Comorbidities in Turkish patients with rheumatoid arthritis: association with the health-related quality of life in terms of disease activity, functional and radiological status, severity of pain, and social and emotional functioning

Garip Y[1], Eser F[2], Bodur H[2]

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ABSTRACT

Aims: The aim of our study was to investigate the comorbidities in Turkish RA patients and evaluate the impact of comorbidities on health-related quality of life (HRQoL) in terms of disease activity, functional and radiological status, severity of pain, and social and emotional functioning.

Methods: In a cross-sectional setting, a total of 160 RA patients who were admitted to our outpatient clinic between December 2013 and February 2014 were consecutively enrolled in the study. Comorbidities were recorded. Disease activity was measured by using Disease Activity Score-28 (DAS28). Stanford Health Assessment Questionnaire (HAQ) was used for determining functional status, Nottingham Health Profile (NHP) for HRQoL, and modified Sharp Score for radiological damage.

Major results: Comorbidities were reported in 107 patients (66.88 %). The most common was peptic ulcer (31.25%). This was followed by osteoporosis (21.25%), dyslipidemia (15.63%), depression (15%), hypertension (13.75%), diabetes mellitus (13.13%), thyroid disorders (%8.13), lung diseases (%6.88), cardiovascular diseases (6.25%), and cancers [(1 breast cancer, 1 malign melanoma, 3 lung carcinoma), 3.13%], respectively. Patients with comorbidities scored significantly higher in DAS28, HAQ, pain, energy and physical mobility subgroups of NHP ($p<0.05$). It was not recorded any statistical significant difference in modified Sharp scores and sleep, social isolation and emotional reactions subgroups of NHP between the patient groups with and without comorbidities ($p>0.05$).

Conclusions: Comorbid conditions of RA are common and associated with more active and severe disease and functional impairment. Comorbidities should be detected and treated earlier to reduce its negative impact on outcome in RA.

Keywords: Rheumatoid arthritis; Quality of life; Comorbidity.

INTRODUCTION

Rheumatoid arthritis (RA) is the most common inflammatory arthritis and is a major cause of disability[1]. Comorbidities are common in patients with RA. Some comorbidities are associated with RA, while others are related to its treatment. Treatment-related comorbidities are accelerated atherosclerosis due to corticosteroids, hyperhomocysteinemia due to methotrexate (MTX), and renal disease and hypertension due to nonsteroidal anti-inflammatory drugs (NSAID) use[2]. Comorbidities increase disability and shorten life expectancy, thereby increasing both the impact and mortality of RA[3]. Increased mortality may result from higher prevalences of cardiovascular disease and infections or the development of certain malignancies in patients with RA[4]. Health-related quality of life (HRQoL) is the gratification taken from life, happiness, and the way human beings perceive their situation within the system of culture and values[5]. World Health Organization defines HRQoL as 'individuals' perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals,

1. Department of Physical Medicine and Rehabilitation, Ankara Basak Medical Center;
2. Department of Physical Medicine and Rehabilitation, Ankara Numune Training and Research Hospital

expectations, standards and concerns. It is a broad ranging concept affected in a complex way by the persons physical health, psychological state, level of independence, social relationships, personal beliefs a nd their relationship to salient features of their environment[6]. HRQoL is an outcome measure that is increasingly being used to evaluate health outcome in clinical studies of patients with rheumatologic disorders including RA[7]. Comorbidities, resulting from RA or its treatment with methotrexate, leflunomide, corticosteroids, sulphasalasine, hydroxychloroquine, and anti-TNF agents, which have potential side effects, have negative impact on HRQoL.

The present study aimed to investigate the comorbidities in Turkish patients with RA and evaluate the association of comorbidities with HRQoL in terms of disease activity, functional and radiological status, severity of pain, and social and emotional functioning.

