometric pattern	No.	%
Restrictive	12	25
Obstructive	4	8.34
Normal	32	66.66

Table 7 shows most common finding is restrictive changes (25%) followed by obstructive changes (8.34%). surprisingly 66.66% patients have normal spirometric pattern.

Table 8 shows most common HRCT findings is ground glass opacity in both lower lobe of lung (16.3%) followed by honey comb patterns in 6.1%. Least finding is prominent pulmonary vasculature. In our study 37 out of

50 RA patient's HRCT imaging are normal pulmonary finding.

Table 8: HRCT findings in RA patients (n=50).

HRCT Findings	No of patients	Percentage (%)
Normal	37	75.5
Ground glass opacity (Both lower lobe)	8	16.3
Honey-comb patterns	3	6.1
Sub pleural reticulations	1	2.05
Prominent pulmonary vasculature	1	2.05

Table 9 showing person having high DAS28 scoring, more chance of pulmonary involvement. That means

patients having high disease activity assess by DAS28 scoring, more chance of pulmonary involvement. Among male and female, higher the DAS28 scores more lung involvement in male than female. That is also statistically significant as p value is 0.045 by chi-Square test (P<0.05).

Table 10 shows among HRCT abnormality, most are Restrictive on spirometry (FEV1/FVC) <80% of predicted value. And this relation is statically significant as P value is 0.001 (<0.05) by Chi-Square test. Other relations show not statistically significant.

Table 11 shows among the 7 abnormal CXR spirometry findings are 2 restrictive and 2 obstructive lesions and this finding is not statistically significant as p value is 0.083 by Chi-Square test (>0.05).

Table 9: Correlation of pulmonary involvement with DAS28 scoring (n=50).

		das28 scoring		Total	P Value (Chi Square test)	
		>5.1	<5.1			
Pulmonary involvement	Yes	Count	14	11	25	
		% within pulmonary involvement	56.0%	44.0%	100.0%	
	No	Count	7	18	25	
		% within pulmonary involvement	28.0%	72.0%	100.0%	
Total	Count	21	29	50		
		% within pulmonary involvement	42.0%	58.0%	100.0%	0.042

Table 10: Correlation of pulmonary involvement in relation of HRCT and Spirometry (FEV1/FVC) findings.

		Spirometry			Total	P Value (Chi Square test)
		Restrictive	Obstructive	Normal		
HRCT	Abnormal	Count	8	0	5	13
		% within HRCT	61.5%	0.0%	38.5%	100.0%
	Normal	Count	4	4	27	35
		% within HRCT	11.4%	11.4%	77.1%	100.0%
Total	Count	12	4	32	48	0.001
		% within HRCT	25.0%	8.3%	66.7%	100.0%

Table 11: Correlation of Chest-X-Ray (CXR) findings with Spirometry findings (FEV1/FVC).

		Spirometry			Total	P Value (Chi Square test)
		Restrictive	Obstructive	Normal		
CXR	Abnormal	Count	2	2	3	7
		% within CXR	28.6%	28.6%	42.9%	100.0%
	Normal	Count	11	2	30	43
		% within CXR	25.6%	4.7%	69.8%	100.0%
Total	Count	13	4	33	50	0.083
		% within CXR	26.0%	8.0%	66.0%	100.0%

DISCUSSION

In our study, we found that the most common age group involved by rheumatoid arthritis between 20 to 40, with

the youngest being 26 years and the oldest being 46 years old. This result corroborates with previous studies, which show that the mean age is fourth to fifth decade of life in South Asian males. Also, this finding is supported by

some epidemiological studies done. Panda et al shows most of the patients from both sexes belonged to the age group of 31 to 40 years (41.7%).

An overwhelming majority of the patients in our study belonged to low socio-economic class. This may be due to the existing demographical profile currently prevalent in this part of rural India. This data supported by study done by Millett et al.⁹

Panda et al, shows most of the patients having pulmonary involvement (41.7%) had their duration of illness between 5 to 10 years. 27.7% of patients had duration between 1 to 5 years. Mean disease duration was 8.1 years.¹⁰ But in our study most patients having pulmonary involvement having duration of illness between 0 to 3 years (66%), followed by 34% between the age more than 3 years. This difference is because of lesser number of sample size included in the study. Vergnenegre et al, reported a significant correlation between abnormal FEF 25-75% and duration of articular disease in non-smokers with RA.¹¹

