Arch Rheumatol 2020;35(x):i-xi
doi: 10.5606/ArchRheumatol.2020.7732

ORIGINAL ARTICLE

# Self-Reported Medication Adherence in Patients With Ankylosing Spondylitis: The Role of Illness Perception and Medication Beliefs

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***ABSTRACT***

**Objectives:** This study aims to investigate medication adherence in Turkish patients with ankylosing spondylitis (AS) and analyze the related factors for non-adherence.

**Patients and methods:** Ninety-nine patients with AS (60 males, 39 females; mean age 41.3±8.4 years; range, 18 to 66 years) were included in the study. Sociodemographic and clinical data were collected. Disease activity (Bath Ankylosing Spondylitis Disease Activity Index, C-reactive protein, and erythrocyte sedimentation rate), functional status (Bath Ankylosing Spondylitis Functional Index), spinal pain and fatigue (visual analog scale), quality of life (Ankylosing Spondylitis Quality of Life), and depression and anxiety (Hospital Anxiety and Depression Scale) were evaluated. Adherence to anti-rheumatic drugs was elicited using the Compliance Questionnaire on Rheumatology (CQR). Medication beliefs were assessed using the Beliefs about Medicines Questionnaire (BMQ), and illness perception using the Brief Illness Perception Questionnaire (B-IPQ).

**Results:** Non-adherence was reported in 64 patients (64.6%). No significant relationship between demographic, clinical, or psychological factors and adherence was found, except for disease duration (p=0.031). High B-IPQ treatment follow-up, illness coherence, and BMQ-Specific necessity scores were associated with good adherence (p=0.007, p=0.039, and p=0.002, respectively). BMQ-General overuse and harm scores showed an inverse correlation with the CQR score (p=0.005 r=-0.278; p=0.029 r=-0.219, respectively). Longer disease duration [odds ratio (OR): 0.98, 95% confidence interval (CI): 0.97-0.99] and higher B-IPQ item-1 score regarding the effect of the illness on the individual's life (OR: 0.58, 95% CI: 0.42-0.81) were important predictors of low adherence.

**Conclusion:** Nearly three out of five AS patients were identified as at risk for non-adherence with the CQR. Medication adherence is influenced by the patient's beliefs about medicines and illness perceptions, and these may be key targets for future interventions to improve medication adherence.

***Keywords:*** Ankylosing spondylitis, beliefs about medicines, illness perception, medication adherence.

Ankylosing spondylitis (AS) is a chronic inflammatory rheumatic disease that mainly affects the sacroiliac joints as well as spine and eventually causes deformity and ankyloses of the spine and joints. Delay in diagnosis or inadequate disease management lead to a limitation of chest expansion, irreversible restriction of spinal mobility, and deterioration of physical functions.[1] AS typically affects people at the most productive time in their lives. Pain, morning stiffness, and functional impairment reduce the quality of life (QoL) and decrease the ability to perform normal

***Received:*** July 22, 2019 ***Accepted:*** November 14, 2019 ***Published online:*** February 07, 2020

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***Citation:***
Tolu S, Rezvani A, Karacan İ, Bugdaycı D, Küçük HC, Bucak ÖF, et al. Self-Reported Medication Adherence in Patients With Ankylosing Spondylitis: The Role of Illness Perception and Medication Beliefs. Arch Rheumatol 2020;35(x):i-xi.

occupational activities, resulting in considerable socioeconomic burden for patients and society.[2] Non-steroidal anti-inflammatory drugs (NSAIDs) in combination with patient education and regular exercise are recommended as the first-line treatment for AS. When conventional treatment has been of limited benefit, biologics have emerged as a highly effective treatment in reducing disease activity and improving function and QoL.[1]

Adherence is defined by the World Health Organization (WHO) as "the degree to which the person's behavior corresponds with the agreed recommendations from a healthcare provider".[3] Adherence is the most important factor that is closely linked with treatment outcomes. Also, poor adherence poses a significant economic burden on healthcare costs worldwide.[4] Of all medication-related hospitalizations in the United States, around one-third to two-thirds are the result of poor medication adherence.[5] There is no gold standard method for monitoring patients' compliance with drug regimens. Direct methods such as the measurement of drug concentrations or metabolites in the blood, serum or urine are very costly, and indirect methods such as the analysis of administrative databases (prescriptions, rate of prescription refills); pill counts; electronic medication monitors; and self-reported measures by the patient (questionnaires, diaries, interviews) may not be feasible on an everyday basis.[6,7]