MATERIAL AND METHODS

A total of 160 RA patients (131 females and 29 males) were included in the study. All of them had a positive diagnosis of RA according to the diagnostic criteria of American College of Rheumatology (ACR) [8]. Patient information regarding age, gender, disease duration and medication was recorded. Comorbidities such as hypertension, dyslipidemia, diabetes mellitus, cardiovascular diseases, peptic ulcer, osteoporosis, thyroid disorders, depression, lung diseases and cancers, extracted from patient records of Ankara Numune Training and Research Hospital, Department of Physical Medicine and Rehabilitation (1995-2014) were assessed. Patient records included serum biochemistry tests; echocardiography and electrocardiogram (ECG); chest x-ray and thoracic computed tomography; upper gastrointestinal endoscopy; dual-energy x-ray absorptiometry (DEXA) and physical examination reports regarding the comorbidities. Rheumatoid factor (RF) seropositivity, number of swollen and tender joints, and erythrocyte sedimentation rate (ESR) levels were evaluated. The quadrivariate Disease Activity Score-28 (DAS28) was used for measuring disease activity. Values under 3.2 were accepted as low, in the range of 3.2-5.1 as intermediate, and over 5.1 as high disease activity[9]. Functional status was assessed by using the Stanford Health Assessment Questionnaire (HAQ)[10]. The Nottingham Health Profile (NHP) was used for evaluating HRQoL[11]. The modified Sharp Score developed by Van der Heijde was used for determining radiological damage[12]. The severity of pain was measured by using 10 cm Visual Analog Scale-Pain (VAS-pain)[13].

STATISTICAL ANALYSES

Descriptive statistics [mean, median, SD (Standard deviation), minimum, maximum and frequencies] were used for assessing the demographics and clinical parameters. Differences between patients with and without comorbidities were assessed using independent samples T-test. A value of $P < 0.05$ was considered statistically significant. All analyses were performed using Statistical Package for the Social Sciences-21.0 (SPSS 21.0) software.

RESULTS

SOCIODEMOGRAPHIC CHARACTERISTICS

A total of 160 RA patients (131 females and 29 males) were included to the study. Female-male ratio was 4.52. Mean age of the patients was 53.63± 11.94 (24-79) years. Mean age was 53.28± 12.27 years for women and 55.17± 10.33 years for men.

CLINICAL FINDINGS AND DISEASE ACTIVITY

The mean disease duration of the patients was 145.36±96.78 months. The mean ESR was 22.39±16 (2-80) mm/h. RF was positive in 137 patients (85.63%). Mean score was 0.73 ±1.52 and 3±4.62 for number of swollen and tender joints, respectively. Mean VAS-pain was 4.26±2.69.

Mean DAS28 score was 3.34±1.36 (median: 3.09). 53 patients (33.13%) were in remission (DAS28 score ≤2.6), 33 patients (20.63%) had mild disease activity (DAS28 score: 2.6-3.2), 55 patients (34.38%) had moderate disease activity (DAS28 score: 3.2-5.1), and 19 patients (11.88%) had severe disease activity (DAS28 score≥5.1).

FUNCTIONAL STATUS AND QUALITY OF LIFE

Mean score was 0.86 ±0.76 for HAQ. The mean ± SD HRQoL scores of the patients were 32.73±31.51, 31.33 ±23.5, 43.44±40.85, 29.31±31.96, 14.25±24.71, 25.78±33.14 in the subgroups of pain, physical mobility, energy, sleep, social isolation, and emotional reaction subgroups of NHP, respectively.

RADIOGRAPHICAL DATA

Radiographs showed structural damage in 146 patients

(91.25 %). The mean modified Sharp Score was 37.06±60.53 (median: 11).

Demographics, clinical and radiographical data are summarized in Table I.

COMORBIDITIES

Comorbidities were noted in 107 patients (66.88 %). The most common was peptic ulcer (50 patients, 31.25%). This was followed by osteoporosis (34 patients, 21.25%), dyslipidemia (25 patients, 15.63%), depression (24 patients, 15%), hypertension (22 patients, 13.75%), diabetes mellitus (21 patients, 13.13%), thyroid disorders (13 patients, %8.13), lung diseases (11 patients, %6.88), cardiovascular diseases (10 patients, 6.25%), and cancers [5 patients (1 breast cancer, 1 malign melanoma, 3 lung carcinoma) 3.13%], respectively (Table II).

MEDICATIONS

One or more synthetic disease-modifying antirheumatic drugs (DMARD) [MTX, leflunomide, sulphasalazine, and hydroxychloroquine] or biological disease-modifying antirheumatic drugs [infliximab, etanercept, adalumimab, rituximab, tocilizumab, and abatacept] were currently being used by 156 patients (97.5%). Of all the patients, 91.88% (147 patients) were under synthetic DMARD therapy, and 11.88% (19 patients) were under biological DMARD therapy. MTX was the most commonly prescribed synthetic DMARD. 72.5% of the patients (116 patients) were under MTX therapy. The ratio of the patients receiving MTX monotherapy was 48.13 % (77 patients). Current medication of the patients is shown in Table III.

