The Relationship Between Disease Activity, Demographic and Characteristic Features in Individuals with Rheumatoid Arthritis

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Abstract

Background: This study was planned to investigate the relationship between disease activity and demographic and characteristic features of a group of Turkish individuals with Rheumatoid Arthritis.

Methods: A total of 143 participants (120 females, 23 males, mean age = 50.32 ± 12.14 years) diagnosed with Rheumatoid Arthritis (RA) according to the American College of Rheumatology 2010 criteria, were included in the study. Demographic features (gender, body mass index) and disease-related characteristics features (duration of disease, morning stiffness, presence of deformity, presence of nodules, dry eye, nail abnormalities, Raynaud’s phenomenon, osteoporosis, dyspnea at rest, exertional dyspnea) of the participants were recorded. Disease activity was calculated using Disease Activity Score 28 (DAS28). According to DAS28, the participants were divided into 3 groups as remission, low disease activity and moderate-high disease activity. Pearson Chi-square test was used to analyze the statistical difference between the disease activity and demographic and possible characteristics features of individuals with RA.

Results: In the analysis of the data, significant difference between remission and moderate-high disease activity was observed in morning stiffness, presence of deformity, presence of nodule, osteoporosis and exertional dyspnea; whereas statistically significant difference between low and moderate-high disease activity was observed in osteoporosis and dyspnea at rest (p < 0.05). In terms of demographic and characteristic features where the difference occurs, It was obtained that osteoporosis and exertional dyspnea, presence of nodüle, presence of deformity and morning stiffness poses a 1.97, 1.64, 1.62, 1.56 and 0.53-fold higher risk for moderate-high disease activity compared to the remission, respectively. It was obtained that osteoporosis and dyspnea at rest poses a 1.52 and 1.40--fold higher risk for moderate-high disease activity compared to the low disease activity, respectively.

Conclusion: It was observed that osteoporosis and dyspnea pose a risk for the active period of RA. According to these results, we think that the risk of developing dyspnea and decrease in bone quality in RA individuals in the active period is high due to inactivity. Therefore, we suggest that RA patients should be encouraged to continue their physical activities and increase their participation in the exercise to reduce their complaints of dyspnea and osteoporosis.

Keywords
Rheumatoid arthritis, Osteoporosis, Dyspnea, Disease, Risk

Objectives

Rheumatoid arthritis (RA) is the most common type of inflammatory arthritis causing pain and destruction, especially in peripheral joints [1]. Although it is a clinical picture characterized by symmetrical polyarticular pain and swelling, prolonged morning stiffness, weakness and fatigue, it shows in systemic involvements. These systemic involvements pose an important risk for the progression of the disease. Rheumatoid nodules, vasculitis, anemia, fatigue, weakness, weight loss, respiratory problems, lung and cardiac involvements may accompany [2–4].

In individuals with RA, symptoms such as pain, fatigue, decreased range of motion, joint damage, morning stiffness, decreased muscle mass, decreased muscle...
strength and endurance cause a decrease in physical activity and physical fitness levels [5].

Rheumatoid arthritis is also a chronic inflammatory disease that progresses with progressive joint deformity, causing osteoporosis and death, causing multiple organ damage [6,7].

Pulmonary manifestations is a very common condition in RA [8]. It has been reported that many drugs used in rheumatoid arthritis can also cause lung involvement [9].

RA can cause significant disability and functional limitations. It is also a great burden for the individual with RA, society and health system. In order to reduce the negative effects of RA on quality of life and socio-economic burden, it should be better understood in every respect. Therefore, there is a need for clinical information on risk factors, comorbidities, epidemiological data and complications. This information is necessary in determining the most appropriate management approach for individuals with RA [10-12]. In recent years, clinical and demographic characteristics features of individuals have been recorded in many countries for better understanding of RA [13-16].

The prevalence of RA in Turkey, according to a study made in 2006 is 0.36% [17]. It is known that RA shows various characteristics features according to the population affected by it. Most of the available information about RA was obtained from studies conducted in Europe and the United States [18,19]. There are very few studies on the Turkish population [20]. Therefore, information regarding demographic and clinical characteristics features of RA individuals in Turkey is not sufficient.

