



RESEARCH ARTICLE

RHEUMATOID ARTHRITIS: A MAJOR DISEASE BURDEN

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ARTICLE INFO

Article History:

Received 05th July, 2016
Received in revised form
20th August, 2016
Accepted 17th September, 2016
Published online 30th October, 2016

Key words:

Rheumatoid Arthritis,
Extra-articular,
DMARDs.

ABSTRACT

Objective: To determine frequency, demographics, laboratory parameters and disease severity in patients with Rheumatoid Arthritis.

Methods: A retrospective analysis of prospectively collected data of patients with a diagnosis of Rheumatoid Arthritis, at the 'Rheumatology Clinic' of Jinnah Postgraduate Medical Centre, from February 2004 to February 2014. Detailed history, examination, laboratory investigations and treatment regimen were recorded in a pre-designed structured proforma. The demographic characteristics, deformities, extra-articular features, associated co-morbidities and disease severity were studied.

Results: A total of 458 patients with the diagnosis of RA, were registered in our 'Rheumatology Clinic' during this period. Among these, 365(79.7%) were females and 93(20.3%) were males. The mean age of patients was reported to be 36.9±11.93 years, while the mean duration of joint pain was 3.49±2.1 years. Treatment regimen included mono-therapy in 131 (28.6%), dual therapy regimen in 221 (48.3%) and triple DMARDs therapy in 11 (2.40%) patients. DMARDs alone were used in 221 (48.3%), while 134 (29.3%) patients received DMARDs with maintenance dose steroids. Extra-articular manifestations were reported in 178 (38.86%) patients. Commonest co-morbidity was hypertension in 38(8.3%) patients. Additionally, out of the 287 patients who could be tested, 211 (73.5%) patients had vitamin-D deficiency as well.

Conclusion: RA constitutes a significant rheumatological disease burden in our population. The demographic features and pattern of joint involvement is similar to the west, but a considerably younger population is affected in our region. The reason for this early disease occurrence needs to be explored. Vitamin-D deficiency may be a trigger in RA pathogenesis.

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Citation: Tasnim Ahsan, Rukhshanda Jabeen, Uzma Erum and Danish Khowaja, 2016. "Rheumatoid arthritis: A major disease burden", *International Journal of Current Research*, 8, (10), 40061-40063.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic, autoimmune disease, with multisystem involvement and variable systemic manifestations. The exact aetiology of the disease is not known. The hall mark of this disease is persistent inflammatory synovitis. It predominantly involves small peripheral joints in a symmetric distribution. The pathological sequence includes hypertrophy and hyperplasia of the synovial cells with perivascular infiltration of inflammatory cells such as macrophages and T-cells that causes release of various cytokines, hence leading to focal vascular changes and edema of the synovial lining. The activation of synovial fibroblasts produces enzymes such as collagenase and cathepsin that degrade the articular matrix. The estimated prevalence of RA

in different populations is approximately 0.5%–1% (Weinblatt *et al.*, 2007). While, 0.55% of RA prevalence has been reported from northern Pakistan (Farooqi and Gibson, 1998). RA is a progressive disease with pronounced impact on functional ability. Therefore, individuals with RA experience considerable physical and psychological distress. The aim of treatment lies at providing highest possible quality of life and ambulation by arresting the disease progression at an early stage. An increased mortality has been reported in RA patients in various epidemiological studies (Wolfe *et al.*, 1994). The present study was designed to report on the demographic features, associated co-morbidities, extra-articular manifestations, pattern of joint involvement and deformities in RA patients. Studies pertaining to clinical characteristics of RA patients in our country are sparse. Highlighting the pattern of disease in our population could be helpful not only in better understanding of the disease course, but also early implementation of treatment strategies in order to prevent deformities and hence improve the quality of life in these patients.

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PATIENTS AND METHODS

Study Design

This study is a retrospective analysis of prospectively collected data of patients registered at the 'Rheumatology Clinic' of JPMC, from February 2004 to February 2014.

Inclusion Criteria

All cases with definitive diagnosis of RA by validated ACR criteria were registered. Data was recorded in a pre-designed structured proforma, including history, examination, laboratory investigations, co-morbidities, treatment and follow-up records.

Data Analysis

Data was analyzed by SPSS version-17. For the descriptive variables like gender, co-morbidities, extra-articular features, joint deformities and treatment regimen, frequency and percentages were calculated, while means were calculated for age and duration of disease.

