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Disease control and its associated factors in outpatients with rheumatoid arthritis

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ABSTRACT

The present study aimed to evaluate disease activity and explore the factors associated with poor disease control among patients with rheumatoid arthritis (RA). This cross-sectional study was conducted at outpatient rheumatology clinics in two teaching hospitals in Jordan. Medication adherence was assessed using the validated five-item compliance questionnaire for rheumatology, and disease activity was assessed using the clinical disease activity Index score. Ordinal regression was performed to explore the factors associated with uncontrolled RA. Most of the participants (n=261) demonstrated moderate to high disease activity (71.2%). Seronegative RA (B=-0.882, CI [-1.584/-0.180], p<0.05) was significantly associated with lower disease activity, while medication non-adherence was significantly associated with poor RA control (B=1.023, CI [0.289-1.756], p<0.01). Future research should explore the factors associated with medication non-adherence. These factors should be targeted in future interventions to improve RA control, particularly in patients who suffer from high disease severity.

Keywords: disease activity, disease control, medication adherence, rheumatoid arthritis, Jordan

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by persistent synovitis, systemic inflammation, and autoantibodies. It initially appears as a symmetrical swelling and tender joints in the hands and/or feet and may include extra-articular manifestations [1]. Disease activity is one of the critical parameters that rheumatologists use to determine the extent of disease control and the modifications required on the therapeutic regimen during patient monitoring. Several methods have been developed to measure RA disease activity in terms of a disease activity score. The most frequently used scores for the estimation of RA disease activity are the disease activity score in 28 joints (DAS28) [2], the simplified disease activity index (SDAI), and the clinical disease activity index (CDAI) [3]. Utilizing these scores allowed the rheumatologists to categorize the status of RA disease into remission, low, moderate, or high disease activity [3, 4]. Since there is no cure for RA, the European league against rheumatism (EULAR) guidelines recommend that therapy with disease modifying anti-rheumatic drugs (DMARDs) should be initiated as soon as the diagnosis of RA is confirmed, preferably within the first three months of symptoms onset, to reach a target of sustained remission or low disease activity in RA patients [5]. Uncontrolled RA was associated with permanent joint deformities, functional disability, poor health-related quality of life (HRQOL), and several other complications [6]. Poor disease control among patients with RA has been reported in earlier studies [7-9]. However, the current study is the first one, which evaluated RA control and explored the factors associated with poor disease management among patients with RA in Jordan. The study findings could be utilized in future interventions to improve RA control and health outcomes in patients with RA.

MATERIALS AND METHODS

Study Design and Settings

The current cross-sectional study was conducted on patients with RA who attended the outpatient rheumatology clinic at King Abdullah University Hospital (KAUH) and Prince Basma Educational Hospital in Irbid/Jordan from February to October 2021.

Patients 18 years or older who had a verified diagnosis of RA for at least four months and received at least one DMARD for four months or more were eligible to participate in the study.

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Patients who had cognitive impairment and those who did not complete the questionnaire were excluded from the study.

The participation was voluntary, and the participants were informed that the study was conducted for research purposes. The participants were also informed that they had the right to withdraw from the study at any time without affecting their medical care and treatment. The collected data was kept confidential in the principal investigator's office. The interview took about 10-15 minutes to complete.

A custom-designed questionnaire was used to collect data about age, gender, marital status, smoking status, occupation, living conditions, income, education level, family history, insurance status, regular exercise, and healthy diet. In addition, medical files and hospital data were used to obtain disease information such as the erythrocyte sedimentation rate (ESR) and rheumatoid factor (RF), as well as RA medications such as biologic and non-biologic DMARDs, corticosteroids, non-steroidal anti-inflammatory drugs (NSAIDs), and other medications.

Study Instruments

Compliance questionnaire for rheumatology

This validated questionnaire is a short version of the 19-item compliance questionnaire for rheumatology (CQR-19) [10] and the only self-report adherence measure designed and explicitly validated for rheumatic diseases. Previous studies used the CQR-5 to assess medication non-adherence in RA patients [11, 12]. The validated Arabic version of the questionnaire used in the present study was adapted after permission from the corresponding author of an earlier study [13]. On a four-point Likert scale, participants rated their degree of agreement with particular statements ranging from "definitely do not agree" (scoring 1) to "definitely agree" (scoring 4), with lower scores suggesting lower levels of adherence.

