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ORIGINAL ARTICLE

Characteristics of Patients With Rheumatoid Arthritis in Turkey: Results From the Turkish League Against Rheumatism Rheumatoid Arthritis Registry

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ABSTRACT

Objectives: This study investigates the demographic and clinical characteristics of patients with rheumatoid arthritis (RA) in Turkey, and attempts to identify strategies for the prevention, treatment, and support of RA.

Patients and methods: A total of 2,359 patients (1,966 females, 393 males; mean age 51.6±12.5 years; range 18 to 75 years) with RA from 36 centers across Turkey, who were recorded in the Turkish League Against Rheumatism (TLAR) RA Registry between September 2007 and March 2011, were evaluated. Patients' demographic and clinical data were recorded. Disease activity, functional status, and radiographic damage were measured using the Disease Activity Score 28, the Health Assessment Questionnaire, and van der Heijde modified Sharp scoring method.

Results: The mean duration of academic education received was 5.2±3.8 years, and 74.6% of the patients were homemakers. Non-biological disease-modifying anti-rheumatic drugs were used by 91.0% of the patients, while 10.2% used biological disease-modifying anti-rheumatic drugs. The mean Disease Activity Score 28, Health Assessment Questionnaire, and Sharp scores were 4.0±1.4, 0.38±0.37, and 31.2±57.1, respectively. Of the patients, 17.8% were in remission and 14.1% had low disease activity rates, while 42.7% and 25.5% had moderate and high disease activity rates.

Conclusion: The majority of patients with RA in Turkey are middle-aged homemakers. Despite the high rates of disease-modifying anti-rheumatic drugs use, the majority of patients had moderate and high disease activity. These findings indicate that treatment needs of RA patients are not met sufficiently.

Keywords: Patient characteristics; registry; rheumatoid arthritis.

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Rheumatoid arthritis (RA) is a chronic inflammatory disease with a prevalence of 1%, which mainly affects the synovial joints. RA can lead to significant functional loss and disability due to joint damage. It is also a great burden on the individual, society, and the health care system. To reduce the negative effects of the disease on the quality of life and socio-economic burden, one should have a better understanding of RA in every aspect. Therefore, epidemiological data, clinical information concerning risk factors, comorbidities, complications and sequelae, and cost analyses are needed. These data are required to adopt the most appropriate management approach for RA patients.[1-3]

Information regarding RA can easily be reached in findings of clinical trials which investigate patients with RA. However, the patients who take part in clinical trials are usually selected according to strict criteria, and therefore are not a true reflection of real-life patients. In recent years, RA registries have been created in many countries to gather information about patients outside of clinical trials, and to be able to follow these patients. The registration of RA patients has provided a better understanding of patients' demographic and clinical characteristics, and the long-term effectiveness and side effects of new drugs.[4-8] In Turkey, the first registry for RA, was initiated in 2007 by Turkish League Against Rheumatism (TLAR).

The aim of this study was to determine the demographic and clinical characteristics of patients with RA in Turkey, and thus to shed light on disease prevention, treatment and support strategies required by this patient group.

PATIENTS AND METHODS

In this study, a total of 2,359 patients (1,966 females, 393 males; mean age 51.6±12.5 years; range 18 to 75 years) in the TLAR RA registry were evaluated. The registry consists of web-based patient data from 36 centers in different regions of Turkey between September 2007 and March 2011. Patients who were over the age of 18 and met the diagnostic criteria of RA according to the 1987 American College of Rheumatology were included.[9]

Before the study began, an interactive meeting consisting of the practical applications was held to ensure that the researchers would carry out the assessments in a standardized fashion. In addition, a booklet for physical and radiographic evaluation methods was prepared for the participating centers. The study was approved by the ethics committees, and informed consents were obtained from all patients.

The evaluations were carried out by physicians in the centers where the patients were being treated and followed-up. The demographic characteristics including age, sex, level of education, employment status, marital status, age at onset, disease duration, smoking and alcohol consumption, tuberculosis history, family history of RA, and exercise habits were recorded. The clinical features including body mass index (BMI), comorbid diseases, extra-articular involvement, history of joint surgery, and drugs used [disease-modifying antirheumatic drugs (DMARDs), biological agents, corticosteroids] were determined. Physical examination consisted of the evaluation of rheumatoid nodules, and all 28 joints for tenderness and swelling. Erythrocyte sedimentation rate (ESR, mm/h) and rheumatoid factor (a value ≥15 IU/ml was accepted positive) tests were performed.