This study was planned and conducted to examine the relationship between disease activity and demographic and characteristic features of a group of Turkish individuals with RA.

Methods

Participants

A total of 143 participants (120 females, 23 males, mean age = 50.32 ± 12.14 years) diagnosed with Rheumatoid Arthritis (RA) according to the American College of Rheumatology 2016 criteria, were included in the study. The inclusion criteria were as follows: (a) Having RA diagnosis according to ACR 2016 criteria [21]. (b) Aged 18-65. (c) Being volunteer to participate in this study. The exclusion criteria were as follows: (a) Having other diseases affecting functions (orthopedic, neurological, cardiovascular and metabolic disease). (b) Comorbidity affecting upper extremity and hand functions (carpal tunnel syndrome, trigger finger, impingement syndrome, thoracic outlet syndrome, lateral and medial epicondylitis, hand osteoarthritis). (b) Cognitive impairments. (c) Pregnancy. (d) Illiteracy.

The ethics of the study was approved by local ethics committee. All individuals were informed verbally and informed consent forms were signed.

Outcome measures

The data were collected by the same rheumatologist and by the same physiotherapist in the same day face to face interview method in approximately 40 minutes.

Evaluations included disease activity and demographic features (gender, body mass index) and disease-related characteristics features (duration of disease, morning stiffness, presence of deformity, presence of nodules, dry eye, nail abnormalities, Raynaud’s phenomenon, osteoporosis, dyspnea at rest, exertional dyspnea).

Disease Activity Score 28 (DAS28) was used to evaluate disease activity. This index is a combination of 28 swollen joints and 28 sensitive joints, assessment of patient’s general medical condition and C reactive protein rate. Swollen and sensitive were assessed for 28 joints (0 = No and 1 = Yes). These 28 joints included 2 shoulder, 2 elbow, 2 wrist, 10 metacarpophalangeal joints, 2 interphalangeal thumbs, 8 proximal interphalangeal joints, and 2 knee joints. DAS28 indicates current condition of the patient in the clinic. A high score represents a high disease activity. (> 5.1 high disease activity; 3.2 < DAS28 ≤ 5.1 moderate disease activity; 2.6 < DAS28 ≤ 3.2 low disease activity; ≤ 2.6 remission) [22].

Participant were divided into 3 groups as “remission”, “low disease activity” and “moderate-high disease activity” according to DAS 28.

Participants were divided into two groups as “normal” and “overweight” according to BMI, as “early stage (≤ 2 years)” and “late stage (> 2 years)” according to duration of disease and as “≤ 60 sec” and “ > 60 sec” according to morning stiffness.

The presence of deformity, presence of nodules, dry eyes, nail abnormalities, Raynaud’s phenomenon, osteoporosis, dyspnea at rest, exertional dyspnea were recorded as “yes” or “no”.

Statistical analysis

The data was analyzed by SPSS packet program. Continuous variables were given as mean ± standard deviation and categorical variables as numbers and percentages. Pearson Chi-square test was used to define the statistical difference between DAS28 and demographic and characteristic features. P value < 0.05 in the 95% confidence interval was considered as statistically significant.

Results

One hundred and forty-three participants (female = 120, male = 23) participating in the study; average age was 50.32 ± 12.15 years. Descriptive data of the demo-
In the analysis of the data, significant difference between remission and moderate-high disease activity was observed in morning stiffness, presence of deformity, presence of nodule, osteoporosis and exertional dyspnea; whereas statistically significant difference between low and moderate-high disease activity was observed in osteoporosis and dyspnea at rest (p < 0.05). In terms of demographic and characteristic features where the difference occurs, it was obtained that osteoporosis, exertional dyspnea, presence of nodules, presence of deformity and morning graphic and disease-related characteristics features of the participants are shown in Table 1.

Descriptive data of the three groups in which the participants were separated according to DAS 28 and are shown in Table 2. Descriptive data of the groups formed according to the demographic and disease-related characteristics features of the participants and are shown in Table 3.

