Original Article

Extra-Articular Manifestations of Rheumatoid Arthritis & its relation with Treatment Outcome: a tertiary care hospital experience

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Abstract

Objective: *This study was done to determine frequency of extra-articular manifestations (ExRA) in patients with rheumatoid arthritis (RA) and its relation with treatment outcome in a tertiary care hospital, Dhaka.* ***Methods:*** *A cross sectional study was conducted upon 50 patients of rheumatoid arthritis of both gender aged ranging 30 to 60 years attending different medicine units of Shaheed Suhrawardy Medical College & Hospital during the period of May to October, 2011 who fulfilled the 1987 American College of Rheumatology criteria for RA. Demographic characteristics, extra-articular manifestations were recorded and some information was gathered by document review according to DAS28 (disease activity score 28.)* ***Results:*** *Among 50 patients female to male ratio was 9:1. The average age was 43.72±10.95 (SD) in years with maximum age 60 years and minimum age 30 years. Extra-articular manifestations were reported in 86.0% of patients. Hematological involvement (82%) was the most common extra-articular manifestation. Average DAS 28 was more in patients who had extra-articular manifestations than patients who had no extra-articular manifestation.* ***Conclusion:*** *Significant proportion of patients with female predominance visited at a tertiary care hospital due to RA. ExRA were present in a substantial proportion of a hospital based sample and is generally associated with a worse disease outcome. Hematological system involvement was the commonest. Early recognition and treatment are important to decrease disease activity.*

Keywords: *Rheumatoid Arthitis, Extra-articular manifestation, Disease outcome, DAS28*

Abbreviations: *ACR, American College of Rheumatology; ANA,antinuclear antibodies; CCP, Cyclic citrullinated peptide; CRP,C- Reactive Protein; DAS28,Disease Activity Score 28;DM,Diabetes Mellitus; DMARDs, Disease modifying anti rheumatic drugs;IHD, Ischemic Heart Disease; RA, Rheumatoid Arthritis; RF, Rheumatoid factor.*

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Conflict of interest: *None*

Introduction

Rheumatoid arthritis is the most common form of poly articular inflammatory arthritis characterized by persistent synovial inflammation, bony erosions and progressive articular destruction leading to varying degree of physical disability[1]. It is an autoimmune disease that has significant progressive morbidity, many extra-articular complications, higher mortality rates than the general population, and considerable socioeconomic costs[2-4]. The estimated prevalence of RA in developing countries is variable. Studies from Nigeria,[5] Indonesia[6] and Africa[7] showed lower prevalence than that reported from the western countries, while the prevalence of RA in India[8] (0.75%) is similar to that reported in white

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population from Manchester[9] (0.8%). In the urban population of southern Pakistan, Karachi, the prevalence of RA is reported to be 0.142%,[10] whereas in northern Pakistan the estimated prevalence is 0.55%[11]. Extra-articular manifestations of rheumatoid arthritis (ExRA) occur in about 40% of patients, either in the beginning or during the course of their disease[12]. The presence of ExRA is associated with severe active disease and increased mortality compared to the general population[13,14]. There are no reliable predictors for the development of ExRA, although many have been suggested[15-17]. They include such constitutional factors as male sex, association with HLA-related shared epitope genes, auto antibodies such as rheumatoid factor (RF), antinuclear antibodies (ANA) and anti-cyclic citrullinated peptide antibody (anti-CCP), as well as environmental factors such as smoking[18-23]. RA shows heterogeneity in presentation, clinical course, extra-articular systemic manifestations and associated co-morbidities[24]. The clinical process can be highly variable, with periods of wax and wane. Most patients have disease fluctuations that vary from weeks to months. Some patients may not have any relief from symptoms, but on rare occasions, others may achieve remission without disease-modifying treatment[3]. Initially RA was treated reactively, focusing on prevention of the progression of symptoms and an attempt to retain functionality. With the advent of biologic therapy, progression of the disease has been slowed, but no cure has been found and sometimes only partial disease-modifying response is achieved[2]. In this study, we reviewed the incidence of ExRA at a tertiary care hospital in Dhaka, Bangladesh and to determine the relation of extra-articular manifestations with its treatment outcome.

Methods & Materials

This cross sectional study was conducted in Medicine units of Shaheed Suhrawardy medical college & Hospital, a tertiary care hospital in Dhaka, Bangladesh. A total 50 cases of RA of both gender and ages in between 30 to 60 years were included. Patient suffering from severe co-morbid conditions like heart failure, IHD, DM, chronic renal disease etc and patients suffering from musculoskeletal problem other than RA were excluded. All patients fulfilled the 1987 modified ACR classification criteria for RA1. All of them were under treatment with DMARDs (single or multiple) as well as steroid for different duration. Every patient was followed up two monthly for six months both clinically and biochemically and treatment response was assessed

by DAS28 calculator[25]. The data was collected in a pre-formed standard printed data collection form included demographic features, clinical findings, disease activity (based on the number of tender /swollen joints)[26], treatment, the presence of articular and extra- articular manifestations of RA, positive family history of RA and laboratory parameters (complete blood count, auto-antibodies [RF and Anti-CCP]) and radiological changes (typical radiological features of involved joints). Statistical analysis was done by Statistical Package for Social Science (SPSS Inc, Chicago, Illinois, USA) software.