In our study the predominant presentation on X-ray chest was a bilateral lower zone diffuse shadow (8%) predominantly reticular and nodular pattern and prominent pulmonary vasculature. These findings are suggestive of an underlying interstitial lung disease. This study is supported by some study like Gabbay and colleagues studied 36 patients with RA of less than 2 years duration using chest films, high-resolution computed tomographic (HRCT) scans, pulmonary function tests (PFTs), BAL characteristics, and technetium- 99m diethylenetriaminepenta acetic acid (Tc-99m DTPA) nuclear scan.¹³ Fifty eight percent of the patients had findings suggestive of ILD by at least one of these modalities. In their study, chest radiographs were abnormal in 6%, HRCT in 33%, PFTs in 22%, BAL in 52%, and Tc-99m DTPA nuclear scan in 15% of the patients.

In 1996, Morrison and colleagues surveyed 104 patients with RA using clinical assessment, chest radiographs, and PFTs and found evidence of ILD in five (4.8%) of the patients.¹² Utilizing only clinical examination and abnormal chest radiographs, Walker and Wright identified ILD in eight of 516 (1.6%) RA patients they studied.¹⁴

Pleural effusion was the second common finding on C-X-R which is the most common asymptomatic pulmonary complication of RA. But in our study, we haven't got any pleural effusion, this contradiction is because of less number of cases is included in our study also, prominent pulmonary vasculature could be due to pulmonary vasculitis which is a less common pulmonary manifestation of RA.

Majority of RA patients had a restrictive pattern on pulmonary function testing (Spirometry) 25%. Which

again highlights the presence of lung fibrosis and an underlying interstitial lung disease.¹⁵ 8% of our RA cases had obstructive pattern with airflow obstruction that was most marked when respiratory volumes were low and trapping of air occurred. The mean forced expiratory volume in 1 second and forced vital capacity are reduced. The combination of tobacco smoking and RA is associated with a much higher prevalence of obstructive pulmonary disease.¹⁶

This finding in our study is supported by some other study. Lake FR et al, shows most common lung abnormality in spirometry in patients of RA is restrictive followed by obstructive.¹⁵ Though one study shown prevalence of obstructive airway disease are highly variable depending on the criteria used to define disease and the population studied.¹⁷

Shen et al, in a retrospective cohort study from Taiwan found a higher rate of chronic obstructive pulmonary disease (COPD) in patients with rheumatoid arthritis compared to those without, particularly in young adults aged 20-34 years.¹⁸

A longitudinal study by Fuld et al evaluating asymptomatic non-smoking patients with rheumatoid arthritis found a slightly higher rate of PFT abnormalities at baseline (8.7% versus 5% of the reference population), but this number did not significantly change over the course of 10 years, leading the authors to question the significance of PFT abnormalities in patients without respiratory symptoms.¹⁹

In present study, on HRCT, majority of RA patients (16%) presented with ground-glass opacity (GGO) which may be the result of air space disease (filling of the alveoli) or interstitial lung disease (ILD) (i.e. fibrosis).

Second common finding on HRCT is the presence of reticular pattern which again indicates fibrosis. Thus, the observations in our study are in agreement with other studies that ILD is the commonest pulmonary manifestation in RA patients.^{13,16,20}

The interstitial lung diseases are comprised of a group of pulmonary disorders characterized clinically by diffuse infiltrates on the chest radiograph and histologically by distortion of the gas exchanging portion of the lung. The physiologic correlates are restriction of lung volumes and impaired oxygenation. In some study conducted by Cortet et al, and Wilczynska MM et al, has demonstrated bronchiectasis on HRCT in ~30% of cases of rheumatoid arthritis, although it may be clinically silent.^{21,22} Bronchiectasis may precede or follow the development of rheumatoid arthritis.²³ But in our study we did not find any bronchiectasis type of lesion on C-X-R or HRCT.

In our study majority of the patients having disease duration less than 40 years (66%). Though lung involvement is much higher in patient having disease

duration more than 3 years. This correlation is statically significant as p value is <0.05. This finding is supported by some other study.

CONCLUSION

High resolution CT thorax is more sensitive modality for detection of pulmonary pathology in rheumatoid arthritis. Because of its' high cost, availability of this imaging technique is beyond the lower socio-economic group where chest X-ray may be useful.

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