

Original Article

MEDICATION ADHERENCE STATUS AMONG RHEUMATOID ARTHRITIS PATIENTS

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ABSTRACT

Objective: Rheumatoid arthritis (RA) is a common disease affecting about 5 in 1,000 people in Malaysia. Medication adherence among RA patients can be as low as 30% and non-adherence of disease modifying anti-rheumatic drugs (DMARD) may result in irreversible joint damage. This study aimed to assess adherence rates and to identify potential factors influencing adherence.

Methods: A cross-sectional study was conducted at Rheumatology Clinic of a tertiary hospital for 8 w from May to June 2014. A total of 51 RA patients using DMARD were recruited in this study. Researcher-assisted questionnaires were utilized. The study assessed adherence by using Compliance Questionnaire on Rheumatology (CQR5) and data retrieved from pharmacy dispensing records which were measured using Medication Possession Ratio (MPR). Questionnaires to assess beliefs about medicines and satisfaction about medicine information were also used. Subsequently, associations between adherence and demographics, socioeconomics, medication, disease and patient-related factors were determined.

Results: The response rate was 75%. Depending on the instruments used, 75% (CQR5) and 60% (MPR) of the patients were adherent to DMARD. Non-adherence was not associated with demographic, socioeconomic and clinical characteristics, satisfaction about medication information and medication concerns. Beliefs about the necessity of medication ($r = 0.372$; $p = 0.007$) and necessity-concerns differential ($r = 0.439$; $p = 0.001$) were moderately associated with adherence.

Conclusion: Patient-related factor was associated with medication adherence in our study population. The necessity-concerns differential of medication beliefs may serve as a possible screening tool for non-adherence or target for adherence-improving intervention among RA patients.

Keywords: Rheumatoid arthritis, Medication adherence, Medication beliefs, DMARD

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INTRODUCTION

Adherence is defined as the extent to which a person's behaviour corresponds with agreed recommendations from a healthcare provider [1]. Rheumatoid arthritis (RA) is a common disease with a prevalence of 0.5% to 1% of the adult population worldwide [2]. According to Arthritis Foundation Malaysia, it affects approximately 5 in 1,000 people in this country. It is a chronic inflammatory disease that is characterized by joint inflammation and is often associated with a poor quality of life [3]. It lays a huge financial burden with more than 50% of patients with RA completely stop working within 10 y of disease onset [3].

Disease-modifying anti-rheumatic drugs (DMARDs) will help in suppressing disease activity, improving functional ability, preventing irreversible joint damage and reducing the risk of extra-articular features such as cardiovascular disease [4]. Adherence to DMARD will determine the success of treatment. However, adherence is only suboptimal and ranges from ranged from 30% to 80%, depending on the definition of adherence and methodology of measurement used [5].

In order to improve adherence, non-adherent individuals have to be identified. The most feasible way to identify non-adherents in clinical practice is by using self-report measures because they are cheaper, minimal participant burden, ease and administrative speed, and flexibility in terms of mode of administration and timing of assessment compare to other measures [6]. There is no gold standard questionnaire for measuring patient adherence at present [7]. Compliance Questionnaire on Rheumatology (CQR) is the only validated rheumatology-specific adherence questionnaire [8]. However, self-report measures tend to overestimate adherence with socially desirable answers and are subjected to recall biases [6, 9]. Therefore, an objective measure such as refill of prescription can also be used to screen RA patients who are likely to be non-adherent [10].

Non-adherent behaviour can be associated with 5 interacting domains which are socioeconomic factors, health professional and health service-related factors, therapy-related factors, disease-related factors and patient-related factors [11]. There is no single factor that can independently predict non-adherence inpatient [1]. Multiple risk factors from different dimensions need to be considered and investigated of their influence on RA patients [11]. Previous studies identified a variety of sociodemographic and clinical variables related to adherence, but none was consistently related in all studies, with sometimes contradictory [6, 11]. The aim of this study was therefore to assess patient's adherence, medication beliefs and satisfaction with medication information of RA patient who was taking DMARD.

MATERIALS AND METHODS

Methods

A cross-sectional survey was conducted at the Rheumatology Clinic of Universiti Kebangsaan Malaysia Medical Centre (UKMMC) over a period of 8 w. RA patients using DMARD were approached based on inclusion and exclusion criteria and researcher-assisted questionnaires were utilised. Convenience sampling was used. All questionnaires including the translated version were piloted on 10 outpatients with RA and were subsequently modified to improve clarity before the actual data collection was started. Each interview started with an assessment of demographics and socioeconomics and clinical characteristics followed by completing three questionnaires: CQR, Satisfaction about Medication Scales (SIMS) and Beliefs about Medicines Questionnaire (BMQ). Ethical approval was obtained from the Research Ethic Committee of UKM (UKM 1.5.3.5/244/NF-002-2014). Written consent was obtained from participants who agreed to participate and they were reassured of the confidentiality of the information provided. Participants in this study were strictly voluntary.

