Research Article

Cardiopulmonary changes in Rheumatoid arthritis

Nigam P[1], Baghel PK[2], Jain MK[3], Kushwaha P[4]

[1]Dr Pradeep Nigam, Assistant Professor, [2]Dr P K Baghel P.K., Professor, [3]Dr MK Jain Professor & Head, Dept. of Medicine, SSMC, Rewa M.P, [4]Dr Prashant Kushawha, Post graduate Student. All are affiliated with Department of Medicine, SSMC, Rewa, MP, India

Address for correspondence: Dr Pradeep Nigam, Email: sonalpragalbh@gmail.com

Abstract

Introduction: Rheumatoid arthritis should be viewed as a multisystem disease affecting multiple organs. Vigilance for lung and cardiac involvement is necessary among rheumatologists and patients. Despite the absence of effective treatment for advanced respiratory and cardiovascular disease, it is possible that therapeutic intervention at an early stage may be beneficial. Keeping in view the above mentioned facts, we have undertaken this study to see the various cardiac and pulmonary changes associated with rheumatoid arthritis and, their age and sex wise distribution in study population. **Objective**: To study prevalence and severity of cardiovascular and pulmonary changes in patients of rheumatoid arthritis in accordance to age and sex. **Method**: All patients fulfilling 1987, revised criteria for diagnosis of rheumatoid arthritis, proposed by American College of Rheumatology were selected without any bias for age, sex, duration, severity of disease. **Result**: Female to male ratio was 2.6: 1 with hypertension as most common co-morbid disease. Anti-cyclic citrullinated peptide was more specific than rheumatoid factor. 40.5% cases had abnormal pulmonary function test results in the form of restrictive and/or obstructive abnormality. 35.7% had abnormal echocardiography with valvular lesions, pericardial effusion and left ventricular dysfunction in decreasing order. Mitral valve was involved in 87.5% of total valvular involvement. **Conclusion:** Cardiopulmonary involvement was restrictive pattern of lung involvement along with mitral valve lesions, pericardial effusion and left ventricular dysfunction. Anti-cyclic citrullinated peptide was more specific than rheumatoid factor.

Key words: Rheumatoid arthritis, Anti-cyclic citrullinated peptide, Rheumatoid factor, Echocardiography, Pulmonary function test.

Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory disease of unknown etiology marked by a symmetric, peripheral polyarthritis. It is the most common form of chronic inflammatory arthritis associated with joint damage and physical disability [1]. RA is multisystem disease, may result in a variety of extraarticular manifestations, including fatigue, subcutaneous nodules, lung involvement, pericarditis, peripheral neuropathy, vasculitis, and hematologic abnormalities. RA affects approximately 0.5–1% of the adult population worldwide. RA occurs more commonly in females than in males, with a 2–3:1 ratio. The incidence of RA increases between 25 and 55 years of age, after which it plateaus until the age of 75 and then decreases [1]. The symptoms of RA typically result of inflammation of the joints, tendons, and bursae. Patients often complain of early morning joint stiffness lasting more than 1 hour and easing with physical activity. The earliest involved joints are typically the small joints of the hands and feet. Extraarticular manifestations may develop even prior to the onset of arthritis.

The most common cause of death in patients with RA is cardiovascular disease. The incidence of coronary artery disease and carotid atherosclerosis is higher in RA patients. Furthermore, congestive heart failure (including both systolic and diastolic dysfunction) occurs at an approximately twofold higher rate in RA. Pericardium is most frequent site of cardiac involvement in RA. However, clinical manifestations of pericarditis occur in less than 10% of patients with RA. Pericardial involvement may be detected in nearly one-half of these patients by echocardiogram or autopsy studies [1]. RA can cause cardiomyopathy and valvular involvement and, mitral regurgitation is the most common valvular

Manuscript received: 14th May 2014
Reviewed: 25th May 2014
Author Corrected: 10th June 2014
Accepted for Publication: 12th June 2014

abnormality in RA [1]. Pleural disease, the most common pulmonary manifestation of RA, may produce pleuritic chest pain and dyspnea, as well as a pleural friction rub and effusion. Interstitial lung disease (ILD) may also occur in patients with RA and is heralded by symptoms of dry cough and progressive shortness of breath. Pulmonary function testing shows a restrictive pattern (e.g., reduced total lung capacity). The presence of ILD confers a poor prognosis. Other less common pulmonary findings include respiratory bronchiolitis and bronchiectasis.

