Progression pattern of rheumatoid arthritis: A study of 500 Pakistani patients

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Abstract: To estimate the most prevalent age of patients and disease status and progression in terms of severity at different age groups in the Pakistani Rheumatoid Arthritis (RA) patients. A total of five hundred (500) RA patients were enrolled during October, 2009 to October, 2013. A screening questionnaire was filled for each patient satisfying America College of Rheumatology (ACR) criteria under the supervision of certified rheumatologists. Epidemiological and demographic variables were statistically analyzed for correlation with progression of the disease using SPSS ver 17.0.1 software. In general, rheumatoid arthritis preferentially affects women with female to male ratio of about 3:1; however, patients with above 60 years of age have equal female to male ratio. The most prevalent age is 45-60 years. The disease severity increases with increase in the age and reaches to its peak in above 60 years of age (p=0.001). The pattern of progression of RA in the Pakistani patients is almost consistent with other relevant studies conducted on European and European derived populations.

Keywords: Rheumatoid Arthritis, epidemiology, auto-immune diseases, disease severity and progression.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic, systemic, inflammatory disease characterized by synovitis and destruction of inflamed joints and bones (Tobon *et al*., 2010). Inflammation of synovial membrane ultimately leads to loss of daily function due to chronic pain and fatigue. The ultimate result is deterioration of cartilage and bone which may eventually lead to permanent disability. Although the exact pathogenesis of rheumatoid arthritis is yet to be properly explored, however, multiple exogenous and endogenous triggers in the presence of background genetic predispositions have be associated with a series of autoimmune responses in the synovium (Jonathan *et al*., 2004).

RA is a multifactorial disease, resulting from the interaction of both genetic (50-60%) and environmental factors, in its occurrence and expression (Alamanos and Drosos, 2005). Various environmental factors involved in the pathogenesis of RA include socioeconomic characteristics, smoking, diet, infectious agents and hormonal factors. Among environmental risk factors smoking shows the strongest association with susceptibility and worse outcomes of RA (Tobon *et al*., 2010). The worldwide prevalence of RA is estimated to be 0.5 to 1.0% (Caporali, 2009). Its prevalence and incidence vary from one population to another (DelPuente *et al*., 1989; Mijiyawa, 1995) and from time to time (Spector, 1991; Silman, 1992). Onset usually occurs between 30 and 50 years of age (Ruddy, 2005) and peaks in individuals aged 40-60 years (Pincus and Callahan, 1985). Rheumatoid arthritis preferentially affects women and the general ratio of female to male patients is approximately 2-4:1. The predominance of RA in females is well documented in European, North American, Asian and Australian population studies, with higher female to male ratio (2-5.6:1) (Lawarence, 1998; Saraus *et al*., 1999; Silman adn Hochberg, 2001; Carmona *et al*., 2002; Gabriel *et al*., 2003; Guillemin *et al.*, 2005). According to epidemiological studies the prevalence of RA varies from 0.2 to 1.0% in various European, North American, Asian and Australian populations (Silman and Hochberg, 2001).

Early diagnosis and disease severity were addressed in the 2010 American College of Rheumatology and the European League Against Rheumatism (2010 ACR/EULAR) classification criteria, as short comings of 1987ACR classification criteria. Therefore, in this descriptive epidemiological study we sought to estimate the most prevalent age group and progression pattern with respect to severity of the disease in the Pakistani RA patients. Which may be helpful in proper care and management of RA in the right age with decreasing the rate of disabilities and hence economical burden on our population.

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MATERIALS AND METHODS

Subjects and methods

Rheumatology departments of Military Hospital and Rahmat Noor Clinic and Arthritis Research Center at Rawalpindi were selected for patients ascertainment. A total of 500 patients satisfying the American College of Rheumatology (ACR) criteria were enrolled during recruitment period from October, 2009 to October, 2013. The mean age of the patients was 40±13 years, while the mean duration of illness was 5-6 years.

All the patients were of Pakistani ethnicity and were enrolled with informed consents. The study was approved by Institutional Review Board (IRB) of Atta-ur-Rahman School of Applied Biosciences, National University of Sciences and Technology, Islamabad Pakistan. All subjects participated in the study were interviewed and data was recorded in a screening questionnaire. Subjects were asked to report the age at onset of symptoms, duration of symptoms, number and kind of affected joints, number of deformities, family history and finally the socio-economic status. The clinical and serological information of the patients was noted. The disease activity score 28 (DAS 28) of the patients was calculated by using standard formula (DAS28 =0.56* sqrt(tender28) + 0.28* sqrt(swollen28) + 0.70* ln(ESR) + 0.014* GH). Three classes of patients, one with remission and lower disease, second with moderate disease and those with DAS28 score higher than 5.3 were called sever and active disease, were made. Based on the amount of radiographic changes the patients were classified to have minor, moderate or severe RA (Saraus *et al*., 2001). Patients were divided in to three groups (minor, moderate and sever disease) according to the DAS28 score and number and amount of radiographic damages and related function loss.