The disease activity was measured using the disease activity score 28 (DAS28), which consists of the examination of tender and swollen joints (from 28 joints), patient global assessment (PGA), measured with a 0-100 mm visual analog scale, and ESR. DAS28 is calculated using the following formula: DAS28= 0.56*sqrt (number of tender joints) + 0.28*sqrt (number of swollen joints) + 0.70*Ln(ESR) + 0.014*PGA.[10] DAS28 values ≤2.6 were considered as indicating disease remission, >2.6 to ≤3.2 as low disease activity, >3.2 to ≤5.1 as moderate disease activity, and >5.1 as high disease activity.[11] The patient's functional status was determined by the self-report Health Assessment Questionnaire (HAQ), for which Turkish validity and reliability studies have been performed. HAQ consists of eight subsections of 20 questions and subsections involving dressing, eating, standing, walking, hygiene, reaching, grasping, and daily activities. Zero to three points were assigned in response to each question (0= ability to perform activity easily, 1= little disability in performing activity,

2= difficulty in performing activity, 3= not able to perform activity). The total score was determined by calculating the mean of the highest points in the subdivisions. If the patient required assistance by another individual or used a device to perform the activity, a score of zero or one given for that question was increased to two.[12,13] Radiological findings were identified according to the van der Heijde modification of the Sharp method using anterior-posterior hand and foot radiographs. Using this method, the erosion score is calculated by studying 16 regions on the hand, and six regions on the foot, and scored between 0-5. Joint narrowing is assessed by studying 16 regions on the hand and six regions on the foot, and scored between 0-4. The total score is 448.[14]

Statistical analysis

Statistical Package for the Social Sciences version 15.0 for Windows (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. A total of 2,359 patients were included in the analysis. Frequency tables were presented for the categorical variables, and descriptive statistics (mean, standard deviation, and median) for the numeric variables.

Table 1. Demographic characteristics of rheumatoid arthritis patients

Characteristic	n	%	Mean±SD
Age (year)			51.6±12.5
Sex			
Female	1966	83.3	
Male	393	16.7	
Education level (year)			5.2±3.8
Occupational status			
Employed	289	12.3	
Unemployed	41	1.7	
Homemaker	1759	74.6	
Retired	252	10.7	
Student	17	0.7	
Marital status			
Single	348	14.8	
Married	2011	85.2	
Disease duration (year)			11.9±8.7
Age at disease onset (year)			41.2±13.6
<16	66	2.8	
≥16	2283	97.2	
Exercises habit	155	7.1	
Smoking habit	356	16.2	
Alcohol consumption	44	2.0	
Family history of RA	479	20.3	
History of tuberculosis	54	2.5	

SD: Standard deviation; RA: Rheumatoid arthritis.

RESULTS

The demographic characteristics of the patients are shown in Table 1, and the clinical features are shown in Table 2. Disease activity, functional status, and radiographic scores are presented in Table 3.

The mean years of received academic education were 5.2±3.8, and 74.6% of the patients were homemakers. The mean disease duration was 11.9±8.7 years. Seven point one percent took regular exercise, 16.2% were smokers and 2% consumed alcohol. The most common extra-articular signs were those involving the eyes (4.8%) and the lungs (3.9%). Comorbid diseases were observed in 57.1% of the patients. Non-biological DMARDs were used by 91.0% of the patients, while 10.2% used biological DMARDs. The mean DAS28, HAQ, and Sharp scores were 4.0±1.4, 0.38±0.37 and 31.2±57.1, respectively. Seventeen point eight percent of the patients