Patients with comorbidities scored significantly higher in DAS28, HAQ, VAS-pain, and pain, energy and physical mobility subgroups of NHP ($p<0.05$). It was not recorded any statistical significant difference in modified Sharp scores and sleep, social isolation and emotional reactions subgroups of NHP between the patient groups with and without comorbidities ($p>0.05$) (Table IV).

DISCUSSION

Our study demonstrates that RA is associated with a high prevalence of comorbidities, which vary widely in different countries worldwide.

In our study, 66.88 % of RA patients had at least one comorbidity. The most common comorbidities were peptic ulcer (31.25%), osteoporosis (21.25%), and dyslipidemia (15.63%). Depression (15%), hyperten-

TABLE I. DEMOGRAPHIC AND CLINICAL PATIENT DATA

	Minimum	Maximum	Mean	Standard deviation	Median
Age	24	79	53.63	11.94	54
Number of swollen joints	0	10	0.73	1.52	0
Number of tender joints	0	26	3	4.62	1
ESR (mm/h)	2	80	22.39	16	18
Disease duration (month)	2	480	145.36	96.78	120
DAS28	0.5	7.6	3.34	1.36	3.09
HAQ	0	3	0.86	0.76	0.75
Modified Sharp Score	0	360	37.06	60.53	11
Pain (VAS,10 cm)	0	10	4.26	2.69	4
NHP-pain	0	100	32.73	31.51	14.29
NHP-physical mobility	0	100	31.33	23.5	25
NHP- energy	0	100	43.44	40.85	50
NHP- sleep	0	100	29.31	31.96	20
NHP-social isolation	0	100	14.25	24.71	0
NHP-emotional reactions	13	100	25.78	33.14	12.5

ESR: Erythrocyte sedimentation rate, DAS28: Disease Activity Score, HAQ: Health Assessment Questionnaire, VAS: Visual Analog Scale, NHP: Nottingham Health Profile

TABLE II. PREVALENCE OF COMORBIDITIES IN 160 RA PATIENTS (N=107)

Comorbidities	Number (percentage)
Hypertension	22 (13.75%)
Dyslipidemia	25 (15.63%)
Cardiovascular diseases (myocardial infarction, stroke)	10 (6.25%)
Diabetes mellitus	21 (13.13%)
Peptic ulcer	50 (31.25%)
Cancers	5 (3.13%)
Lung diseases (asthma, chronic obstructive pulmonary disease)	11 (6.88%)
Thyroid disorders	13 (8.13%)
Depression	24 (15%)
Osteoporosis	34 (21.25%)

TABLE III. DRUG USE IN 160 RA PATIENTS

	Number	Percentage
Methotrexate	116	72.5
Sulphasalazine	21	13.13
Leflunomide	22	13.75
Hydroxychloroquine	33	20.63
Infliximab	1	0.63
Etanercept	12	7.5
Adalimumab	2	1.25
Rituximab	1	0.63
Tocilizumab	1	0.63
Abatacept	1	0.63
Azathiopurin	1	0.63
Corticosteroids	89	55.63

TABLE IV. THE RELATION BETWEEN PRESENCE OF COMORBIDITIES AND CLINICAL AND RADIOLOGICAL PARAMETERS

	Comorbidities		
	Present (n=107)	Absent (n=53)	P value
DAS28	3.53±1.32	2.96±1.38	0.012*
HAQ	1.02±0.73	0.54±0.73	0.001**
Modified Sharp Score	41.09±59.54	28.91±62.26	0.23
VAS-pain	4.87±3.04	2.56±2.53	0.001**
NHP-pain	38.56±31.36	20.96±1.38	0.001**
NHP-physical mobility	36.09±22.21	21.69±23.27	0.001**
NHP- energy	49.66±40.04	32.07±39.33	0.012*
NHP- sleep	30.74±32.92	26.41±30.01	0.42
NHP-social isolation	14.76±24.62	13.21±25.09	0.71
NHP-emotional reactions	28.15±32.67	20.99±33.85	0.19

DAS28: Disease Activity Score, HAQ (Health Assessment Questionnaire): Functional Status Health Assessment Questionnaire, VAS: Visual Analog Scale, NHP: Nottingham Health Profile, *: P < 0.05 (significant), **: P < 0.01 (highly significant)

sion (13.75%), diabetes mellitus (13.13%), thyroid disorders (8.13%), lung diseases (6.88%), cardiovascular diseases (6.25%), and cancers [5 patients (1 breast cancer, 1 malign melanoma, 3 lung carcinoma) 3.13%], followed these, respectively.