Patients were recruited if they were diagnosed with RA, aged 18 y old and above and were taking at least one DMARD. Patients were excluded from the study if they were just recently started on DMARD (less than 1 y), were unable to give informed consent and unable to read or understand English, Malay or Mandarin, with documented cognitive impairment or psychiatric illness and were not responsible for their own medication taking (relied on a carer).

Targeted sample size was 140 subjects with 10 subjects per variable studied. The 14 factors to be assessed in our study were age, race, sex, employment status, education level, household income, marital status, duration of illness, pain intensity, the number of medicines prescribed, beliefs about medicines (2 subscales) and satisfaction with medication information (2 subscales).

Data collection

Instruments

a) Beliefs about medicines questionnaire (BMQ)

Patients' beliefs about medicines were assessed using the BMQ. It has been validated for use in patients with various chronic illnesses [9]. Only part one BMQ was used and it consisted of two 5-item subscales. Item 1 to 5 was utilised to assess patients' beliefs about the necessity of prescribed medication for controlling their disease while item 6 to 10 were utilised to assess their concerns about potential threats of taking it. Participants indicated their degree of agreement with each statement on a 5-point Likert scale, ranging from 1 = strongly disagree to 5 = strongly agree. The total scores were ranged from 5 to 25 for both necessity and concerns scales with higher scores indicating stronger beliefs. BMQ necessity-concerns differential was calculated by subtracting the concerns subscale score from the necessity subscale score and the difference between the necessity and the concerns scales were ranged-20 to+20. This differential could be thought of as the cost-benefit analysis for each patient, for whom costs (concerns) were weighed against their perceived benefits (necessity beliefs).

b) Compliance questionnaire on rheumatology (CQR5)

Adherence was assessed with CQR and computerized pharmacy refill records. The 5-item CQR (CQR5) was previously modified from the 19-item CQR, which was validated with Medication Event Monitoring System (MEMS device) in patients with inflammatory rheumatic diseases [8, 12]. CQR5 is a condensed questionnaire that would be quicker and easier to be utilised and able to reduce the patients' burden but maintain a good level of reliability and validity. Each 5 item in CQR presents a statement, which is related to adherence rated on a 4-point Likert scale ranging from 1 (do not agree at all) to 4 (agree very much). By using CQR5 Adherence Calculator, an estimation of whether the patient is a "high adherer" or a "low adherer" was calculated and the results were presented in dichotomous scale.

c) Medication possession ratio (MPR)

MPR of DMARD was calculated from automated pharmacy dispensing records as a proportion of day's supply obtained over a period of refill intervals for the past one year. MPR was then calculated by a number of days for which DMARD(s) were dispensed between the start and the end date divided by the total number of days elapsed between the intervals. The obtained ratio was multiplied by 100%, and it was defined as poor adherence if refill adherence was less than 80% [13].

d) Satisfaction with information about medicines scale (SIMS)

SIMS consists of 17 items to assess the extent to which patients feel they have received enough information about different aspects of their prescribed medicines from health care provider [14]. For each item, participants were asked to indicate whether the amount of information they had received was "too much", "about right", "too little", "none received", or "none needed". The SIMS items are divided into two subscales: the action and use (Item 1-9) and the potential problems of medication (Item 10-17). Total satisfaction score can be obtained from each subscale by summing the scores for each item with higher scores indicating a higher degree of overall satisfaction with the amount of medication information received. A

score of 1 if satisfied ("about right" or "none needed") and score 0 if dissatisfied ("too much", "too little", or "none received").

Statistical analysis

Descriptive data were presented in mean (\pm SD) or median (25th-75th percentile) depending on the parametric distribution of measured variables. Data transformations were performed if possible. Comparisons between risk factors of adherent and non-adherent patients were done using Mann-Whitney U test, Chi-square test and Independent-samples t-test depending on the scale and normality of tested variables. All statistical tests were two-tailed and p-value<0.05 was considered statistically significant. The relationship between variables and adherence were tested using Spearman or Pearson correlation. All variables with p-value<0.10 in the bivariate analysis were entered in the multivariate analysis performed by the binary logistic regression. Data were analyzed using SPSS version 21.