Table 2. Clinical characteristics of rheumatoid arthritis patients

Characteristic	n	%	Mean±SD
Body mass index (kg/m²)			28±5.3
Extra-articular involvement			
Pulmonary	85	3.9	
Ocular	106	4.8	
Renal	13	0.6	
Neurologic	6	0.3	
Sjögren's syndrome	34	1.6	
Cardiac	17	0.8	
Vasculitis	7	0.3	
Lymphedema	3	0.1	
Comorbidities			
Diabetes mellitus	175	8.0	
Heart disease	131	6.0	
Hypertension	591	26.6	
Thyroid disease	164	7.5	
Peptic ulcer	296	13.4	
Rheumatoid factor positivity	1633	69.2	
Subcutaneous nodule	69	3.2	
Joint surgery	377	31.6	
Drug use			
Non-biological DMARDs	2061	91.0	
Methotrexate	1451	64.1	
Sulfasalazine	755	33.3	
Leflunomide	464	20.5	
Chloroquine/ hydroxichloroquine	357	15.8	
Biological DMARDs	230	10.2	
Anti-TNF-α	223	9.8	
Others	7	0.4	
Corticosteroid	987	51.4	

SD: Standard deviation; DMARDs: Disease-modifying anti-rheumatic drugs; TNF-α: Tumor necrosis factor-alpha.

Table 3. Disease activity, disability, and radiographic scores of rheumatoid arthritis patients

Characteristic	n	%	Mean±SD	Median	Minimum-Maximum
Disease activity score 28			4.0±1.4	3.96	0.0-8.5
EULAR disease activity					
Remission	415	17.8			
Low	329	14.1			
Moderate	996	42.7			
High	595	25.5			
Health assessment questionnaire			0.38±0.37	0.2	0.0-1.5
Total Sharp score (n=682)			31.2±57.1	6.0	0.0-445.0

SD: Standard deviation; EULAR: European League Against Rheumatism.

were in remission, 14.1% had low disease activity rates, while 42.7% and 25.5% had moderate and high disease activity rates, respectively.

DISCUSSION

The data of 2,359 patients were obtained from TRASD-IP, within the scope of TLAR, which is the first RA registry in Turkey. Clinical and demographic characteristics were evaluated using this data.

Rheumatoid arthritis registries evaluate patients' health status, disease course, mortality, drug side effects, costs, and labor productivity. Arthritis registries were first created in the 1980s. The RA registries may vary according to the characteristics of the patients, and may be based on rheumatic diseases,[15-17] early arthritis,[8] early RA,[17-19] established RA,[7,20] and biological agent,[5,21,22] or DMARD[23] registries. In the TLAR registry, all patients older than 18 years of age with any kind of therapy or disease stage were recorded and monitored, and their real-life data was collected.

The mean age in the RA registries from other countries is between 50-68 years. That of the TLAR registry was also similar, although slightly younger (51.6 years).[15,24] In a study by Sokka et al.,[25] which contains data from 15 countries, the mean age of the RA patients in Turkey was younger than in other countries. This is an expected result due to Turkey's largely young population.

Rheumatoid arthritis is three times more frequent in women than in men. Hormonal factors are thought to be responsible for this phenomenon.[26] This rate was similar in the TLAR and other RA registries.[24,25]

The mean disease duration was 11.9 years, which is similar to the findings of other studies.[24,25] RA has been considered to begin at 40-50 years of age. In this study, the age of onset was 41.2 years, which is lower than that of other RA registries.[5,15]

Some studies have shown that the level of education may affect the prognosis of RA.[27] It is thought that low levels of education may be associated with poor compliance to treatment. Therefore, the high disease activity of patients in the TLAR registry may be associated with a low level of education.

The vast majority of patients in the RA registry in Turkey are women. Therefore, RA can lead to dysfunction in the roles of housewives, which in turn will cause loss of labor at home, resulting in an increase in the indirect costs of the disease.[28]

Exercise enhances the maintenance of range of motion, and improves the muscle strength and coordination. Furthermore, exercise has been shown to reduce pain and ESR in patients with RA.[29] The low rate of regular exercise taken by the population in our study suggests that patients need to be better educated on the importance of taking regular exercise.

Smoking is recognized as a risk factor for RA development and poor outcomes.[30,31] In this study, the rate of smoking was lower compared to some RA registries, while it was higher than some of them.[24] All the patients with RA should be informed about the negative effects of smoking on RA. The use of alcohol, which may increase DMARDs-induced liver toxicity, was not common among the patients.

First degree relatives of patients with RA have been reported to have an increased risk of

developing RA.[32] Approximately one fifth of the patients had a family history of RA.

Latent tuberculosis, which continues to be a major problem in Turkey, should be screened prior to administering biological treatments. Therefore, the guide for national tuberculosis screening is applied to the patients before starting any biological treatment. Even so, 2.5% of the patients had a history of tuberculosis. In Turkey, this issue should be kept in mind before commencing treatment with biological agents.