Adherence for rheumatic diseases is influenced by many factors, including illness perception, beliefs about the necessity of medicines, and concerns about their potential adverse effects. Illness perceptions are cognitive and emotional representations or beliefs that patients have about their illnesses. Each patient has their own preconceptions about the identity, cause, timeline or the consequences of the illness and beliefs about its treatment and controllability.[8,9] Beliefs about medicines and illness perception were shown to predict adherence more strongly than sociodemographic or clinical factors.[10,11]

The risks for non-adherence in rheumatic diseases such as rheumatoid arthritis (RA), AS, psoriatic arthritis (PsA), systemic sclerosis (SSc), juvenile idiopathic arthritis, and systemic lupus erythematosus have been investigated in several studies.[6,8,10-14] For AS, medication adherence has been shown to be associated with older age, white race, illness perception, beliefs about medication, QoL, choice of drugs and route of administration.[10,12-14] To the best of our knowledge, no studies have assessed medication adherence and analyzed related factors for non-adherence in patients with AS in Turkey. Therefore, in this study, we aimed to investigate medication adherence in Turkish patients with ankylosing spondylitis (AS) and analyze the related factors for non-adherence.

## PATIENTS AND METHODS

A total of 99 patients with AS (60 males, 39 females; mean age 41.3±8.4 years; range 18 to 66 years) at Bezmialem Vakıf University, Physical Medicine and Rehabilitation outpatient clinic were included in the study between September 2017 and March 2018. Patients who were diagnosed as having AS using the 1984 modified New York Classification Criteria[15] for at least six months were enrolled for analysis if they were treated with at least one conventional and/or biologic therapy, including any NSAID, conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs), and/or tumor necrosis factor-alpha (TNF-α) inhibitor therapy. The sample size was determined pragmatically with all patients agreeing to be involved in the study over the six-month period. The exclusion criteria were as follows: *(i)* age <18 years, *(ii)* any diagnosis of psychiatric disorders and receiving psychiatric treatments and cognitive dysfunctions, *(iii)* patients who were not taking any medication or were lost to follow-up (defined as not visiting a rheumatologist in the last 18 months), *(iv)* inability to read and understand the questionnaires, and *(v)* patients with any significant comorbidity (e.g., advanced cancer, stroke). The study protocol was approved by the Bezmialem Vakıf University Ethics Committee (54022451-050.05.04). A written informed consent was obtained from each patient. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Demographic characteristics such as age, sex, marital and working status, years of education, and medical comorbidities were provided by the patient. Disease characteristics including current use of anti-rheumatic medications, duration of disease, and morning stiffness were noted.

Disease activity was evaluated using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) concentration.[16] For BASDAI, a cut-off score of ≥4 indicates active disease. Physical functions were assessed using the Bath Ankylosing Spondylitis Functional Index (BASFI).[17] Spinal pain and fatigue were scored using a visual analog scale (VAS, 0-10 cm). The Ankylosing Spondylitis Quality of Life (ASQoL) questionnaire was used for the assessment of disease-related QoL in patients with AS.[18] The Hospital Anxiety and Depression Scale was used for the assessment of depression and anxiety symptoms.[19]

Self-reported questionnaires were used to evaluate medication adherence and the potential associated factors for non adherence to anti-rheumatic drug therapy. The Compliance Questionnaire on Rheumatology (CQR) is the only questionnaire validated to measure treatment adherence in patients with rheumatic diseases. This 19-item questionnaire measures patients' agreement with certain statements through a four-point Likert scale, ranging from "strongly disagree" (scored as 1) to "strongly agree" (scored as 4). Final scores range from 0 (no adherence) to 100 (perfect adherence).[20] The patients were grouped as adherent and non-adherent using a cut-off score of 80% according to previous studies.[12,21] The CQR has been translated and validated in Turkish.[22]

Patients' illness perceptions were measured using the Brief Illness Perception Questionnaire (B-IPQ), which explores the cognitive and emotional aspects of illness across eight items using a 0 to 10 scale and an additional item, which investigates the causal factors. The first five items form the questions on cognitive illness representations, namely, consequences (how much does your illness affect your life?), timeline (how long do you think your illness will continue?), personal control (how much control do you feel you have over your illness?), treatment control (how much do you think your treatment can help your illness?), and identity (how much do you experience symptoms from your illness?). Two of the items form the emotional illness perceptions, namely, concern (how concerned are you about your illness?) and emotions (how much does your illness affect you emotionally?). One item assesses illness coherence. In the last item, the assessment of the causal representation is through an open-ended response that asks patients to list the most important causal factors of their illness. A higher score reflects that a patient feels more threatened by the illness.[23,24]