Method

The study included carefully selected 50 patients of rheumatoid arthritis, was carried out in Department of Medicine, S. S. Medical College and Associated S.G.M. Hospital, Rewa (MP).over a period of 20 months from February 2010 to October 2011, either attending outpatient department or admitted in medicine wards. Written and informed consent was taken from each patient. The study was conducted in accordance with protocol approved by the institutional review board.

Inclusion Criteria:

All patients fulfilling 1987, revised criteria for diagnosis of rheumatoid arthritis, proposed by American College of Rheumatology were selected without any bias for age, sex, duration, severity of disease.

Results

Our study on 50 R.A. patients showed that 14 were males and 36 were females, with female to male ratio was 2.6: 1 with 33 patients (66%) in age group of 31-60 yrs (P<0.05).

Table No 1: Distribution according to Educational Status

Educational status	Number	Percentage %
Illiterate	10	20
Upto 10^{th} class	24	48
$>10^{th}$ class	16	32
Total	50	100

P <0.05, significant

Table No. 2: Distribution according to Socio Economic status

Socio Economic status	Number	Percentage %
Low	18	36
Middle	24	48
High	08	16
Total	50	100

P <0.05, significant

The literacy status were 10 (20%) cases illiterate, 24 (48%) were up to 10^{th} std. and 16 (32%) were more than 10^{th} std suggesting that persons with higher level of education had lesser incidence (P<0.05). Most cases belonged to middle [18 (36%)]and low socioeconomic status [24 (48%)] (P <0.05).

R.A. patients had co morbid diseases in 17 (34%) cases, of them 9 (52.9%) cases had HTN, 4 (23.5%) cases had DM, 3 (17.6%) cases had CAD, another 3 (17.6%) had COPD and 1 (5.9%) case had CVA.

RA factor was positive in 31 (62%) and negative in 19 (38%) of cases (P<0.05). In the present study both the antiCCP and RA factor reports were available in only 30 cases. Of the 31 RA factor positive cases in this study, antiCCP was done in

17 cases of which 15 were positive and 2 were negative. Of the 19 RA factor negative cases, antiCCP was done in 13 cases of which 6 were positive and 7 were negative. Thus antiCCP detected additional 6 (46.1%) out of 13 rheumatoid factor negative RA patients, it shows that antiCCP is more specific than RA factor positivity

Table No. 3: Distribution according to RA factor and Anti CCP

R A factor	Number (%)	Anti CCP (n=30)
Reactive	**31 (62)**	
	a. 15 (48.38%)	Positive
	b. 02 (6.46%)	Negative
	c. 14 (45.16%)	Not done
Non-Reactive	**19 (38)**	
	a. 06 (31.6%)	Positive
	b. 07 (36.8%)	Negative
	c. 06 (31.6%)	Not done
Total	**50 (100)**	

Table No. 4: Distribution according to joint involvement

Manifestations	Number	Percentage %
Pain/ morning stiffness	28	56
Swelling	12	24
Deformity	10	20
Total	50	100

P <0.05, significant

Our study showed pain /morning stiffness 28 (56%) was most common presenting complain followed by swelling in 12 (24%), and deformity in 10 (20%) (P<0.05).

Table No. 5: Distribution of cases according to X-ray finding of joints

X-ray findings	Number	Percentage %
Normal	**28**	**56**
Abnormal	**22**	**44**
a. Only soft tissue swelling	03	13.6
b. Only juxtaarticular osteopenia	09	41
c. Loss of articular cartilage	10	45.4
Total	**50**	**100**

P <0.05, significant

The abnormal joint X-ray rest were found in the 22 (44%) cases (P<0.05). Of the 22 cases with abnormal X- ray in this study, 10 (45.4%) had loss of articular cartilage, 9 (41%) had juxta-articular osteopenia, and 3 (13.6%) had soft tissue swelling.