STATISTICAL ANALYSIS

Epidemiological and clinical variables were statistically analyzed using Statistical Package for Social Sciences version 17.0.1 (SPSS 17.0.1). Descriptive statistical analysis was performed by frequency tabulation and cross tabulation of the variables of interest and relevance for this study. *P* value less than 0.05 was considered statistically significant.

RESULTS

A total of five hundred RA patients were ascertained in a period of three years including 370 females and 130 males patients giving a female to male ratio of ~3:1(table 1). Clinical presentation of the patients revealed that small joints of hands and legs like fingers, knee and wrists were frequently involved. Patients with severe clinical conditions had severely deformed bones with RA specific pattern.

In order to determine the most prevalent age of onset; patients were stratified by age into four groups i.e., Group-A (15-30 years), Group-B (31-45 years), Group-C (46-60 years) and Group-D (60 years +) (fig. 1). The age-based stratification showed high Female to Male ratio in each age group and the average age of disease occurrence that is ~40 and ~50 years in female and male, respectively. The onset of symptoms occur approximately 10 years earlier in women than in men, while in the Group-D almost equal ratio was seen in females and males (table 1, fig. 2).

Furthermore, we observed that RA is a disease of all ages but signs and symptom may more prominently appear in subjects aged above 35 years (fig. 2) and severity in disease status increases with increase in age and reaches to its peak above 60 years (p=0.001) (fig. 3) where the bones of inflamed joints may be severely deformed.

DISCUSSION

RA is a multifactorial disease, resulting from the interaction of both genetic and environmental factors. Several environmental factors have been studied as possibly related to an increased risk of RA, as well as to worse or improved prognosis of the disease (Alamanos and Drosos, 2005).[3] Various environmental factors involved in the pathogenesis of RA include socioeconomic status, smoking, diet, infectious agents and hormonal factors (Tobon *et al*., 2010). The worldwide prevalence of RA is estimated to be 0.5-1.0% (Caporali *et al*., 2009) and 0.1-0.2% in the Pakistani population (Baig, 2003). However, the prevalence and incidence vary from one population to another (DelPuente *et al*., 1989; Mijiyawa, 1995) and from time to time (Spector, 1991; Silman, 1992) possibly due to variations in environmental conditions and genetic predisposition of the patients. Low prevalence of rheumatoid arthritis was previously reported in an urban Pakistani population (Hameed *et al*., 1995) and higher prevalence in Pakistanis living in England but not as high as the prevalence in ethnic English populations (Hameed and Gibson, 1997).

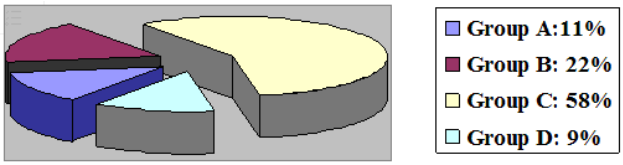

Fig. 1: Stratification of patients by age in to four groups; Group A (15-30 years), Group B (31-45 years), Group C (46-60 years), Group D (60 years +)

To our knowledge, this is a first descriptive epidemiological study undertaken in a small pool of Pakistani samples to determine the pattern of progression of RA in the Pakistani patients. Rheumatology departments of two hospitals in Rawalpindi were selected

for enrolment of the subjects. All the patients were subjected to physical and clinical examination and detailed history of disease was collected by using a specially designed Performa. Demographic details which include the duration of disease, age at onset, gender and disease severity were statistically interpreted by using Statistical Package for the Social Sciences (SPSS) computer program.