Treatment beliefs were assessed using the Turkish version of the Beliefs about Medicines Questionnaire (BMQ). The BMQ is an 18-item questionnaire with four scales: the BMQ Specific-necessity (patients' beliefs about the necessity of the prescribed medication for controlling their illness), the BMQ Specific-concerns (patients' concerns about the potential adverse effects of taking medication), the BMQ General-overuse (scoring the statement that medicine is overused), and the BMQ General-harm (scoring beliefs that medication is harmful and poisonous). Each item is scored on a five-point Likert scale (1=strongly disagree; 5=strongly agree), and higher scores emphasize stronger beliefs. A necessity-concerns differential (necessity beliefs) is calculated as the difference between the necessity and the concern scales. This differential can be thought of as an indicator of how the individual judges their personal need for the treatment relative to their concerns about taking medicine.[25,26]

**Statistical analysis**

Data were analyzed using the IBM SPSS for Windows version 23.0 software (IBM Corp. Armonk, NY, USA). The Shapiro-Wilk test was used to evaluate the normality of data. Frequency, percentage, mean, median, standard deviation, and interquartile range (IQR) were used for descriptive statistics. For two-group comparisons (adherent vs. non-adherent), we used the Chi-square test for categorical variables, the independent-sample t-test for continuous data if normal distribution of variables existed, and the Mann-Whitney U test in other cases. Correlations were evaluated using Spearman's rank correlation analyses. A $p$ value of $<0.05$ was considered statistically significant. Multivariate logistic regression analysis was performed to determine risk factors for adherence. The $p$ value for a factor to be included in the regression model was 0.05 using the forward conditional method, and the p value for exclusion was 0.1. Suitability of the regression model was reviewed with

**Table 1.** Demographic and clinical characteristics of patients with ankylosing spondylitis subdivided according to adherence rate (≤80% and >80%)

| | Whole sample (n=99) | | | | | Non-adherent (CQR score ≤80%) (n=64) | | | | | Adherent (CQR score >80%) (n=35) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | n | % | Mean±SD | Median | IQR | n | % | Mean±SD | Median | IQR | n | % | Mean±SD | Median | IQR | *p* |
| Age (year) | | | 41.3±8.4 | | | | | 40.1±7.9 | | | | | 43.5±8.9 | | | 0.054* |
| Sex | | | | | | | | | | | | | | | | 0.341† |
| Male | 60 | 60.6 | | | | 41 | 64.1 | | | | 19 | 54.3 | | | | |
| Single/divorced | 23 | 23.2 | | | | 15 | 23.4 | | | | 8 | 22.9 | | | | 0.948† |
| Working status | | | | | | | | | | | | | | | | 0.281† |
| Have regular job | 61 | 61.6 | | | | 43 | 67.2 | | | | 18 | 51.4 | | | | |
| Unemployed | 28 | 28.3 | | | | 16 | 25.0 | | | | 12 | 34.3 | | | | |
| Retired\left work due to illness | 10 | 10.1 | | | | 5 | 7.8 | | | | 5 | 14.3 | | | | |
| Years of education | | | | | | | | | | | | | | | | 0.990† |
| ≤8 years | 51 | 51.5 | | | | 33 | 51.6 | | | | 18 | 51.4 | | | | |
| >8 years | 48 | 48.5 | | | | 31 | 48.4 | | | | 17 | 48.6 | | | | |
| Comorbidities | 40 | 40.4 | | | | 23 | 35.9 | | | | 17 | 48.6 | | | | 0.221† |
| Disease duration (month) | | | | 96 | 72-144 | | | 120 | 72-168 | | | | | 84 | 72-110 | 0.031‡ |
| Patients currently taking AS-related drugs by category | | | | | | | | | | | | | | | | 0.072† |
| NSAID monotherapy | 32 | 32.3 | | | | 24 | 37.5 | | | | 8 | 22.9 | | | | |
| csDMARD monotherapy | 6 | 6.1 | | | | 5 | 7.8 | | | | 1 | 2.9 | | | | |
| TNF-α inhibitor monotherapy | 36 | 36.4 | | | | 17 | 26.6 | | | | 19 | 54.3 | | | | |
| NSAID-csDMARD combination | 18 | 18.2 | | | | 12 | 18.8 | | | | 6 | 17.1 | | | | |
| TNF-α inhibitor-NSAID combination | 7 | 7.1 | | | | 6 | 9.4 | | | | 1 | 2.9 | | | | |
| Erythrocyte sedimentation rate (mm/h) | | | | 11 | 5-16 | | | | 11 | 5-15 | | | | 11 | 5-22 | 0.654‡ |
| C-reactive protein (mg/L) | | | | 0.31 | 0.07-0.82 | | | | 0.29 | 0.08-0.74 | | | | 0.42 | 0.04-1.83 | 0.260‡ |
| BASDAI (0-10 cm) | | | | 3.05 | 1.45-4.42 | | | | 3.21 | 1.69-4.40 | | | | 2.85 | 0.82-4.45 | 0.394‡ |
| BASDAI ≥4 | 31 | 31.3 | | | | 20 | 31.3 | | | | 11 | 31.4 | | | | 0.985† |
| BASFI (0-10 cm) | | | | 1.80 | 0.40-4.0 | | | | 2.10 | 0.50-3.87 | | | | 1.0 | 0.30-4.04 | 0.484‡ |
| BASFI ≥4 | 25 | 25.3 | | | | 15 | 23.4 | | | | 10 | 28.6 | | | | 0.574† |
| Morning stiffness (second) | | | | 15 | 0-30 | | | | 17.50 | 0-30 | | | | 15.0 | 0-30 | 0.757‡ |
| Spinal pain (0-10 VAS) | | | | 3 | 1.5-6 | | | | 3 | 2-6 | | | | 3 | 1-6 | 0.340‡ |
| Fatigue (0-10 VAS) | | | | 3 | 1-6 | | | | 4 | 2-6 | | | | 3 | 1-6 | 0.197‡ |
| ASQoL | | | | 6 | 3-10 | | | | 5 | 3-9.75 | | | | 7 | 2-13 | 0.689‡ |