RESULTS

A response rate of 75.0% was reported among RA patients who have fulfilled inclusion criteria. Race and gender were not further analyzed for their association with adherence due to insufficient sample or did not meet the assumption of most statistical tests. Only 4 male patients were recruited in our study. Subject's characteristics are described in table 1.

The majority of the participants (51%) used single traditional DMARD, 45% used traditional combination DMARDs and 4% used biological DMARD. Most patients used methotrexate (70.7%), sulfasalazine (35.4%), leflunomide (33.5%) and hydroxychloroquine (9.8%) as DMARD. The majority of participants were women (92.2%). A total of 70.6% of patients were younger than 65 y old. The majority of patients were retired (49%). Meanwhile, 15.7% of participants had a monthly household income of less than RM 1000 with most of them depended mainly on their pensions. 82.4% of participants were married and not staying alone. Participants have large pill burden with a median of 8 medications per day and long disease duration with 13.7 mean years.

Based on CQR5, 74.5% of the patients were adherent with prescribed medicines. Using MPR, 60.8% of the patients were rated as adherent. CQR5 and MPR were found to have a moderate association with each other (Spearman's rho = 0.315, p = 0.025). In other words, people who collected medication on time tending to report more adherence to medications.

A number of variables were tested for possible associations with adherence, measured with the CQR5 (table 2).

Adherence between employment and marital status, age, the number of medications prescribed, pain intensity, disease duration, medication concerns score and satisfaction with information about medications were found to be non-significant. There was no association between adherence with monthly household income (Spearman's rho = 0.127, p = 0.375) and education level (Spearman's rho = 0.037, p = 0.798). Only beliefs about the necessity of the medication ($t = 2.169$, $p = 0.047$) and necessity-concerns differential ($t = 3.420$; $p = 0.001$) were found to be significantly higher for the adherent group in our study. Both showed significant moderate association with adherence. Necessity-concerns differential has a higher positive correlation with adherence ($r = 0.439$; $p = 0.001$) than BMQ necessity score ($r = 0.372$, $p = 0.007$). However, only necessity-concerns differential seemed to be powerful enough to predict low adherence in our study (table 3).

In our study, the majority of the participants (69.0%) believed in the necessity of their arthritis medication to maintain their health (table 4). Almost 85% of patients believed medications were able to protect them from becoming worse. Although there was no association between adherence and medication concerns, however, overall 55.7% reported concerns about potential adverse consequences of taking their medication. Nearly 75% of participants expressed their concern about potential long-term adverse effects and becoming too dependent on their medications. There was much less concern about inconveniences and disruption to life's routines associated with taking arthritis medications

Table 1: Demographic, socioeconomic, clinical and patient characteristics (n = 51)

Characteristic	Finding
Age in years, mean (\pm SD)	58.6 (\pm 10.8)
Gender, n (%)	
Male	4 (7.8)
Female	47 (92.2)
Race, n (%)	
Malay	25 (49.0)
Chinese	15 (29.4)
Indian	6 (11.8)
Others	5 (9.8)
Education level, n (%)	
Never	2 (3.9)
Primary	11 (21.6)
Secondary	31 (60.8)
University/College	6 (11.8)
Postgraduate	1 (2.0)
Employment status, n (%)	
Working at present	14 (27.5)
Retired	25 (49.0)
Never worked	9 (17.6)
Unemployed due to disease	2 (3.9)
Unemployed due to other reasons	1 (2)
Marital status, n (%)	
Married/living together	42 (82.4)
Married/living alone	2 (3.9)
Single/living together	2 (3.9)
Single/living alone	5 (9.8)
Monthly household income, n (%)	
RM 1000 and below	8 (15.7)
RM 1001-RM2000	21 (41.2)
RM 2001-RM3000	11 (21.6)
Above RM 3000	11 (21.6)
Years of disease duration, mean (\pm SD)	13.7 (\pm 9.2)
Pain VAS, mean (\pm SD)	4.2 (\pm 2.5)
No. of medicines, median (IQR)	8 (5-11)
BMQ necessity score, mean (\pm SD)	17.8 (\pm 3.1)
BMQ concerns score, mean (\pm SD)	16.1 (\pm 3.4)
BMQ necessity-concerns differential, mean (\pm SD)	1.7 (\pm 4.4)
SIMS action score, mean (\pm SD)	6.4 (\pm 1.8)
SIMS adverse effects score, median (IQR)	2.0 (1.0-4.0)