Table 1: Descriptive data of the participants' demographic and disease related characteristics features.

| Variables                              | Min.-Max. | X ± SD          |
|----------------------------------------|-----------|-----------------|
| Age (years)                            | 20 - 65   | 50.32 ± 12.14   |
| Body height (m)                        | 1.34 - 1.78 | 1.61 ± 0.07     |
| Body mass (kg)                         | 45 - 170  | 72.98 ± 15.16   |
| Body mass index (kg/m²)                | 17.76 - 58.82 | 28.08 ± 5.72   |
| Duration of disease (years)            | 0.04 - 30.00 | 7.98 ± 7.17    |
| Morning stiffness (sec)                | 0.00 - 180.00 | 32.90 ± 44.38  |

Table 2: Distribution and descriptive data of the participants according to Disease Activity Score 28.

| Disease Activity Score 28 | n (%)   | Min. - Max. | X ± SD     |
|---------------------------|---------|-------------|-----------|
| Remission                 | 67 (46.9) | 0.96 - 4.17 | 1.78 ± 0.53 |
| Low disease activity      | 24 (16.8) | 2.62 - 3.19 | 2.94 ± 0.19 |
| Moderate-high disease activity | 52 (36.5) | 3.24 - 6.52 | 4.36 ± 0.93 |

Table 3: Descriptive data of the groups allocated according to the demographic and disease-related characteristics features of the participants.

| Variables                              | Total n (%) | Remission n (%) | Low DA n (%) | Moderate-High DA n (%) |
|----------------------------------------|-------------|-----------------|--------------|------------------------|
| Gender- Female                          | 120 (83.9)  | 54 (80.6)       | 19 (79.2)    | 47 (90.4)              |
| -Male                                   | 23 (16.1)   | 13 (19.4)       | 5 (20.8)     | 5 (9.6)                |
| BMI - Normal                            | 45 (31.5)   | 26 (38.8)       | 5 (20.8)     | 14 (26.9)              |
| -Owerweight                             | 98 (68.5)   | 41 (61.2)       | 19 (79.2)    | 38 (73.1)              |
| Duration of disease (years)             | 41 (28.7)   | 18 (26.9)       | 6 (25.0)     | 17 (32.7)              |
| -Early stage (≤ 2 years)                | 102 (71.3)  | 49 (73.1)       | 18 (75.0)    | 35 (67.3)              |
| -Late stage (> 2 years)                 | 124 (86.7)  | 63 (94.0)       | 20 (83.3)    | 41 (78.8)              |
| Morning stiffness (sec) < 60 sec         | 19 (13.3)   | 4 (6.0)         | 4 (16.7)     | 11 (21.2)              |
| > 60 sec                                | 124 (86.7)  | 63 (94.0)       | 20 (83.3)    | 41 (78.8)              |
| Presence of deformity -Yes              | 49 (34.3)   | 17 (25.4)       | 9 (37.5)     | 23 (44.2)              |
| -No                                     | 94 (65.7)   | 50 (74.6)       | 15 (62.5)    | 29 (55.8)              |
| Presence of nodules -Yes                | 24 (16.8)   | 8 (11.9)        | 2 (8.3)      | 14 (26.9)              |
| -No                                     | 119 (83.2)  | 59 (88.1)       | 22 (91.7)    | 38 (73.1)              |
| Dry eye -Yes                            | 65 (45.5)   | 30 (44.8)       | 9 (37.5)     | 26 (50.0)              |
| -No                                     | 78 (54.5)   | 37 (55.2)       | 15 (62.5)    | 26 (50.0)              |
| Nail abnormalities -Yes                 | 39 (27.3)   | 18 (26.9)       | 6 (25.0)     | 15 (28.8)              |
| -No                                     | 104 (72.7)  | 49 (73.1)       | 18 (75.0)    | 37 (71.2)              |
| Raynaud's phenomenon -Yes               | 30 (21.0)   | 9 (13.4)        | 7 (29.2)     | 14 (26.9)              |
| -No                                     | 113 (79.0)  | 58 (86.6)       | 17 (70.8)    | 38 (73.1)              |
| Osteoporosis -Yes                       | 43 (30.1)   | 15 (22.4)       | 4 (16.7)     | 27 (51.9)              |
| -No                                     | 97 (67.8)   | 52 (77.6)       | 20 (83.3)    | 25 (48.1)              |
| Dyspnea at rest -Yes                    | 28 (19.6)   | 11 (16.4)       | 2 (8.3)      | 15 (28.8)              |
| -No                                     | 115 (80.4)  | 56 (83.6)       | 22 (91.7)    | 37 (71.2)              |
| Exertional dyspnea -Yes                 | 64 (44.8)   | 24 (35.8)       | 10 (41.7)    | 30 (57.7)              |
| -No                                     | 79 (55.2)   | 43 (64.2)       | 14 (58.3)    | 22 (42.3)              |