CQR: Compliance Questionnaire on Rheumatology; SD: Standard deviation; IQR: Interquartile range; AS: Ankylosing spondylitis; NSAID: Non-steroid anti-inflammatory drug; csDMARD: Conventional synthetic disease-modifying anti-rheumatic drug; TNF-α: Tumor necrosis factor alpha; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; VAS: Visual analog scale; ASQoL: Ankylosing Spondylitis Quality of Life; * Independent-sample t-test; † Chi-square tests; ‡ Mann-Whitney U test; $p<0.05$ was considered statistically significant.

**Table 2.** Psychological factors of patients with ankylosing spondylitis subdivided according to adherence rate (≤80% and >80%)

| | Whole sample (n=99) | | | Non-adherent (CQR score ≤80%) (n=64) | | | Adherent (CQR score >80%) (n=35) | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Mean±SD | Median | IQR | Mean±SD | Median | IQR | Mean±SD | Median | IQR | *p* |
| Variable | | | | | | | | | | |
| HAD-Anxiety | 7.8±4.6 | | | 8.0±4.3 | | | 7.5±5.1 | | | 0.626* |
| HAD-Depression | | 5 | 3-9 | | 6 | 3-9 | | 5 | 3-9 | 0.837† |
| HAD-Total | 13.9±8.2 | | | 14.0±7.6 | | | 13.6±9.3 | | | 0.844* |
| B-IPQ | | | | | | | | | | |
| Consequences | | 4 | 2-7 | | 4.5 | 3-7.75 | | 4 | 2-6 | 0.196† |
| Timeline | | 10 | 9-10 | | 10 | 8-10 | | 10 | 10-10 | 0.185† |
| Personal control | | 5 | 3-7 | | 5 | 3-7 | | 5 | 3-8 | 0.255† |
| Treatment control | | 8 | 5-10 | | 7 | 5-9 | | 9 | 7-10 | 0.007† |
| Identity | | 5 | 3-8 | | 5 | 3-8 | | 5 | 3-7 | 0.671† |
| Understanding, concern | | 6 | 4-9 | | 6 | 4.25-8.75 | | 5 | 4-10 | 0.935† |
| Illness coherence | | 10 | 8-10 | | 10 | 8-10 | | 10 | 10-10 | 0.039† |
| Emotions | | 7 | 3-9 | | 6 | 3-8 | | 8 | 3-10 | 0.276† |
| B-IPQ total | 52.1±11.5 | | | 51.0±11.8 | | | 54.0±10.9 | | | 0.209* |
| BMQ-Specific | | | | | | | | | | |
| Concerns | 3.2±0.8 | | | 3.2±0.8 | | | 3.2±0.8 | | | 0.658* |
| Necessity | | 4 | 3.4-4.6 | | 3.80 | 3.20-4.20 | | 4.20 | 3.80-4.60 | 0.002† |
| Necessity beliefs (necessity-concern differential) | | 0.68 | -2.40-3.60 | | 0.40 | 0-1.2 | | 1.0 | 0.40-1.40 | 0.020† |
| BMQ-General | | | | | | | | | | |
| Overuse | | 2.5 | 2.25-3.0 | | 2.75 | 2.25-3.25 | | 2.50 | -2.75 | 0.003† |
| Harm | | 2.5 | 2-3.25 | | 2.75 | 2.25-3.25 | | 2.50 | 2-3 | 0.151† |
| BMQ-Total | 3.1±0.5 | | | 3.1±0.5 | | | 3.2±0.5 | | | 0.437* |