The mean BMI was high. Since a high BMI is associated with poor outcomes in patients with RA and causes negative effects on the treatment, care should be taken to maintain weight control.[33,34]

Extra-articular involvement also plays an important role in the follow-up and treatment of patients with RA. The most common comorbid diseases in the current study were hypertension and peptic ulcers. In the Giese registry, the most common comorbid disease was hypertension as well.[5] In patients with RA, the increased risk of coronary heart disease due to inflammation may be affected adversely by the presence of hypertension. Therefore, the regulation of blood pressure is extremely important. The increased rate of peptic ulcer disease may be related to the drug treatment for RA, and particularly the use of NSAIDs and corticosteroids.

Rheumatoid factor positivity was detected in 69.2% of the patients, which is consistent with the literature.[13,21] In the Norwegian DMARD registry, 19.7% was positive for rheumatoid nodules, whereas in our RA registry, the rheumatoid nodule rate was extremely low at 3.2%.[23] Joint surgery was performed in 31% of the patients. Surgery also increases the cost of the disease. When compared to past data, the rate of joint surgery seems to have increased.[35] This is likely due to the increased access to surgical treatment.

In recent years, the proposed approach for RA is to start DMARD therapy in the early stages of onset, before permanent joint damage occurs.[36] Ninety-one percent of the patients were using a non-biological DMARD, whereas 10% were treated with biological DMARDs. When compared with the other registries, the non-biological DMARD use was higher, whereas the use of biological DMARD was lower.[15,23,37] Half of the patients were on corticosteroid therapy. This is lower when compared to some of the RA registries, and higher than others.[24] In a previous study from Turkey, use of biological agents was 6.9%.[35] The recent data indicate that use of biological drugs has increased in Turkey, as well as all over the world. These data reflect the status 3 years previously and show that the disease activity was high and the use of biological agents was low. Presently, we believe that biological agents are used more frequently. Although it is not consistent with the current treatment strategy, patients showing moderate activity and unresponsiveness to DMARDs are not included in the repayment cover in our country.

Methotrexate remains the gold standard DMARD in the treatment of RA, and it has also been reported to be the most commonly used DMARD in the treatment of RA in various studies.[5,23,38] In this registry, methotrexate was the most commonly used DMARD, with a higher utilization rate compared to other studies (64.1%). Corticosteroid and methotrexate utilization rates were similar to the past data from Turkey.[35] The most commonly used DMARDs second to methotrexate were sulfasalazine, leflunomide, chloroquine and hydroxychloroquine, respectively. Azathioprine, auronophine, cyclosporine, gold thiomalate and d-penicillamine, which were all used in the 1980s and 1990s, are no longer in use in RA patient recorded the registry.

According to EULAR disease activity criteria, more than half of the patients had a moderate or high level of disease activity. This may suggest that, in Turkey, medical treatment is insufficient despite the frequent use of DMARDs, and that the course of the disease is more severe and resistant to treatment. In the study of Sokka et al.,[25] in which data from many countries were evaluated, the mean DAS28 was 4.0. In the same study, the mean DAS28 for Turkey was 4.1. These values are similar to the results of the present study.

Although the disease activity was high in the majority of the patients, it was surprising that the disability levels and the radiographic pathology results were not at an advanced level. RA can lead to functional disability by causing joint deformity and destruction. The disability levels associated with the disease as

measured by the HAQ were low (0.38). This rate of disability is low compared to the majority of the clinical trials on RA, and past data from Turkey.[24,25,35,39] The fact that the radiographic findings and levels of disability were low as expected.

This study is important because it contains the results of the first RA register created in Turkey, and includes accessible national data on patients with RA in Turkey. These data may shed light on the prevention, treatment, and support strategies required by these patients. The analysis of the follow-up results of the registry may provide data on the long-term course of the disease, drug side effects, and cost-effectiveness.

The majority of patients with RA in Turkey are middle-aged and homemakers. Higher levels of education may be necessary for compliance to and success of treatment. Despite the high use of DMARDs, the majority of the patients had moderate or high disease activity. These findings indicate that treatment needs for RA patients are not met sufficiently. Thus, we may conclude that the RA register may aid significantly in obtaining true clinical information.

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Declaration of conflicting interests

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