Beliefs about medicines questionnaire

Beliefs about medicines questionnaire (BMQ) specific has two five-item scales: the necessity scale, which assesses patients' beliefs about the necessity of their prescribed medications to control the disease (specific-necessity), and the scale of the concern, which evaluates patients' concerns about potential medication adverse effects (specific-concerns).

On a five-point Likert scale, patients expressed their level of agreement with each statement, with 1 indicating significant disagreement and 5 indicating strong agreement. Each scale had a score ranging from 5 to 25, with higher values indicating stronger convictions [14]. The validated Arabic version of the questionnaire was utilized in this study [15].

Clinical disease activity index

CDAI score was manipulated by rheumatologists working in the hospitals we recruited our participants from; therefore, CDAI score was used in the current study to evaluate disease activity in the study participants [3]. Participants were classified as having low (3-10 points), moderate (>10-22 points), or high (>22 points) disease activity based on CDAI.

Data Analysis

The statistical package for the social sciences (SPSS version 27 from IBM, Chicago, IL, USA) was used to run descriptive and analytical statistics [16]. Descriptive analysis was used to describe continuous variables in terms of the mean and standard deviations (SDs) or median (25^{th}-75^{th} quartiles) depending on the normality of data tests using the Kolmogorov-Smirnov and Shapiro-Wilk statistical tests and in terms of frequencies (percentages) for the categorical variables.

We used Chi-square test for categorical variables and the Spearman correlation test for continuous variables to find the variables significantly associated with uncontrolled RA in terms of disease activity level manifested by CDAI (low, moderate, or high disease activity). Factors significantly associated with poor disease control in the univariate analysis were included in the ordinal regression model to explore variables significantly and independently associated with poor disease control. A p-value of <0.05 was considered statistically significant.

Appendix A shows the results of univariate analysis of factors associated with disease control.

RESULTS

A total of 313 patients were invited to participate in the study. Of those, thirty-two patients refused to participate, four did not finish the questionnaire, sixteen did not receive DMARD, and the remaining 261 completed the survey, yielding an 83.4% response rate. The majority of the study participants were females (86.6%), married (77.0%), unemployed (83.1%), insured (78.5%), living with their families (96.6%), had low education level (63.6%), had a monthly income of less than 700 USD (64%), did not eat a healthy diet (63.6%), did not engage in regular physical activity (78.5%), had a negative family history of RA (73.2%) and were nonsmokers (80.1%). The age range of the study population was 19 to 83 years old, with a mean of 48.7 years (SD=12.57).

Table 1. Demographic characteristics of participants (n=261)

Characteristics		Frequency (%)
Gender	Male	35 (13.4)
	Female	226 (86.6)
Education level*	Low	166 (63.6)
	High	95 (36.4)
Occupation	Employed	44 (16.9)
	Unemployed	217 (83.1)
Living condition	Alone	9 (3.4)
	Not alone	252 (96.6)
Insurance	Yes	205 (78.5)
	No	56 (21.5)
Marital status	Married	201 (77.0)
	Other†	60 (23.0)
Income	<700 USD	167 (64.0)
	700-1,400 USD	82 (31.4)
	>1,400 USD	12 (4.6)
Smoking status	Smoker	52 (19.9)
	Non-smoker	209 (80.1)
Healthy diet	Yes	95 (36.4)
	No	166 (63.6)
Regular exercise	Yes	56 (21.5)
	No	205 (78.5)
Family history of RA	Yes	70 (26.8)
	No	191 (73.2)

Note.*High educational level includes a diploma degree or higher; low educational level includes illiterate, primary, secondary, & high school; †Single includes unmarried, divorced, & widow; RA: Rheumatoid arthritis; Age: Mean (SD)=48.7 (12.57); & Body mass index: Mean (SD)=30.04 (6.52)

Table 2. Medical characteristics of participants (n=261)

Variable		Frequency (%) or Median (IQR)
Presence of other chronic disease(s)	Yes	177 (67.8)
	No	84 (32.2)
Type of comorbidities	Hypertension	77 (29.5)
	Diabetes mellitus	53 (20.3)
	Hypothyroidism	20 (7.7)
	Atherosclerotic disease	15 (5.7)
	Chronic respiratory disease	24 (9.2)
	Herniated disc	15 (5.7)
Presence of any complications of RA	Yes	243 (93.1)
	No	18 (6.9)
Type of complications	Joint deformity	55 (21.1)
	Arthroplasty	36 (13.8)
	Peripheral neuropathy	202 (77.4)
	Osteoporosis	98 (37.5)
	Eye problems	122 (46.7)
	Cardiovascular disease	13 (5.0)
Positive RF		81 (31)
Disease activity estimated by CDAI	Low	53 (20.3)
	Moderate	88 (33.7)
	High	98 (37.5)
	Missing	22 (8.5)
Duration since RA diagnosis (years)		10 (4.0-16.5)
Number of comorbidities other than RA		2.0 (1.0-3.0)
ESR (mm/hour)		44.0 (30.0-65.0)
CDAI score		19.0 (11.0-26.0)