RESULTS

A total of 458 patients were registered with the diagnosis of RA according to the ACR criteria. Out of these, 365(79.7%) were females and 93(20.3%) were males. The mean age was 36.9±11.93 years; the commonest affected age group was second and third decade, representing 141 (30.8%) and 135 (29.5%) patients respectively (Fig-1).

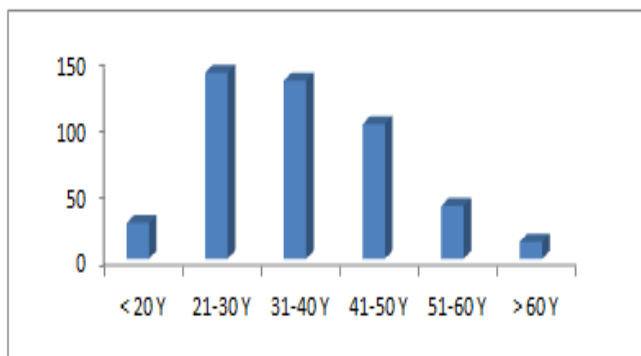


Fig 1. Age Distribution among RA patients

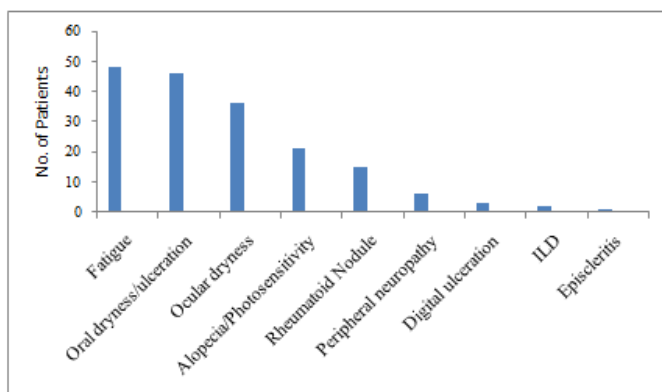


Fig. 2. Extra-articular manifestations in RA patients

The mean duration of joint pain was 3.49±2.1 years. Rheumatoid factor was positive in 364 (79.5%) patients. Commonest joint deformity was Ulnar drift of fingers in 64 (14%) patients, followed by Boutonniere in 48 (10.5%); Swan neck in 44 (9.6%); Palmar subluxation in 30 (6.6%); and Z-deformity in 12 (2.6%) patients. Extra-articular manifestations were reported in a total of 178 (38.86%) patients; these included oral dryness and ulceration in 46 (10.04%); ocular dryness in 36 (7.8%); alopecia and photosensitivity in 21 (4.5%) patients. Rheumatoid nodule was reported in only 15 (3.3%) patients and fatigue was reported in 48 (10.48%) patients. Interstitial lung disease (ILD), peripheral neuropathy, episcleritis and digital ulceration was reported in few patients. (Fig-2). Serum vitamin-D levels were reported in 287 patients, out of which 211 (73.5%) patients had vitamin-D deficiency or insufficiency. Out of the 458 patients, only 85 (18.5%) were on some treatment, including erratic DMARDs, steroids and NSAIDs; the rest were treatment naïve before registration in our clinic.

Treatment and follow-up record revealed that, 221 (48.3%) patients were treated with DMARDs and bridging steroids, and 134 (29.3%) were given DMARDs with either low dose maintenance steroids or regular NSAIDs. One patient received biological agent namely Tocilizumab. Treatment regimen included mono-therapy in 131 (28.6%), while dual or triple therapy regimen was instituted in 221 (48.3%) and 11 (2.40%) patients respectively. Commonest drugs used were dual therapy with Methotrexate and Hydroxy-chloroquine in 143 (31.2%) patients. While, Methotrexate and sulphasalazine in 37 (8.07%); Sulphasalazine and Hydroxychloroquine in 27 (5.89%) and Methotrexate as monotherapy was used in 95 (20.7%) patients. Other patients received either of the above mentioned drugs, either alone or in combination. Associated co-morbidities included hypertension in 38(8.3%) patients; diabetes in 10 (2.2%) and hypothyroidism in 5 (1.1%) of patients. Other diseases like chronic hepatitis B and C, tuberculosis, asthma and hyperthyroidism were reported in less than 1% of patients.