CQR: Compliance Questionnaire on Rheumatology; SD: Standard deviation; IQR: Interquartile range; HAD: Hospital Anxiety and Depression Scale; B-IPQ: Brief Illness Perception Questionnaire; BMQ: Beliefs about Medicines Questionnaire; * Independent-sample t-test, † Mann-Whitney U test; $p<0.05$ was considered statistically significant.

the Hosmer-Lemeshow test. The regression model was considered statistically suitable if the *p* value found with the Hosmer-Lemeshow test was <0.05. The 95% confidence intervals (CIs) were calculated for the odds ratios (ORs) [Exp(B)]. Wald statistical analysis was conducted to determine the significance of coefficient B.

## RESULTS

The median (IQR) disease duration was 96 months (range, 72-144 months). Median (IQR) BASDAI was 3.05 (range, 1.45-4.42), and BASFI (IQR) was 1.80 (range, 0.40-4.0). Of the patients with AS, 32 (32.3%) used NSAID monotherapy, and 36 (36.4%) used TNF-α inhibitor monotherapy. There were no significant differences between the adherent and non-adherent groups in terms of demographic and clinical characteristics, and only disease duration was significantly longer in the non-adherent group (p=0.031). The proportion of non-adherence in younger patients (aged ≤40 years; 69.4%) was nearly the same as that recorded in patients aged >40 years (60%). The demographic and clinical characteristics of patients with AS are presented in Table 1.

Sixty-four patients (64.6%) were considered as non-adherent (CQR score ≤80%), 35 patients (35.4%) were considered as adherent (CQR score >80%). The mean CQR score was 73.59 (range, 21.05-92.98). The results from the HAD, B-IPQ, and BMQ are shown in Table 2.

Treatment control and illness coherence dimension scores of B-IPQ were significantly higher in the adherent group (p=0.007, p=0.039, respectively). BMQ-Specific necessity and necessity beliefs scores were significantly higher in the adherent group (p=0.002, p=0.020, respectively). BMQ-General overuse score was significantly higher in the non-adherent group (p=0.003).

Table 3 shows the correlation analyses between the CQR and B-IPQ dimensions. The CQR score was positively correlated with treatment control (r=0.285, p=0.004), illness coherence (r=0.239, p=0.017), emotions dimension (r=0.214, p=0.033), and total B-IPQ scores (r=0.246, p=0.014).

Table 4 demonstrates the correlation analyses between the CQR and demographics, disease,

**Table 3.** Correlation coefficients between Compliance Questionnaire on Rheumatology and Brief Illness Perception Questionnaire subscales

| B-IPQ | CQR score |
|---|---|
| Consequences | 0.042 |
| Timeline | 0.157 |
| Personal control | 0.034 |
| Treatment control | 0.285* |
| Identity | 0.127 |
| Understanding, concern | 0.097 |
| Illness coherence | 0.239** |
| Emotions | 0.214** |
| Total score | 0.246** |

B-IPQ: Brief Illness Perception Questionnaire; CQR: Compliance Questionnaire on Rheumatology; * Correlation is significant at 0.05 level; ** Correlation is significant at 0.01 level.