DA: Disease activity.
stiffness poses a 1.97, 1.64, 1.62, 1.56 and 0.53-fold higher risk for moderate-high disease activity compared to the remission, respectively. It was obtained that osteoporosis and dyspnea at rest poses a 1.52 and 1.40-fold higher risk for moderate-high disease activity compared to the remission, respectively. It was obtained that increased BMI in RA has an effect on many morbidity. Comparing normal and overweight RA patients, it was concluded that the rates of rheumatoid cachexia and osteopenia increased significantly in overweight patients [32]. High BMI with RA has been associated with worse scores in patients and has been reported to negatively affect treatment [33,34]. It has been reported that increased BMI in RA should be treated and the solution is not just to lose weight [35]. We think that better results can be obtained by doing diet programs and exercise applications together in controlling increased weight gain in individuals with RA.

Yazıcı, et al. reported that the duration of morning stiffness reflects functional limitations and increased pain scores [36]. While the duration of morning stiffness was found to be significantly associated with DAS28 in the study by Orange, et al. [37]; Boers, et al. reported a low correlation in their study [38]. In parallel with the literature, we have seen that the increase in disease activity in individuals with RA is effective on the duration of morning stiffness.

Although direct evidence is limited, there is evidence between disease activity, functional status, and radiographic damage, and persistent synovitis in the hands has been reported to be a parameter associated with erosive changes [39,40]. In their study with 62 RA patients, Karaçavuş, et al. found that patients with high DAS28 scores had more peripheral joint involvement (mean 11/8 joints) than the patients with low disease activity [41]. In our study, we have concluded that the presence of deformity in RA poses a risk for the active

| Variables | Remission and low disease activity | Remission and moderate-high disease activity | Low and moderate-high disease activity |
|-----------|---------------------------------|-------------------------------------------|--------------------------------------|
| Gender (Female/Male) | OR (95% CI) | p’ | OR (95% CI) | p’ | OR (95% CI) | p’ |
| BMI (Normal/Overweight) | 0.80 (0.39 - 1.63) | 0.537 | 1.12 (0.74 - 1.69) | 0.571 | 1.17 (0.86 - 1.56) | 0.310 |
| Duration of disease (Early stage/late stage) | 0.93 (0.34 - 2.06) | 0.859 | 1.66 (0.76 - 1.78) | 0.489 | 1.11 (0.82 - 1.52) | 0.497 |

OR: Odds Ratio, CI: Confidence Interval, *Pearson Chi-square test.
period of the disease. In order to obtain this result, there is a need for further investigation on which of the parameters used in the calculation of DAS28 (the number of swollen joints and/or the number of sensitive joints and/or patient’s general medical condition and/or CRP) is more effective.

From studies evaluating demographic and clinical characteristics in individuals with RA, Mota, et al. reported the presence of rheumatoid nodules 15.38% and Bal, et al. 3.2% [24,20]. Corbett, et al. and Mota, et al. have associated the increase in the incidence of rheumatoid nodules with the active period [24,42]. They reported that nodules were more common in severe RA and they tended to disappear with the regression of articular involvement [43]. While we determined the presence of nodules as 16.8% in our study, we obtained that the presence of nodules poses 1.62-fold higher risk for moderate-high disease activity compared to the remission, Bal, et al. declared eye involvement as 4.8% in their study examined demographic and clinical characteristics of patients with RA in Turkey; Mota, et al. noticed the symptoms of sikka as 13.84% [20,24]. We determined the dryness of the eyes as 45.5% in the sample group of our study.