DISCUSSION

RA compromises an individual's functional capability and poses a significant financial burden on the individual, as well as on the health care delivery system in the public sector. It constitutes a major disease burden of our Rheumatology Clinic. The demographic features of RA are almost same as reported in earlier studies, but a considerably younger population is affected here. Over 60% of our patients were in the second and third decade of life. Diagnosis is often delayed from several months to several years after the onset of symptoms. A median lag time of 36 weeks has been reported (Chan *et al.*, 1994). This time lag is an important contributor to disease progression, functional disability and extra-articular involvement in individual patients of RA. Being a population with prevalent vitamin-D deficiency, the predisposition to RA might be linked to low vitamin-D levels. Other studies from various parts of the world have also reported a high associated prevalence of low vitamin-D levels in RA patients (Kostoglou *et al.*, 2012; Rossini *et al.*, 2010). A large number of our patients presented with established hand deformities. So far no study from Pakistan has reported the occurrence of hand deformities in RA. Hand deformities are important because of considerable disability that accrues. The devastating secondary outcomes of these deformities can be minimized by an early comprehensive

and aggressive treatment strategy. A study from Sweden reported that, 31 patients out of the 100 had developed either one or more deformities during a 2 year follow-up after RA diagnosis (Ebrehardat *et al.*, 1991). Extra-articular manifestations variably occur during the course of rheumatoid disease, and the frequency differs among different populations. A linear relation exists, reflecting longer the disease duration, greater the frequency of extra-articular manifestations. The presence of extra-articular features is more frequent in patients with severe active synovitis and is associated with high mortality, and needs early and aggressive treatment.

A considerable number of patients had extra-articular features in our study, reflecting their disease severity. Turesson *et al.* reported extra-articular features in 42.7% of RA patients in a follow-up period of 11.8 years (Turesson *et al.*, 2006). Rheumatoid nodules are reported to be the commonest extra-articular feature in approximately 30%; while secondary Sjögren's syndrome, and pulmonary manifestations in 6-10% of RA patients (Young and Koduri, 2007). On the contrary rheumatoid nodules were seen in a very small percentage of our patients, despite most patients having moderate to severe disease. Persistent oral and ocular dryness has been reported in 11.6% of RA patients (Wolfe *et al.*, 2008). These might be related to secondary Sjögren's syndrome, seen frequently in RA patients. Another important factor is RA associated interstitial lung disease (ILD), which is a source of substantial morbidity and mortality in these patients. Pulmonary involvement was seen in very few of our patients. The incidence of lung involvement might have been higher, had we screened all patients rather than only those who had persistent overt respiratory symptoms. An Indian study reported ground glass opacities or reticular changes on HRCT chest in 19% patients of the RA cohort (Fatima *et al.*, 2013). The commonest co-morbidity reported was hypertension. It may be because RA is an autoimmune inflammatory state hence the systemic nature of the disease leads to inflammation of blood vessels as well, leading to atherosclerosis and hypertension.

Fatigue is a frequent and overwhelming issue for most RA patients. A considerable number of our patients reported fatigue. Although, subjective differences exist between the pain perception and depressive feelings, a linear relation lies between individual's functional capability and depressive feelings. However, prompt social support as well as appropriate treatment may have a buffering effect on the level of stress and fatigue. Studies also reported, and linked it mainly to pain and depression. Fatigue is a considerably treatable target in the management of RA to have a better quality of life (Hewlett *et al.*, 2005; Pollard *et al.*, 2006; van Hoogmoed *et al.*, 2010). Despite the current management guidelines supporting an early and aggressive management of RA to prevent joint destruction, disease progression and associated co-morbidities. In a developing country with poor health care resources, treating RA patients in a public sector hospital is very difficult but not entirely unmanageable. Cost-effective management of RA patients becomes an important issue as so, as to prevent incapacity and hence the capability of gainful employment and unaided existence. Paucity of trained rheumatologists and inaccessibility to health care facilities are added hurdles in the delivery of cost-effective treatment. Despite not being able to use biological agents at an early disease course because of

expense, most of our patients received conventional DMARDs as the main treatment arm and benefited significantly from them.

Conclusion

The disease burden and pattern of RA as seen in a public sector 'Rheumatology Clinic' has been reported here. It provides clue to better understanding of the nature of disease progression and its varied manifestations in our population. High frequency of extra-articular manifestations, points towards early and severe progressive disease course. Associated vitamin-D deficiency may be a triggering factor for RA in our patients.

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