Note. RA: Rheumatoid arthritis; RF: Rheumatoid factor; ESR: Erythrocyte sedimentation rate; CDAI: Clinical disease activity index; & IQR: Interquartile range

Table 1 shows the demographic characteristics of the participants.

As demonstrated in **Table 2**, the study findings revealed that peripheral neuropathy (77.4%), eye problems (46.7%), and osteoporosis (37.5%) were the most common complications of RA. In terms of disease activity, more than one-third of the patients (37.5%) had high disease activity, with a median CDAI score of 19 (11-26). Methotrexate (67.8%) was the most commonly administered conventional DMARD, followed by sulfasalazine (28%), while leflunomide was the least frequently prescribed one (0.4%). More than a third of the research participants (36.7%) were using biologic DMARDs as monotherapy or combined with other treatments, and more than half received a single DMARD (51.7%). The majority of the patients were using corticosteroids or NSAIDs to decrease inflammation and relieve pain (75.1%).

Table 3 describes the medication-related characteristics of the study participants. According to CQR-5, more than one-third of the participants (43.3%) were found non-adherent.

Several characteristics of the study participants influenced disease activity. The univariate analysis results revealed that low monthly income, low education level, the presence of complications from RA, having peripheral neuropathy, cardiovascular disease, receiving corticosteroids/NSAIDs, receiving three DMARDs or more, having a seropositive RA, medication non-adherence, higher number of RA and total medications, and higher number of RA complications were significantly associated with poor diseases control. However, smoking status and the presence of other chronic diseases were not associated with disease control in the present study. Variables significantly associated with disease control in the univariate analysis were included in the ordinal regression model (**Table 4**).

Table 3. Medications received by participants (n=261)

Variable		Frequency (%) or Median (IQR)
Medications for RA	Methotrexate	177 (67.8)
	Sulfasalazine	73 (28.0)
	Hydroxychloroquine	32 (12.3)
	Azathioprine	14 (5.4)
	Leflunomide	1 (0.4)
	Biologic DMARDs	96 (36.8)
	Corticosteroids/NSAIDs	196 (75.1)
Number of DMARDs	Single DMARD	135 (51.7)
	Double DMARDs	96 (36.8)
	Triple DMARDs	27 (10.3)
	Quadruple DMARDs	3 (1.2)
Frequency of medication administration	Monthly	1 (0.4)
	Biweekly	7 (2.7)
	Once weekly	115 (44.1)
	Once daily	48 (18.4)
	Twice daily	90 (34.5)
Number of RA medications		2.0 (2.0-3.0)
Number of total medications		6.0 (4.0-8.0)
Duration of medications intake (years)		8.0 (2.0-14.0)

Note. RA: Rheumatoid arthritis; DMARD: Disease-modifying anti-rheumatic drug; NSAIDs: Non-steroidal anti-inflammatory drugs; & IQR: Interquartile range

Table 4. Multivariate analysis of factors associated with poor disease control

Variable	ORC	95% CI		p-value
		Lower	Upper	
Seronegative RA	-0.882	-1.58	-0.18	0.014 *
Medication non-adherence	1.023	0.29	1.76	0.006 †
Number of total medications	-0.017	-0.168	0.134	0.829
Number of RA medications	0.138	-0.468	0.743	0.656
Number of complications	0.179	-0.139	0.497	0.270
Having CVD	-1.386	-3.175	0.403	0.129
Monthly income	0.556	-0.201	1.314	0.150
Receiving corticosteroids/NSAIDs	-0.285	-1.242	0.671	0.559
Receiving triple DMARDs	-0.294	-1.764	1.177	0.696
Having neuropathy	-0.158	-1.095	0.778	0.740
Having RA complications	-0.203	-1.745	1.339	0.797
Education level	0.168	-0.646	0.981	0.686

Note. CI: Confidence interval; CVD: Cardiovascular disease; DMARD: Disease-modifying anti-rheumatic drug; RA: Rheumatoid arthritis; *Significance at p<0.05; †Significance at p<0.01; & ORC: Ordinal regression coefficient

Results revealed a strong and negative association between seronegative RA and disease activity (p<0.05). Medication non-adherence was also significantly associated with high disease activity (p<0.01), indicating that patients with low adherence levels had more severe disease than patients who reported high adherence levels.