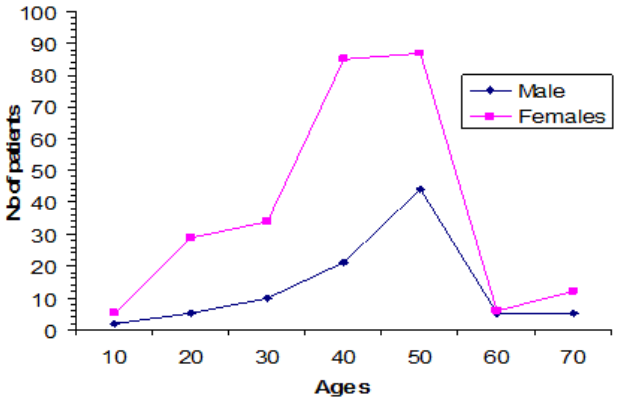

Fig. 2: Age-specific progression of RA in males and females

We observed that rheumatoid arthritis preferentially affects women, with female to male ratio of ~3:1 which is consistent with the previously reported female to male ratio of i.e., approximately 2-3:1(Pedersen *et al.*, 2007) while this ratio is almost equal at 60-75 years of age. The similarity in ratio between females and males in older age group may be due to increased mortality rate at this age and decrease in immune responses. Studies have indicated that RA incidence increases with age and in the oldest age groups equal rates are seen in females and males (Doran *et al.*, 2002). Moreover, we have observed that the onset of RA occurs about 10 years earlier in women than in men which was found consistent with previous studies (Deborah, 2002). The exact mechanism of the gender differences in the onset of RA is not fully understood but is presumed to be the cause of hormonal milieu on immune function (Silman and Hochberg, 2001).

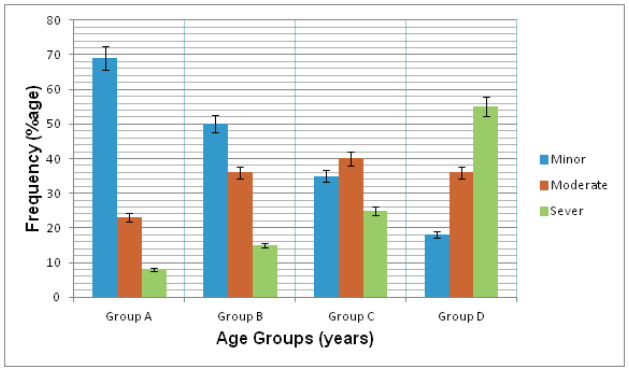

Fig. 3: Progression of disease in terms of severity in different age groups; Group-A (15-30 years), Group-B (31-45 years), Group-C (46-60 years), Group-D (60 years +)

Aging is a ultimate risk factor for RA and the frequency of autoimmune diseases increase with age due to the decline of normal immune surveillance and dysregulation (Hakim and Gress, 2007; Goronzy *et al*,. 2007)**.** The incidence of RA may occurs at any age, rises dramatically during adulthood and reaches to its peak in individuals aged 40-60 years (Khurana and Berney, 2005). Similarly, we noticed that RA is more prevalent in 45-60 years of age.

The severity of disease severity can be defined by the number and amount of organs damage and the loss of their function. There is no standard guidelines exist in literature for the assessment of disease status in RA (Wolfe *et al.*, 2001), however, previously Saraux *et al* suggested that the patients meeting ACR criteria would follow three clinical patterns of disease progression (Saraux *et al.*, 2001). Based on the amount of organs

Table 1: Distribution of Subjects according to Demographic Variables

	Number of patients (n=500)	Percentage of patients out of total	Male patients (n=130)	Female patients (n=370)	*P*- Value
Age Groups					
15-30	55	11%	10	45	
31-45	110	22%	15	95	
45-60	290	58%	85	200	
61-75+	45	9%	20	30	
Age at onset of symptoms					
<20years	85	17%	22	63	
20-40years	150	30%	27	126	
>40years	265	52%	81	181	
Disease Severity					
Minor	250	50%	80	170	0.01
Moderate	155	31%	25	130	
Sever	95	19%	25	69	

involved and radiographic changes we classified our sample in to minor, moderate and sever disease. Minor is a self-limited disease, moderate is a mild-disease that can be controlled with traditional therapies and severe is a progressive disease that can not been controlled by traditional therapies. From this stratification we observed that severity in disease status increases with increase in age and reach to its peak above 60 year of age where the affected joints specially hands and feet bones severely deformed forming RA specific pattern in older age. we have found more severe disease symptoms in female subjects then male which may be because of certain reasons. Pakistani women due to social customs, do not participate in activities like both indoor and outdoor games, not they go to gyms and nor do daily exercises to keep their body physically active. Majority of women are involved in caring their homes and kids, let them to avoid the outdoor activities, resulting in the vulnerability of their body to immunological diseases. This may not only led to the high disease ratio in Pakistani women but also increasing the mortality rate in women as compare to men in the older age.

CONCLUSION

The disease burden of Rheumatoid Arthritis is increasing due to lack of proper disease management and treatment. However, a significant proportion of RA cases still remains undiagnosed in our community. Therefore substantial research is required for proper diagnosis and management of the RA patients that will help in alleviation of symptoms of RA in our population.

ACKNOWLEDGEMENTS

The work was funded by the Higher Education Commission (HEC), Islamabad, Pakistan. We wish to thank the Patients for their cooperation.

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