Table No. 6: Distribution of cases according to Pulmonary Function Test (n=42)

Pulmonary Function Test	Number	Percentage %
Normal	25	59.5
Abnormal	**17**	**40.5**
a. Mild obstructive and mild restrictive	04	23.
b. Mild obstructive and severe restrictive	06	35.
c. Severe obstructive mild restrictive	03	17.6
d. Severe obstructive and severe restrictive	04	23.5

P<0.05 significant.

PFT was performed in 42 cases of which 17 (40.5%) cases had abnormal PFT in the form of restrictive and/or obstructive abnormalities (P<0.05). Most had mixed pattern with mild obstructive and severe restrictive pattern in 6 (35.3%) cases followed by mild obstructive and mild restrictive pattern, and severe obstructive and severe restrictive pattern in 4 (23.5%) cases each and 3 (17.6%) had severe obstructive and mild restrictive pattern. Abnormal PFT had positive correlation with increasing age and in advanced age group restrictive pattern was more common.

Table No 7: Results of 2D-ECHO (n=42)

2D-ECHO	Number (%)
Normal	27 (64.3)
Abnormal	15 (35.7)
a.Valvular lesions	08 (53.3)
1.Mitral	07 (87.5)
2.Tricuspid	01 (12.5)
b. Pericardial effusion	08 (53.3)
c.LV dysfunction	05 (33.3)

P<0.05, significant

The 2d-echo was done in 42 cases of which 15 (35.7%) had abnormal 2d-echo and rest were normal (P<0.05). 8 (53.3%) cases had valvular lesions, another 8 (53.3%) had pericardial effusion and 5 (33.3%) had LV dysfunction. Of the 8 valvular lesions mitral valve was involved in 7 (87.5%) and were having mitral incompetence, and 1 (12.5%) had involvement of tricuspid valve incompetence.

Discussion

Our study had females preponderance, with female to male ratio was 2.6: 1. (p<0.05) which could be because of estrogen effect, similar to the Shah A et al study (2012) [2, 3]. Our study showed that persons with higher level of education had lesser incidence (P<0.05) finding similar to the study by Mathew A J et al (2009),who found that 41.4% patients were educated less than high school, 48.3% up to high school and 10.3% up to tertiary level [4]. The reason is not known but it could be because of negligence and lack of awareness regarding disease and its complication in less educated group and early treatment in higher educated group. The maximum cases belonged to middle (36%) and low socioeconomic status (48%) (P<0.05). This could be due to overcrowding, cross infection and molecular mimickery. This supported by Bengtsson C et al (2005) observation that for manual laborers had 20% more risk of developing rheumatoid arthritis [5].

The most common co-morbid disease was hypertension in our study. Other co morbid diseases were in decreasing order were diabetes mellitus, coronary artery disease, chronic obstructive pulmonary disease and cerebrovascular disease. The generalized inflammatory process and inflammatory mediators are the probable reasons. Petri H et al (2010) found hypertension in 40.3%, diabetes in 12%, chronic obstructive pulmonary disease in 6.4%, coronary atherosclerosis in 6.9% in RA. They found no relation between rheumatoid arthritis and CVA. Only 14% had family history suggestive of rheumatoid arthritis in this study [6]. It could be because large number of patients belonging to lower socioeconomic status and education. Shah A et al (2012) found that RA is 2–10 times greater in first-degree relatives [2]. The study revealed rheumatoid factor positivity in 62% and negative in 38% of cases ($P < 0.05$), this finding is similar to finding of Cortet B et al (1997) who studied 68 patients with rheumatoid arthritis and rheumatoid factor was positive in 52 patients (76.5%) [7]. Eustice C (2011) mentioned that up to 20% of rheumatoid arthritis patients remain negative for rheumatoid factor [8]. In the present study both the antiCCP and RA factor reports were available in only 30 cases. Our study had anti-cyclic citrullinated peptide positive in 70% and negative in30% ($P <0.05$), similar to 67% positive anti-cyclic citrullinated peptide in RA patients in Nishimura K et al (2006) study [9]. We found anti-cyclic citrullinated peptide is more specific than rheumatoid factor. Joshi L et al (2009) observed that out of 37 RA patients 23 (62%) were rheumatoid factor positive and all were anti-cyclic citrullinated peptide positive [10].