DISCUSSION

Assessment of RA severity is critical to monitor the clinical course of the disease, evaluate the effectiveness of the prescribed treatment, prevent long-term destruction of the joints [17], and avoid the negative impact of the increased disease activity on patients' health such as the increased risk of infections [18]. Nevertheless, limited data is available about the degree of disease control in patients with RA and the factors associated with poor disease control in these patients. Therefore, this study aimed to evaluate disease control and to

explore the factors that were significantly associated with uncontrolled disease in RA patients.

The majority of the participants had moderate to high disease activity (71.2%), which reflects poor disease control. Comparable results were reported in previous studies. A Turkish study found that 58.5% of the participants showed moderate or severe disease assessed by the DAS28 score [7]. Another study that enrolled over one thousand RA patients reported that most patients (62%) had moderate to high disease activity [8]. A study investigating the association between the polymorphism in genes involved in methotrexate metabolism and disease activity in RA patients on methotrexate therapy showed that genetic polymorphisms significantly affected disease activity, with around 66% of the participants found to have moderate to high disease activity [19]. Therefore, the higher percentage of methotrexate users in the US study could justify the similar finding about disease control between the two studs. In addition, a higher proportion of patients with moderate to high disease activity was found in a Moroccan study (85.4%) [9].

RF is a protein produced by the immune system that attacks self-body tissues [20]. High blood concentration of RF was associated with higher disease activity [21], depression [22], and poor prognosis [23] in RA patients. In addition, a prospective cohort study reported that was autoantibodies such as RF were associated with higher disease activity in pregnant women with RA [24]. A clinical-controlled trial conducted in Russia reported that patients with seropositive RA, which indicates an elevated RF serum level, had significantly higher joint destruction than seronegative RA patients [25]. The current study found that the participants with seropositive RA had more active disease than participants who had seronegative RA. RF was found to induce inflammatory cytokines such as tumor necrosis factor TNF-α, aiding the inflammation process and increasing disease activity [26]. In addition, seropositive RA was associated with a higher risk for mortality, primarily driven by cardiovascular or respiratory deaths in a cohort study [27]. Similarly, another cohort study reported that being a seropositive RA patient strongly predicted cardiovascular diseases and mortality [28]. Therefore, the therapeutic goals of RA should focus not only on inflammation reduction ad symptoms relief, but also on the conversion of seropositive RA patients to a seronegative state, given its efficacy in decreasing disease activity as demonstrated in a previous study [29], and to reduce the risk for mortality among this subgroup of patients.

Results of the present study revealed that non-adherence was significantly associated with higher disease activity. Consistent results were reported in earlier studies [30-32]. A Japanese study reported a higher risk of disease flare among non-adherent RA patients with early- or short-duration disease [33]. In addition, a multicenter prospective cohort study reported that RA patients who were non-adherent to their biological medications had poor disease control and clinical outcomes [34]. Furthermore, a systematic review and meta-analysis study reported that medication non-adherence was significantly associated with higher disease activity in patients with RA [35]. A randomized controlled trial demonstrated that disease activity was significantly reduced in the adherent RA patients compared to non-adherent patients over the study period [36]. Medication non-adherence was also associated with poor disease control in chronic diseases such as hypertension [37,38] and type 2 diabetes [39]. Medication non-adherence is not only associated with uncontrolled disease, but also affects the physicians' treatment decisions, increasing the cost burden on the healthcare system [40]. Therefore, clinical pharmacists should focus on improving medication adherence by exploring the factors associated with medication non-adherence and targeting it in individualized pharmaceutical care programs aiming to improve health outcomes among patients with RA.

Study Limitations

The self-report method used to assess medication adherence may have overestimated adherence due to social desirability bias. Furthermore, a larger sample size would help to draw more robust conclusions from the present study. Despite these limitations, the current study provides baseline data on the predictors of poor disease control among patients with RA in Jordan.

CONCLUSIONS

The current study demonstrates poor disease control among the majority of the study participants. Factors such as seropositive RA and medication non-adherence were significantly associated with poor disease control in the present study. In addition, future management programs should focus on the seroconversion of seropositive RA patients to a seronegative status, improving medication adherence, and hence disease control among patients with RA.