**Table 4.** Correlation coefficients between Compliance Questionnaire on Rheumatology and demographic, clinical and psychological variables of patients with ankylosing spondylitis

| Variables | CQR score |
|---|---|
| Age (year) | 0.191 |
| Disease duration (months) | -0.131 |
| C-reactive protein (mg/L) | 0.229* |
| Erythrocyte sedimentation rate (mm/h) | 0.031 |
| BASDAI | 0.051 |
| BASFI | 0.147 |
| Morning stiffness (second) | 0.105 |
| Spinal pain (0-10 VAS) | 0.016 |
| Fatigue (0-10 VAS) | -0.016 |
| BMQ-Spesific concerns | 0.103 |
| BMQ-spesific necessity | 0.508** |
| BMQ-General overuse | -0.278** |
| BMQ-General harm | -0.219* |
| BMQ-Total | 0.148 |
| HAD-Anxiety | 0.033 |
| HAD-Depression | 0.041 |
| HAD-Total | 0.041 |
| ASQoL | 0.157 |

CQR: Compliance Questionnaire on Rheumatology; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; VAS: Visual analog scale; BMQ: Beliefs about Medicines Questionnaire; HAD: Hospital Anxiety and Depression Scale; ASQoL: Ankylosing Spondylitis Quality of Life; * Correlation is significant at 0.05 level; ** Correlation is significant at 0.01 level.

**Table 5.** Regression model for medication adherence

| | | | | | 95% CI for EXP(B) | |
|---|---|---|---|---|---|---|
| | Wald | df | *p* | Exp(B) | Lower | Upper |
| Age (year) | 7.1 | 1 | 0.008 | 1.10 | 1.03 | 1.18 |
| Disease duration (month) | 8.0 | 1 | 0.005 | 0.98 | 0.97 | 0.99 |
| CRP (mg/L) | 4.7 | 1 | 0.031 | 1.81 | 1.06 | 3.11 |
| BMQ-Specific necessity | 4.6 | 1 | 0.033 | 2.50 | 1.08 | 5.77 |
| B-IPQ total | 7.1 | 1 | 0.008 | 1.12 | 1.03 | 1.22 |
| B-IPQ item-1 consequences | 10.7 | 1 | 0.001 | 0.58 | 0.42 | 0.81 |
| Constant | 14.6 | 1 | 0.000 | 0.00 | | |

df: Degrees of freedom; CI: Confidence interval; Exp(B): Odds ratio; CRP: C-reactive protein; BMQ: Beliefs about Medicines Questionnaire; B-IPQ: Brief Illness Perception Questionnaire.

and mental health-related factors of patients with AS. The CQR score was positively correlated with CRP concentrations and BMQ-Specific necessity scores (r=0.229, p=0.023; r=0.508, p<0.001). BMQ-General overuse and harm scores showed an inverse correlation with the CQR score (r=-0.278, p=0.005; r=-0.219, p=0.029).

The multivariable regression analysis revealed that age, disease duration, CRP, medication beliefs (BMQ-Specific necessity score) and illness perception [score for B-IPQ item-1 (consequences) and B-IPQ total] were the important predictors of medication adherence (Nagelkerke R2=0.458, Hosmer-Lemeshow test p=0.971). Older age (OR: 1.10, 95% CI: 1.03-1.18), elevated CRP (OR: 1.81, 95% CI: 1.06-3.11), higher illness perception (OR: 1.12, 95% CI: 1.03-1.22) and belief in the necessity of medications (OR: 2.50, 95% CI: 1.08-5.77) were significantly associated with better treatment adherence. Longer disease duration (OR: 0.98, 95% CI: 0.97-0.99) and higher B-IPQ item-1 score regarding the effect of the illness on the individual's life (OR: 0.58, 95% CI: 0.42-0.81) were important predictors of low adherence (Table 5). Illness perception and beliefs about medications may be regarded as important targets in efforts to improve treatment adherence.

## DISCUSSION

Medication adherence is a primary determinant of treatment success. Numerous studies have been performed on various auto-immune rheumatic diseases in recent years to assess rates of medication adherence and factors that potentially influence these rates.[6,10-14,21] To the best of our knowledge, this is the first cross-sectional study in Turkey to evaluate medication adherence in patients with AS and analyze the relationship with patient, disease and mental-health related factors.