The study showed pain /morning stiffness was most common presenting complain followed by swelling and deformity ($P < 0.05$) similar to study by Lipsky P E (2008) who mentioned that pain in affected joints, aggravated by movement, is the most common manifestation of established RA [1]. Of the 22 cases with abnormal X- ray in this study, 45.4% had loss of articular cartilage, 41% had juxta-articular osteopenia, and 13.6% had soft tissue swelling. Joshi L et al (2009) observed that out of 37 RA patients, 26 (70%) patients demonstrated radiological erosions and/or typical articular deformity [10]. Pulmonary function test was abnormal in 40.5% in the form of restrictive and/or obstructive abnormalities ($P <0.05$). This finding is nearly similar to Gabbay E et al (1997) who studied 36 rheumatoid arthritis patients and found 21 (58%) to have abnormal findings on PFT consistent with interstitial lung disease [11]. All had mixed pattern with mild obstructive and severe restrictive pattern was most common type of abnormality in 35.3% cases. Imeruz N et al (2007) studied 93 rheumatoid arthritis patient and interstitial lung disease was found in 27.7% of RA patients but it was present in 6.6% (4/60) of the control patients [12]. Nannini C et al (2008) reported prevalence of subclinical and symptomatic interstitial lung disease in RA varies depending on the method of detection and ranges between 1 and 58% [13]. The female outnumbered male with mild obstructive and severe restrictive pattern were more common in females and all patterns were equally present in males with exception of severe obstructive and mild restrictive pattern which was absent. The abnormal pulmonary function test had positive correlation with increasing age and in advanced age group restrictive pattern was more common.

In our study had abnormal 2d-echocardiography in 35.7% and rest were normal ($P < 0.05$). The valvular lesions were found in 53.3%, another 53.3% had pericardial effusion and 33.3% had left ventricular dysfunction. The mitral incompetence was found in 87.5% and 12.5% had incompetence of tricuspid valve. Dinsmore WW et al (1983) found fourteen patients (42%) with small pericardial effusion, and 9 patients (27%) with abnormalities of the mitral valve motion in the form of regurgitant lesion. They also found increased left ventricular diameter/LV dysfunction in 5 (15%) patients. Tlustochowicz W et al (1997) reported 26 out of 100 patients with rheumatoid arthritis had pericardial effusion, and 3 had valvular heart disease [14]. But they did not mention which valve was most commonly involved. Mody G M et al (2008) studied 101 patients with RA and found that 5 6%) patients had pericardial effusion and in 10 (13%) abnormalities of the mitral valve were noted [15].

Roldan C A et al (2007) studied 34 volunteers with RA and observed that 20 (59%) had mainly left-sided valvular lesions which equally affected the aortic and mitral valves [16]. Valve regurgitation manifested as mild aortic regurgitation in 4 patients, moderate mitral regurgitation in 4 patients, and moderate tricuspid regurgitation in 1 patient. Mitral and aortic valve stenosis occurred in 1 patient (3%).11 (32%) patients had left sided valve nodules. No correlation was found between valve lesions and duration, activity, severity, pattern of onset and course, extra-articular disease, serology, or therapy of RA.

RA is autoimmune disease which results in persistent chronic inflammatory disease responsible for multisystem involvement and could be responsible above changes seen in the study.