BMQ: Beliefs about Medicines Questionnaire; SIMS: Satisfaction about Medication Scales; VAS: Visual Analog Scale

Table 2: Comparison between sociodemographic, disease, therapy and patient-related factors of adherent and non-adherent patients (n = 51)

Characteristic	Adherence expressed as dichotomous variable			p-value
	Adherent(n = 38)	Non-adherent(n = 13)	Statistics	
Sociodemographic factors				
Age in years, mean (\pm SD)	59.5 (\pm 9.9)	55.9 (\pm 13.3)	t = 1.024	0.311
Employment status, n (%) Working at present Retired/Not working	9 (23.7)29 (76.3)	5 (38.5)8 (61.5)	Yates' χ^2 = 0.450	0.502
Marital status, n (%) Married Single	32 (84.2)6 (15.8)	12 (92.3)1 (7.7)	Yates' χ^2 = 0.070	0.791
Disease-related factors				
Years of disease duration, mean (\pm SD)	14.5 (\pm 9.4)	11.2 (\pm 8.4)	t = 1.147	0.257
Pain VAS, mean (\pm SD)	4.3 (\pm 2.5)	4.0 (\pm 2.9)	t = 0.336	0.738
Therapy-related factor				
No. of medicines, median (IQR)	8 (5-12)	7 (5-9)	Z = -0.695	0.487
Patient-related factors				
BMQ necessity score, mean (\pm SD)	18.5 (\pm 2.4)	15.8 (\pm 4.1)	t = 2.169	0.047*
BMQ concerns score, mean (\pm SD)	15.7 (\pm 3.2)	17.5 (\pm 3.9)	t = -1.634	0.109
BMQ necessity-concerns differential, mean (\pm SD)	2.8 (\pm 3.8)	-1.6 (\pm 4.6)	t = 3.420	0.001*
SIMS action score, mean (\pm SD)	6.2 (\pm 1.8)	6.9 (\pm 1.8)	t = -1.161	0.251
SIMS adverse effects score, median (IQR)	2.0 (1.0-5.0)	2.0 (2.0-3.5)	Z = -0.574	0.566

Z=Mann-Whitney U test; χ^2 = Chi-square test; t= Independent-samples t-test; *p<0.05 denotes statistical significance. BMQ: Beliefs about Medicines Questionnaire; SIMS: Satisfaction about Medication Scales; VAS: Visual Analog Scale

Table 3: Logistic regression predicting likelihood of reporting non-adherence

Characteristic	Odds Ratio	95% CI for odds ratio	p-value
BMQ necessity score	1.095	0.838-1.431	0.505
BMQ necessity-concerns differential	1.267	1.108-1.508	0.048*

*p<0.05 denotes statistical significance. BMQ: Beliefs about Medicines Questionnaire

Table 4: Percentage of participant agreeing or strongly agreeing with Beliefs about Medicines Questionnaire (BMQ) statements (n = 51)

BMQ statements	% agreeing or strongly agreeing
<i>Necessity Scale</i>	
My health, at present, depends on my medicines	76.5
My life would be impossible without my medicines	58.8
Without my medicines I would become very ill	60.8
My health in the future will depend on my medicines	64.7
My medicines protect me from becoming worse	84.3
<i>Concern Scale</i>	
Having to take medicines worries me	56.9
I sometimes worry about the long-term effects of my medicines	74.5
My medicines are a mystery to me	39.2
My medicines disrupt my life	33.3
I sometimes worry about becoming too dependent on my medicines	74.5

On the other hand, patient satisfaction was highest regarding information on how to obtain follow-up prescriptions and on how to use the medication (>90% satisfied patients) (table 5). Patients were least satisfied (<70% satisfied patients) with information provided for the majority of the items regarding potential problems of

medication. Only non-Muslims were assessed for information regarding alcohol use. A total of 13.7% of patients were dissatisfied about information received regarding the potential risk of teratogenicity of arthritis medications, and two of them were in their childbearing age.

Table 5: Satisfaction about medicine information in both adherent and non-adherent patients

Effects and usage	n	% satisfied	Potential problems	n	% satisfied
Medicine name	51	80.4	Any side effects	51	41.2
Indication	51	84.3	Side effect risk	51	37.3
Effects	51	80.4	What to do when side effects occur	51	29.4
Mechanism	51	74.5	Drug interactions	51	9.8
Onset of action	51	31.4	Alcohol use	26	37.3
Perceived effects	51	43.1	Drowsiness	51	19.6
Duration medicine use	51	35.3	Effects on the unborn child	51	86.3
Instruction of use	51	96.1	Missed doses	51	27.5
Follow-up prescriptions	51	98			

DISCUSSION

RA has been consistently found to be three times more common in women than men [15] but the ratio of male to female RA patients presented to our Rheumatology Clinic was approximately one-sixth, and this has not yet included male patients that did not fulfill inclusion criteria or unwilling to take part in the study.