Author contributions: ASJ: conceived and designed study, supervised project, conducted research, provided research materials, & wrote initial & final draft of article; **WA-Q:** validated instruments, organized, analyzed, & interpreted data, & reviewed manuscript; **SRAH:** designed study, collected, organized, analyzed, & interpreted data, & wrote initial & final draft of article; **KA & TLM:** conceived study & reviewed final draft of article; & **AA:** conceived study, reviewed final draft of article, co-supervised project, & provided logistic support. All authors have agreed with the results and conclusions.

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Ethical statement: The study has been carried out in accordance with the Declaration of Helsinki (1964) for experiments involving human subjects. The study received ethical approval from the Institutional Review Board in KAUH at Jordan University of Science and Technology (Ref. # 58/132/2020), and an informed consent form was obtained from all participants agreed to participate in the study.

Declaration of interest: No conflict of interest is declared by authors.

Data sharing statement: Data supporting the findings and conclusions are available upon request from the corresponding author.

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APPENDIX A

Table A1. Results of univariate analysis of factors associated with disease control

Variable		n (%)			p-value
		Low	Moderate	High	
Gender	Female	41 (19.9)	79 (38.3)	86 (41.8)	0.099
	Male	12 (36.4)	9 (27.2)	12 (36.4)	
Income [a]	Low	23 (14.8)	55 (35.5)	77 (49.7)	<0.001*
	High	30 (35.7)	33 (39.3)	21 (25.0)	
Education level [b]	Low	27 (17.5)	55 (35.7)	72 (46.8)	0.020*
	High	26 (30.6)	33 (38.8)	26 (30.6)	
Regular physical activity	No	38 (20.3)	66 (35.3)	83 (44.4)	0.118
	Yes	15 (28.8)	22 (42.4)	15 (28.8)	
Family history	No	34 (19.5)	66 (37.9)	74 (42.6)	0.275
	Yes	19 (29.2)	22 (33.9)	24 (36.9)	
Healthy diet	No	38 (26.0)	50 (34.3)	58 (39.7)	0.189
	Yes	15 (16.1)	38 (40.9)	40 (43.0)	
Living conditions	Live alone	1 (11.2)	4 (44.4)	4 (44.4)	0.708
	Live with family	52 (22.6)	84 (36.5)	94 (40.9)	
Smoking	No	42 (21.5)	72 (36.9)	81 (41.6)	0.873
	Yes	11 (25.0)	16 (36.4)	17 (38.6)	
Occupation	Employed	12 (28.6)	11 (26.2)	19 (45.2)	0.256
	Unemployed	41 (20.8)	77 (39.1)	79 (40.1)	
Insurance	No	13 (24.5)	16 (30.2)	24 (45.3)	0.525
	Yes	40 (21.5)	72 (38.7)	74 (39.8)	
Marital status	Married	40 (22.1)	65 (35.9)	76 (42.0)	0.841
	Single [c]	13 (22.4)	23 (39.7)	22 (37.9)	
Presence of any RA complications	No	8 (44.4)	8 (44.4)	2 (11.2)	0.012*
	Yes	45 (20.4)	80 (36.2)	96 (43.4)	
Peripheral neuropathy	No	17 (29.3)	26 (44.8)	15 (25.9)	0.025*
	Yes	36 (19.9)	62 (34.2)	83 (45.9)	
Eye problems	No	33 (25.8)	49 (38.3)	46 (35.9)	0.174
	Yes	20 (18.0)	39 (35.1)	52 (46.9)	
Joints deformity	No	46 (24.6)	70 (37.4)	71 (38.0)	0.117
	Yes	7 (13.5)	18 (34.6)	27 (51.9)	
Arthroplasty	No	50 (24.4)	76 (37.1)	79 (38.5)	0.069
	Yes	3 (8.8)	12 (35.3)	19 (55.9)	
CVD	No	52 (22.9)	87 (38.3)	88 (38.8)	0.009*
	Yes	1 (8.3)	1 (8.3)	10 (83.4)	
Osteoporosis	No	29 (19.5)	63 (42.3)	57 (38.2)	0.073
	Yes	24 (26.7)	25 (27.8)	41 (45.5)	
Presence of chronic diseases other than RA	No	14 (18.7)	33 (44.0)	28 (37.3)	0.287
	Yes	39 (23.8)	55 (33.5)	70 (42.7)	
Hypertension	No	39 (23.8)	65 (39.6)	60 (36.6)	0.121
	Yes	14 (18.7)	23 (30.7)	38 (50.6)	
Diabetes mellitus	No	42 (22.3)	75 (39.9)	71 (37.8)	0.104
	Yes	11 (21.6)	13 (25.5)	27 (52.9)	
Chronic respiratory disease	No	48 (22.1)	83 (38.3)	86 (39.6)	0.302
	Yes	5 (22.7)	5 (22.7)	12 (54.6)	
Hypothyroidism	No	49 (22.3)	80 (37.3)	91 (41.4)	0.880
	Yes	4 (21.1)	8 (42.1)	7 (36.8)	
Herniated disc	No	53 (23.5)	80 (35.4)	93 (41.1)	0.069
	Yes	0 (0.0)	8 (61.5)	5 (38.5)	
Receive methotrexate	No	18 (22.8)	30 (38.0)	31 (39.2)	0.927
	Yes	35 (21.9)	58 (36.2)	67 (41.9)	
Receive sulfasalazine	No	37 (21.8)	66 (38.8)	67 (39.4)	0.591
	Yes	16 (23.2)	22 (31.9)	31 (44.9)	
Receive hydroxychloroquine	No	44 (21.0)	78 (37.1)	88 (41.9)	0.459
	Yes	9 (31.0)	10 (34.5)	10 (34.5)	
Receive azathioprine	No	50 (22.2)	82 (36.5)	93 (41.3)	0.881
	Yes	3 (21.4)	6 (42.9)	5 (35.7)	
Receive biologic DMARD	No	40 (26.1)	58 (37.9)	55 (36.0)	0.055
	Yes	13 (15.1)	30 (34.9)	43 (50.0)	
Receive corticosteroids/NSAIDs	No	26 (43.3)	18 (30.0)	16 (26.7)	<0.001*
	Yes	27 (15.1)	70 (39.1)	82 (45.8)	
Receive single DMARD	No	22 (17.9)	40 (32.5)	61 (49.6)	0.019*
	Yes	31 (26.7)	48 (41.4)	37 (31.9)	