Conclusion

Rheumatoid arthritis is a chronic inflammatory disease of unknown etiology marked by symmetric, peripheral polyarthritis. It is the most common form of chronic inflammatory arthritis associated with joint damage and physical disability. It is disease of most productive age groups between 25 to 55 years, an early diagnosis and interventions can significantly delay and prevent disability adjusted life years (DALYS).

Funding: Nil
Conflict of interest: Nil
Permission from IRB: Yes

References

1. Lipsky P E, Rheumatoid Arthritis in Harrison text book of InternalMedicine,McGraw-Hill2008;17:2083-87

2. Shah A, St-Clair E W.Rheumatoid Arthritis in Harrison text book of Internal Medicine, *McGraw-Hill* 2012;18:2738.

3. Dinsmore W W. The heart in rheumatoid arthritis (rheumatoid disease) - an echocardiographic study. *Ulster Med J*. 1983; 52 (1): 54–57.

4. Mathew A J, Antony J, Eremenco S, Paul B V, Jayakumar B, Philip J. Health-related quality of life in rheumatoid arthritis patients in South India.*Singapore Med J.* 2009; 50 (8) : 801.

5. Bengtsson C, Nordmark B, Klareskog L, Lundberg I, Alfredsson L. Socioeconomic status and the risk of developing rheumatoid arthritis: results from the Swedish EIRA Study. *Ann Rheum Dis*. 2005;64:1588–1594.

6. Petri H, Maldonat D, Robinson N J. Data-driven identification of co-morbidities associated with rheumatoid arthritis in a large US health plan claims database. *BMC Musculoskeletal Disorders.* 2010, 11:247

7. Cortet B, Perez T, Roux N. Pulmonary function test in high resolution CT of lungs in patients with Rheumatoid Arthritis. *Ann Rheum Dis*.1997;56:596-600.

8. Eustice C. What Is Rheumatoid Factor.80% of Rheumatoid Arthritis Patients Test Positive By Carol Eustice*, About.com Guide* Updated June 29, 2011;5:12.

9. Nishimura K, Sugiyama D, Kogata Y, et al. "Meta-analysis: diagnostic accuracy of anti-cyclic citrullinated peptide antibody and rheumatoid factor for rheumatoid arthritis*" Ann. Intern. Med.*2006; 146 (11) : 797–808.

10. Joshi L, Chopra A. Is There an Urban-Rural Divide? Population Surveys of Rheumatic Musculoskeletal Disorders in the Pune Region of India Using the COPCORD Bhigwan Model. *The Journal of Rheumatology* 2009; 36:3.

11. Gabbay E, Tarala, R. Will et al., "Interstitial lung disease in recent onset rheumatoid arthritis," *American Journal of Respiratory and Critical Care Medicine*.1997;156 (2) part 1:528–535.

12. Imeryüz N, . Yazici H, Koçak H, Erk M, Özder A, Karcier S M. Pericardial and pulmonary involvement in rheumatoid arthritis in Turkey. *CLINICAL RHEUMATOLOGY*. 2007;13 (2) :239-243.

13. Nannini C. Pulmonary manifestations of the rheumatic diseases. *Practitioner* 2008;220:51–5.

14. Tłustochowicz W, Cwetsch A, Cholewa M, Raczka A, Nowak J. Echocardiographic evaluation of cardiac structures in patients with rheumatoid arthritis; *Pol Arch Med Wewn*.1997;97 (4) :352-8.

15. Mody GM, Cardiel MH. Challenges in the management of rheumatoid arthritis in developing countries. Best Practice & Research. *Clin Rheumatol*. 2008;22 (4) :621-41.

16. Roldan CA, DeLong C, Qualls CR, Crawford MH. Characterization of valvular heart disease in rheumatoid arthritis by transesophageal echocardiography and clinical correlates. *Am J Cardiol.* 2007;100 (3) :496-502

How to cite this article?

Nigam P, Baghel PK, Jain MK, Kushwaha P. Cardiopulmonary changes in Rheumatoid arthritis. *Int J Med Res Rev* 2014;2(3):228-233. doi:10.17511/ijmrr.2014.i03.6.