In our study, the most commonly observed comorbidity was peptic ulcer with a ratio of 31.25%. In COMOrbidities in Rheumatoid Arthritis (COMORA) study, performed in RA patients from different countries worldwide, the prevalence of peptic ulcer was 10.8 among overall RA patients, ranging from 1% in Morocco to 17% in Hungary. The most common comorbidity was depression (15%). It was similar to the prevalence of depression in Turkey. The rate of depression varied widely among countries (from 2% in Morocco to 33% in the USA). The frequency of hypertension was reported as 11.2%. Hyperlipidemia (8.3%), lung diseases (6.6%), cardiovascular diseases (6%), and cancers (4.5%) followed it, respectively[4].

The prevalence of overall comorbidities in Turkish RA patients was 66.8%. Similarly, in a study performed in USA, the rate of cardiovascular disease, diabetes or

hyperlipidemia was reported as 67% in RA patients[14]. On the other hand, Al Bishri *et al.* noted the frequency of overall comorbidities in Saudi RA patients as 66%. The five most common comorbidities were hypertension (36%), diabetes mellitus (31%), osteoporosis (26%), dyslipidemia (19%), and peptic ulcer disease (10%)[15]. In a study from Taiwan, comorbid conditions were reported as 63.5%. The most common was hypertension (51.2%)[16].

Among drug therapy, single drugs or combinations of drugs including corticosteroids, synthetic and biological DMARDs are used for treating RA. Currently, MTX is accepted as first-choice DMARD[15]. In our study, MTX was the most prescribed DMARD, with a rate of 72.5%. Hydroxychloroquine (20.63%), leflunomide (13.75%), and sulphasalazine (13.13%) followed it, respectively.

The present study investigated the impact of comorbidities on HRQoL including physical, social, and emotional functions, and pain. The relationship between the presence of comorbidities and disease activity, functional status, pain, and radiological damage was evaluated. Patients with comorbidities scored significantly higher in the DAS28, HAQ, VAS-pain, and pain, energy and physical mobility subgroups of NHP. Presence of comorbidities was found to be associated with disease activity, functional status, pain and physical domains of HRQoL. It was not associated with mental domains of HRQoL such as sleep, social isolation and emotional reactions. This is concordant to the other studies in the literature. Radner *et al.* investigated HRQoL and functional status in 380 patients with established RA in Austria. They reported that comorbidities affected physical functions and physical domains of HRQoL[17]. Similarly, Rupp *et al.* suggested that comorbidities led to a worse HRQoL in RA patients. HRQoL was estimated with the Short form-36 (SF--36)[18]. Ranganath *et al.* evaluated disease activity by using Clinical Disease Activity Index (CDAI) in RA patients in North America and reported strong association between the presence of comorbidities and disease activity, confirming our data[19]. On the other hand, Van den Hoek *et al.* noted an association between comorbidity and physical impairment, which was evaluated by using HAQ[20]. Also in another study of Radner, which assesses the impact of comorbidities on physical function in RA patients, it was reported that comorbidities had a negative impact on physical function, irrespective of disease activity[21].

The limitation of this study is related to retrospective data analysis. Due to the fact that it is difficult to investigate the risk factors for comorbidities such as the use of glucocorticoids and NSAIDs, retrospectively, we could not clearly identify which comorbidities were associated with RA or its treatment. Further studies with prospective design will help us reach a more precise decision on this matter.

To our knowledge, this study is the first to investigate association with comorbidities and radiological findings in RA patients. We found no association between the presence of comorbidities and radiological damage.

CONCLUSIONS

Comorbid conditions of RA are common and associated with more active and severe disease and functional impairment. Also, they negatively affect the physical domains of HRQoL. Therefore, comorbidities should be detected and treated earlier to reduce its negative impact on outcome in RA. Monitoring of comorbidities should be regularly performed in clinical practice.

CORRESPONDENCE TO
Yesim Garip
Yasamkent Mah. 3250. Cad. Karevler B blok no:10
Ankara, Turkey
E-mail: dryesimgarip@gmail.com

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