Table A1 (Continued). Results of univariate analysis of factors associated with disease control

Variable		n (%)			p-value
		Low	Moderate	High	
Receive double DMARDs	No	35 (22.0)	59 (37.1)	65 (40.9)	0.991
	Yes	18 (22.5)	29 (36.3)	33 (41.2)	
Receive triple DMARDs or more	No	50 (23.5)	82 (38.5)	81 (38.0)	0.027*
	Yes	3 (11.5)	6 (23.1)	17 (65.4)	
Frequency of administration	Monthly	0 (0.0)	1 (100.0)	(0.0)	0.626
	Biweekly	1 (16.7)	1 (16.7)	4 (66.6)	
	Weekly	23 (22.8)	41 (40.6)	37 (36.6)	
	Once daily	9 (19.6)	19 (41.3)	18 (39.1)	
	Twice daily	20 (23.5)	26 (30.6)	39 (45.9)	
RF	Negative	28 (37.3)	24 (32.0)	23 (30.7)	0.020*
	Positive	16 (20.3)	23 (29.1)	40 (50.6)	
Adherence level (CQR-5)	Low	10 (9.7)	38 (36.9)	55 (53.4)	<0.001*
	High	43 (31.6)	50 (36.8)	43 (31.6)	
Spearman's correlation coefficient					
Age		0.061			0.348
BMI		0.088			0.177
Disease duration		0.166			0.073
Number of complications		0.178			0.006*
Number of comorbidities		0.107			0.098
Number of DMARDs		0.081			0.213
Number of RA medications		0.221			0.001*
Number of total medications		0.218			0.001*
Duration of medication intake		0.061			0.346
Necessity score		0.079			0.226
Concerns score		0.057			0.380

Note. RA: Rheumatoid arthritis; CVD: Cardiovascular disease; DMARD: Disease-modifying anti-rheumatic drug; NSAIDs: Non-steroidal anti-inflammatory drugs; RF: Rheumatoid factor; CQR: Compliance questionnaire for rheumatology; BMI: Body mass index; *Significant at 0.05 level; [a]Low: Less than 700 USD; High: 700 USD or more; [b]High educational level: Diploma degree or higher; Low educational level includes illiterate; Primary, secondary, & high school; & [c]Single: Include unmarried, divorced, & widow