The adherence rate of 60% to 75% to DMARD in this study is in agreement with the previous study.⁶ Lower adherence rate was reported with MPR compared to CQR in our study. Possible explanations are the input of data into pharmacy administrative database may not be comprehensive especially during busy hours and for prescriptions that were amended manually, manual prescriptions would have been used, and medications would had been dispensed bypassing computerized pharmacy dispensing records. Therefore, MPR may underestimate adherence in our study. This explained moderate rather than strong association between MPR and CQR. Besides, possessions did not guarantee that medications were taken by patients using MPR measure. Despite limitation with MPR, it was still being used as an additional adherence tool to reduce the effect of bias with self-reported questionnaire alone.

Non-adherence of DMARD is hard to be identified using general characteristics [1, 6, 11, 16, 17] as results from our study suggested that only beliefs about necessity of medications and perceived necessity greater than medication concerns were associated with

adherence and these was consistent with previous studies that they seem to convince patients of the need for medications [6, 16-18]. Patients' motivation to commence and to continue with medication is influenced by the way in which they evaluate their need for treatment [9, 18]. Adherent patients had greater necessity-concerns differential. They seemed to engage in an implicit cost-benefit analysis that balanced their concerns about the potential threats against perceptions of the necessity of arthritis medication [9, 18].

The cost-benefit analysis was powerful enough as predictor and screening tool for non-adherence in our study and was consistent with previous finding [9, 18]. Therefore, it served as a possible target for adherence-improving interventions. Despite strong beliefs about the necessity of their medication to decrease the symptoms of pain and fatigue, prevention of functional loss and cure of the disease, more than half of the RA patients in this sample reported strong concerns about potential adverse effects, particularly in the long term and becoming too dependent which were also consistent with previous findings [6, 18].

Adherence-improving interventions were reported not very successful in RA patients [19]. Our findings suggested that effective intervention should be tailored to overcome the perceptual barrier such as fear of possible adverse effects and fear of dependence, increase the understanding and reason why medication is needed as for this group of patients with the aim of increase the perceived benefit of treatment and reduce perceived threats at the same time [1].

Not all items in SIMS were used; item "whether the medication will affect your sex life" was replaced with "effects on the unborn child" [6] because asking the irrelevant question can increase the concerns and thereby influencing adherence [20]. RA impacts on the sexual lives by limitations on sexual intercourse because of fatigue and pain with the disease itself [21] rather than arthritis medication. Although not related to adherence, there were around two-third of patients dissatisfied with the information provided regarding potential problem of arthritis medications. This needs to be highlighted as side effects of DMARDs can be detrimental e. g. serious hepatotoxicity, bone marrow suppression and pulmonary complications [22]. Furthermore, the risk of liver damage increases with alcohol consumption but two-third of non-Muslims patients were not informed regarding alcohol use [23] and the majority of them were put on methotrexate and leflunomide. The majority of samples were on leflunomide and methotrexate, but not all the childbearing age women were informed regarding the increased risk of foetal death and teratogenicity risk of their arthritis medications. Therefore, providing sufficient information is important because it will help in prompt discontinuation and seek for early treatment in patients experiencing side effects.

Our study has highlighted several findings; however, it has several limitations. Limited sample size may lead to insufficient power and results in non-significant findings. A study from single centred Rheumatology Clinic would limit the generalization of the findings and caution must be exercised before applying to other settings. In addition, there may be a possible overestimation of adherence with self-report adherence due to Hawthorne effect [6] and the self-reported measure was subjected to recall biases [9]. Furthermore, adherence is a dynamic process and patients' beliefs can change over time. A longitudinal study with a larger sample are required as the cross-sectional study did not measure changes over time [6].

In conclusion, our findings demonstrated that a significant proportion of RA patients did not adhere to their DMARD prescription. Interventions and the educational programme should incorporate personal beliefs about medication and by improving adherence to DMARD will subsequently improve the efficacy of medical treatments. Although not related to adherence, our study suggested that patients require more information regarding their arthritis medication than what they currently received to facilitate the appropriate medication use. Similar to medication concerns, this should also be addressed during drug counseling.

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CONFLICT OF INTERESTS

Declare none

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