The reported rates of adherence varied widely from 9.3 to 94% with results depending on the rheumatic disease and methodology used for estimating medication adherence.[11] In a systematic literature review, there were the same wide variations with reported adherence in AS between 4.12% and 85.2%.[11] In our study, the adherence rate to anti-rheumatic drugs was 35.3% according to the CQR. The measurement of adherence to pharmacologic treatment may be evaluated in several methods, though each has its own advantages and disadvantages. Self-questionnaires, as an indirect method, have the advantage of being an easy, cheap, and quick method.[11] Currently, the only self-reported questionnaire for assessing the compliance of patients with the rheumatic disease is the CQR.[22] In a study of patients with AS, it was reported that 38.3% of patients complied with biologic agent therapy, as measured using the CQR.[12]

Adherence is a dynamic process that changes over time and is influenced by many different factors. The WHO published an overview of adherence issues and recommended a hand model for improving treatment adherence in a variety of conditions needing long-term therapies. In this model, there were five domains, including patient, therapy, mental health, health system, and socioeconomic-related factors.[27]

Having an understanding of the complex problems that affect compliance and making recommendations to solve them could help to increase medication adherence in patients. Some modifiable factors such as frequency of dosing, route of administration, anxiety and depression, disease-related patient knowledge, and beliefs about medicines were reported to be efficient in improving medication adherence.[28] In the present study, we identified the patient, disease, and mental health-related factors in patients with AS. Although patient demographic factors such as sex, education level, marital and working status were found significantly associated with good or poor adherence, older patients were more likely to be adherent. Previous studies reported that older patients with rheumatic disease presented higher compliance with medication, and non-adherence behavior or reduced persistence over time occurred more often in the younger population.[27,29,30] It was hypothesized that busier lifestyle and more focus on professional and social life than on illness might be the possible reasons for poorer treatment adherence among younger patients.[30] On the other hand, some studies reported no association between drug adherence and age.[10,12,13]

At present, few studies have addressed illness perceptions among patients with AS. In our study, only two variables of B-IPQ, 'treatment control' and 'illness coherence' dimension scores, were found significantly higher in patients with good adherence and positively correlated with CQR score. High scores on the treatment control and coherence dimensions represent positive beliefs about the controllability of the illness, trust in the treatment, and a personal understanding of the disease. This means that only patients who self-reported a good understanding of AS and its treatment to control their disease demonstrated good adherence behavior. For patients with RA, increased perception of treatment control was shown as an independent predictor of increased adherence to treatment.[31,32] Morgan et al.[31] stated that patients with RA with established disease realized of the cyclical nature of the disease had a high level of illness coherence, and adopted a large number of coping strategies. They also thought that the extensive experience might have made these patients keep taking medication even when they felt better.

In the present study, the B-IPQ 'emotions' dimension score, indicating the emotional impact of illness on the patient, was positively correlated with the CQR score but was not significantly different between the adherent and non-adherent groups. By contrast, Smolen et al.[10] reported a significant association between higher emotional responses and poor medication adherence in patients with AS. Suh et al.[33] also showed that greater emotional responses to RA encouraged non-adherence to medications. Consequently, holding positive illness perceptions may decrease distress and predict good adherence in these circumstances.

Our new finding was that perceiving AS as having greater consequences on the patient's life (higher B-IPQ consequences score) encouraged non-adherence to medications. On the other hand, higher total illness perception score reflecting that a patient feels more threatened by AS was associated with better adherence. Similarly, Dalbeth et al.[34] reported that adherence to urate-lowering therapy was inversely associated with perceived consequences of disease in patients with gout. Patients with AS may worry about the more severe forms of the disease leading to limited neck movement, increased stiffness of the entire spine, loss of normal posture and development of thoracic kyphosis. Therefore, the patient education individually tailored to the patient's specific needs and priorities (such as medication, pain, fatigue, activity, work, and prognosis) may improve the understanding of their illness and improve adherence.

Patients undertake a cost benefit analysis about both the necessity of medications for maintaining health and the potential adverse effects of taking them. Positive and increased beliefs in medication necessity were more consistently associated with good adherence and may also offer greater predictability than any other demographic or clinical factors.[10,33,35,36] In the present study, higher BMQ-Specific necessity and necessity beliefs score were associated with good adherence. In rheumatic diseases, high necessity has been generally related to high adherence and great concerns to low adherence.[10,11,31] A large cross-sectional study found that highly adherent patients with RA, PsA, and AS had higher necessity scores.[10] Similarly, it was proved that highly adherent patients with SSc had higher

necessity beliefs scores.[35] Therefore, patient education on the pathophysiology of disease and the mechanism of action of therapeutics may be a good strategy to improve treatment adherence of patients with low necessity beliefs.