The first case-controlled study to identify nail changes significantly related to the disease in RA was conducted by Michel, et al. In our study, we identified nail abnormalities as 27.3% in individuals with RA [44]. We believe that information on this subject is lacking in the literature and more research is needed.

RA is not frequently reported among the underlying causes of secondary Raynaud’s phenomenon; however, some studies have shown that the Raynaud’s phenomenon occurs much more in RA patients than thought [45]. Among the studies evaluating demographic and clinical characteristics features in individuals with RA, Mota, et al. found that 18.46% had a Raynaud’s phenomenon; Saraux, et al. found that 54 of 332 RA individuals (17.2%) had a Raynaud’s phenomenon [24,46]. When the patients with Raynaud’s phenomenon are examined, it is revealed that the RA rate is between 5 and 7% [46]. We have found the presence of Raynaud’s phenomenon in patients with RA at a high rate, such as 21.0%.

It has been reported that axial and appendicular bone loss starts from the first 6 months of RA. Clinical inflammation usually progresses with bone erosion, leading to functional limitations. Synovial osteoclastic formation results in bone erosion [47,48]. Osteoporosis is one of the major complications encountered in RA and there are studies reporting that individuals with RA have an increased risk of bone fracture in the literature [49-51]. According to the results of our study, osteoporosis is seen at 30.1% in RA. We obtained that the osteoporosis poses 1.97-fold higher risk for moderate-high disease activity compared to remission and poses 1.52-fold higher risk for moderate-high disease activity compared to low disease activity. It is known that the effect of physical activity is quite high in the prevention of osteoporosis [52]. The World Health Organization emphasizes that sufficient calcium and vitamin D, as well as strengthening exercises, are important for preventing osteoporosis [53]. It has been reported in the literature that exercise increases bone density, reduces the risk of fractures and significantly improves quality of life [54]. In addition to sunbathing and calcium supplementation, exercise is also recommended to prevent falls against osteoporosis, which is common in RA [55].

In a study by Doyle, et al. it was reported that 12% of individuals had hypoxia in lung involvement in RA [56]. People often avoid breathing-causing activities in order not to increase their symptom severity and maintain their current status. Fear of movement due to dyspnea leads to a decrease in physical activity levels and functional capacities, and not performing daily living activities. Zu Wallack and his colleagues defined the "dyspnoea-inactivity vicious circle" in their work [57]. In the systematic review conducted by Tierney, et al. It was found that physical activity level in RA patients was lower compared to healthy individuals [58]. According to the results of our study, dyspnea was the second parameter that posed the highest risk for the active period in RA.

Exercise therapy is recommended as a part of non-pharmacological treatment in rheumatic diseases [59]. In a review that examines the relationship between exercise and inflammation, exercise has been shown to produce anti-inflammatory responses, and positive adaptation to the muscles has been demonstrated if exercise is continued regularly [60,61]. It has been reported in the literature that exercise is effective in reducing the level of dyspnea and fatigue [62]. It has been shown that regular exercise increases aerobic capacity and physical fitness in RA patients [63,64]. In addition, exercise is recommended in RA treatment by being effective in coping with the disease [65,66].

**Conclusion**

In our study, it was observed that osteoporosis and dyspnea pose a high risk in the active period of RA. According to these results, we think that the risk of developing dyspnea and decrease in bone quality in RA individuals in the active period is high due to inactivity. Therefore, we suggest that RA patients should be encouraged to continue their physical activities and increase their participation in the exercise to reduce their complaints of dyspnea and osteoporosis. We also recommend that exercise be made a part of life and be done regularly.
Conflicts of Interest

The author reports no conflicts of interest in this work.

Author Contributions

EGK, UBA, and BBC designed the study. EGK and CK searched databases and performed the selection of studies; EGK and MT collected data; EGK and BBC analyzed the data; EGK, CK and BBC wrote the manuscript; UBA and VC contributed to writing and critically uprising the manuscript and approved the last version.

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