Results

Out of 50 patients, forty five (90%) were females. Age ranged from 30- 60 years with an average age of 43.72 ± 10.95 (SD) in years. Thirty six (72%) were from lower socio-economic condition and fourteen (28%) were from middle socio-economic condition.
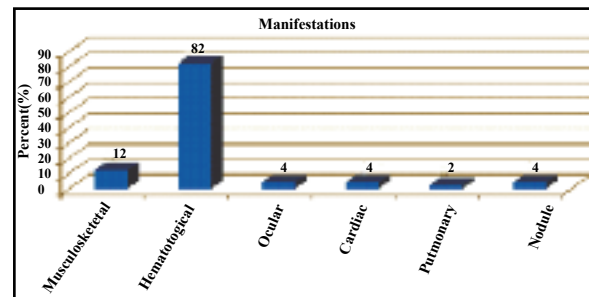

Figure I: Frequency of extra-articular manifestations among the study subjects

Fourteen (28%) of them had positive family history of rheumatoid arthritis. One (2%) of the study subjects was smoker. Thirty five (70%) of them had normal BMI. Among others, less than one third (28%) were overweight. Only one (2%) was found as obese. Among study subjects, forty three (86%) had single or multiple extra-articular manifestation of RA. Among those who had Ex RA, hematological involvement was a common feature, affecting forty one (82%) patients. Extra-articular musculoskeletal system involvement was found in six (12%) patients. Two (4%) had ocular, two (4%) had nodule and another two (4%) had cardiac manifestations. Pulmonary manifestations were the least frequent feature found in our series, occurring in one (2%) patient only (Figure-l). CRP was found positive in 46 (92%), 39 (78%) and 32 (64%) subjects in 1st, 2nd and 3rd follow which was found positive in 48 (96%) subjects at baseline. Forty three (86.0%) had extra-articular manifestations and only seven (14.0%) had no

extra-articular manifestation. DAS 28 was high in patients who had extra-articular manifestations with scores of 6.78 ±0.72 (SD), 6.31± 0.55 (SD), 5.81± 0.61 (SD) and 5.52 ±0.57 (SD) found in baseline, 1st, 2nd and 3rd follow up respectively. Among the patients who had no extra-articular manifestation average DAS was found low, which was 5.97 ±1.18 (SD), 4.97 ±1.38 (SD), 4.90± 0.96 (SD) and 4.29± 0.75 (SD) in base line, 1st, 2nd and 3rd follow uprespectively. Regarding treatment response DAS score reduced in both arms at the end of study but was still high in subjects with ExRA [5.52 ±0.57 (SD) vs 4.29± 0.75 (SD)]. These differences were statistically significant. (Table-l).

Table l: Relation of extra-articular manifestation and DAS 28

Variable	Extra -articular manifestation		t- test	df	P
	Present Mean ± SD	Absent Mean ± SD			
Baseline DAS 28	6.78±0.72	5.97±1.18	2.491	48	0.016
DAS 28 in 1 st follow up	6.31±0.55	4.97±1.38	4.631	48	0.000
DAS 28 in 2 nd follow up	5.81±0.61	4.90±0.96	3.333	48	0.002
DAS 28 in 3 rd follow up	5.52 ±0.57	4.29±0.75	5.053	48	0.000

Discussion

Rheumatoid arthritis (RA) is the most common form of chronic inflammatory arthritis. It is an inflammation of synovial tissue with symmetric involvement of peripheral joints, hand, feet, and wrists. It can also affect non-articular muscular structures such as tendons, ligaments, and fascia[27]. It affects 0.5-1% of population all over the world[1]. The prevalence is about 2.5 times higher in females than males[11]. A hospital based study shows a considerable female predominance of RA from all communities of Karachi. The mean age of onset in that study group of patients with RA was found to be 38.5 years in females and 44.8 years in males[28]. In our study, forty five (90%) were female and five (10%) were male. The average age was 43.72±10.95 (SD) years with maximum age 60 years and minimum age 30 years.

Conclusion

This demonstrated that extra-articular manifestations are present in a substantial proportion and are generally associated with a worse disease outcome. Hematological and extra-articular musculoskeletal system involvements were the commonest. Though this study had limited sample and short duration follow up, it gives insight that ExRA needs to be recognized and managed early to improve the disease outcome.

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