High BMQ-General overuse scores were significantly associated with non-adherence in our patients. Both BMQ-General overuse and harm scores were also negatively correlated with CQR score. In a previous study with RA, AS, and PsA, adherence was reported to be highest for patients with low treatment harm beliefs or concerns.[10] A possible explanation might be that general beliefs are most relevant when new and unfamiliar treatment is prescribed. Their influence may be diminished when patients become more familiar with their treatment and are informed by trusted healthcare professionals.

Disease-related factors (e.g., disease duration and activity, functional disability and comorbidities, health-related QoL) being consistently associated with adherence have been extensively investigated. Laboratory parameters and disease activity indexes are used for assessing the severity of rheumatic diseases and can be potentially used for adherence screening. The relationship between adherence and disease activity can be bidirectional because disease activity could be both the cause and result of adherence behavior. In the present study, CRP, ESR, and BASDAI were used for assessing disease activity. We found no association between BASDAI and adherence, but CRP concentrations were positively correlated with CQR scores and elevated CRP was significantly associated with better treatment adherence. Morning stiffness, spinal pain, and fatigue levels also had no apparent influence on adherence; however, we found that disease duration was significantly longer in non-adherent patients and longer disease duration increased the risk of low adherence. Arturi et al.[13] noted that neither disease duration nor disease activity (using BASDAI) nor functional disability (using BASFI) was associated with adherence in AS. Similarly, Smolen et al.[10] found no disease and medication-related factors across patients with RA, AS, and PsA. However, some previous studies on patients with RA found a negative association between disease duration, disease activity, and medication adherence.[31] This may be explained by the beliefs about the disease progression despite the treatment and having strong views that the long-lasting nature of the rheumatic diseases would not improve over time.

Patients with rheumatic diseases use complex treatment regimens. The relationship between therapy-related factors and adherence has been investigated in many studies.[10,11,13,14,21,29-33] Anghel et al.[11] reported that medication adherence was related to taking fewer medicines and the type of medication used. Our findings revealed no differences between treatment regimens, but the highest rate of adherence was obtained from the group taking the TNF-α inhibitor monotherapy. Although Arturi et al.[13] found no differences between patients receiving biologics and non-biologics, Smolen et al.[10] showed that TNF-α inhibitor monotherapy or in combination with csDMARDs had the highest predicted probability of good adherence in patients with AS. The reason for a higher observed adherence to TNF-α inhibitor therapy could be explained by the favorable balance between perceptions of treatment necessity versus concerns about adverse effects.[10,11,32] This might also be related to the route of administration, dosing frequency, and enthusiasm toward feeling better, alleviating severe pain and morning stiffness, as well as the expectation of stopping the disease progression and increasing long-term health-related QoL.[32,37] Administration route was one of the common factors reported as a cause of non-adherence; previous studies supported that self-injectable subcutaneous forms of TNF-α inhibitor drugs were effective and well-tolerated and increased the adherence behavior due to the ease of administration.[11,37,38] Therefore, it is recommended that biologic drugs should be prescribed for carefully selected patients without delay if first-line treatments can inadequately control disease activity.[1,2]

This study has some limitations. Firstly, the sample size was too small to find significant correlations with other risk factors. Future studies with increased patient numbers are needed to determine the factors affecting medication adherence. Secondly, although self-reported questionnaires for adherence are the most commonly used method, this method may lead to overestimation of adherence as compared with direct methods because patients may not admit to non-adherence in order to avoid the

disappointment or anger of their physician. Therefore, a combination of different methods, such as pill count, medication monitoring system, or pharmacy claims data may be useful to evaluate accurate medication adherence. Thirdly, we only enrolled the patients receiving subcutaneous TNF-α inhibitor drugs. Patients receiving intravenous TNF-α inhibitor or oral Janus kinase inhibitor treatments were not included. Finally, no evaluation was performed regarding age at diagnosis, drug experiences (drug-related adverse events, length of treatment, and changing of medical treatment), socio-economic (cost of treatment, social support, type of health insurance, socioeconomic status), and health system-related factors (quality of patient-physician relationship, understand/lack of medical instructions).

In conclusion, we found a low medication adherence rate in patients with AS. We detected that medication adherence in Turkish patients with AS was a product of greater belief in the necessity of medication and perceptions of treatment control and illness coherence. Also, less beliefs in the overuse and harm of medication seem to be related to good adherence. Before the beginning of medical treatment, beliefs about medication and illness perception can be checked to anticipate adherence behavior. Patients with low scores should be educated about the disease and importance of current medication for improving subsequent clinical outcomes.

**Declaration of conflicting interests**

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

**Funding**

The authors received no financial support for the research and/or authorship of this article.

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