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Research Article

Determinants of Adherence to cDMARDs in Patients of Rheumatoid Arthritis at a Tertiary Care Hospital of Lahore, Pakistan

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Abstract

Background: Rheumatoid Arthritis (RA) is a chronic autoimmune disease characterized by inflammation of joints, with associated joints pain, swellings, damage and disability. Adherence to these prescribed drugs is important to improve joint function, productivity of work, and health-associated quality of life. This approach may also reduce likability of joint damage, disability, and morbidity, with improvement in life expectancy.

Objective: To understand the determinants of adherences to treatment with disease modifying anti-rheumatic drugs (cDMARDs) in Rheumatoid arthritis patients.

Methods: This cross-sectional study was conducted at Rheumatology and Immunology department of Shaikh Zayed Hospital Lahore Pakistan for three months. Total of 163 RA patients were enrolled after following inclusion and exclusion criteria. After taking the informed consent, multiple questionnaires were filled by the patients. All the data was entered and analyzed using SPSS 23. The p value of < 0.05 was taken as significant.

Results: The mean age of the patients was 43.11 ± 12.11 years. There were 31(19%) male and 132 (81%) female patients. MARS score was high in females than males. Low disease activity groups had lowest MARS score with statistically significant difference from other disease activity group ($p = 0.045$; $p < 0.05$).

Conclusion: Female rheumatoid arthritis patients had significantly higher adherence scores than males. All factors of BMQ and SIMS and feature of emotional representation from IPQ show significant difference with regard to gender.

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Key Words: Conventional diseases modifying anti-rheumatic drugs (cDMARDs), Rheumatoid Arthritis (RA), Medication Adherences Report Scales (MARS)

Introduction

Rheumatoid Arthritis (RA) is a chronic autoimmune disease characterized by inflammation of joints with associated joints pain, swellings, damage, and disability[1]. About 0.5-1% of the world's population has RA[2]. and in Pakistan the prevalence of RA is in between 0.14 and 0.22%[3]. Symptoms prevention comprises of disease reduction and disability prevention. RA is commonly treated with conventional disease modifying anti-rheumatic drugs (cDMARDs), corticosteroids, and non-steroidal anti-inflammatory

drugs (NSAIDs)[4]. Present recommendations indicate use of conventional disease-modifying anti-rheumatic drugs (cDMARDs) for rheumatoid patients within three months of diagnosis[5].

Adherence to these prescribed drugs is important to improve joint function, productivity of work, and health-associated life quality. This approach may also reduce probability of joint damage, disability, and morbidity with improvement in life expectancy[6]. Adherence to medications is found to be influenced by different factors such as medication characteristics, socioeconomic and demographic factors, perceptions and cognitions about illness and medication, doctorpatient relationship & disease features, Although evidence exists regarding factors linked with meager or effective medication adherence, recognition of patients with high risk of non-adherence is still intrica-te[7]. High adherence rate was reported by Arshad et al.[8], and Ragab et al.[9], who found that 77% and 62.-5% of RA patients were adherent to DMARDs resp-ectively. According to a study by Mahran et al.[10], 42.-5% of their patients were highly adherent to prescri-bed DMARDs and 26% were moderately adherent. A similar kind of study was conducted by Xia et al.[11], which reported the adherence ratio to be 38% in Chinese patients suffering with rheumatoid arthritis. On the other hand, Prudente et al.[12], found that only (16.4%) of RA patients were adherent to treatment and Naqvi et al.[3], found adherence ratio of 23%.

Limited studies are available Pakistan in the context. This study was conducted to understand the determinant of adherence to conventional disease modifying anti-rheumatic drugs (cDMARDs) in Rheumatoid arthritis patients. These determinants included medication features, beliefs, socioeconomic and demographic factors, disease features, and doctor-patient relationship. This study will help the rheumatologists in identifying the factors for adherence and may use for better treatment plans and follow-ups.

Objective

To understand the determinants of adherence to treatment with conventional disease modifying anti-rheumatic drugs (cDMARDs) in patients of Rheumatoid arthritis

Methods

This cross-sectional study was conducted from October 2019 to January 2020 at the Rheumatology and Immunology department of Shaikh Zayed Hospital, Lahore, Pakistan, after obtaining permission from the Institutional Review Board of the hospital. The sample size of 163 was calculated by using Z = 2.58 at 99% confidence interval, P = anticipated DMARD adherence = 60% (13), and absolute Precision: 0.10. Non-probability consecutive sampling technique was used. The patients aged 18 years and above (both males & females), fulfilling the ACR criteria of Rheumatoid Arthritis, and taking at least one cDMARD for three months according to their medical history were included in this study. Patients presenting with any other rheumatic and inflammatory diseases were excluded. Informed written consent was taken from all the patients.

All demographic data was collected (including gender, age, occupation & education) with clinical data as well as disease activity scores (DAS28-ESR). DAS28-ESR, which involves 28 tender & swollen joints count (SJC and TJC), assessment of patient disease activity (visuals analogs scales [VAS]) and erythrocytes sedimentations rates (ESR), were observed. A number of questionnaires were filled by participants such as Medication Adherence Report Scales (MA-RS-6), Beliefs about Medicines Questionnaires (BMQ), Satisfaction with information about Medica-tions Scales (SIMS) and Illness Perceptions Questio-nnaires (IPQ) (14, 15).

Operational Definitions

Adherences: Medication adherence to the extent of coherence between an individual's behavior and provided recommendations from a health care worker[16].

Determinants of adherence: These include complexity and treatment duration, illness characteristics, costs and effect of treatments, characteristics of health service provision, interaction between practitioner and patients and socio-demographic variables.

cDMARDs: Conventional Diseases-modifying anti-rheumatic drugs (cDMARDs) are a group of medications commonly used in patients with RA. The commonly used conventional cDMARDs are Methotrexate, Sulfasalazine, Hydroxychloroquine, and Leflunomide, Azathioprine and Cyclosporine.

Medication Adherence Report Scale (MARS-6): It involves 6 patterns of non-adherent behaviors that respondents scored on a five-point Likert scale. Scores were added and totals ranged from 6 to 30, with higher scores signifying higher self-reported adherence [14].

The Beliefs about Medicines Questionnaire (BMQ): To evaluate an individual's concepts regarding specific medicine and comprises of 19 questions on a two point scale (with 1= Agree, 2 = Disagree). A higher score specifies stronger apprehensions[17].

The Satisfaction with Information about Medication (SIMS): It comprises of 17 items to evaluate kind of information required to help in self management of medicines by patients. Contributors were supposed to indicate received information on the basis of a five-point scale[15].

The Illness Perceptions Questionnaires (IPQ): It measures the representation of perceptions about illness. Responses of patients were recorded against 38 questions on a five-point scale [18].

All the data was entered and studied with SPSS version[23]. Categorical data was summarized as percentages and frequency, whereas means and standard deviations were used to present quantitative data. The t-test and Mann-Whitney tests were used to assess the relationship between the demo graphic data and SIMS/BMQ/IPQ. Mann-Whitney and Kruskal Wa-llis tests were used to evaluate the MARS score for categorized variables (followed by Dunn's test wher-ever applicable). Spearman correlation was used to evaluate the relationship of continuous variables with MARS score. The p value of < 0.05 was taken as statistically significant.

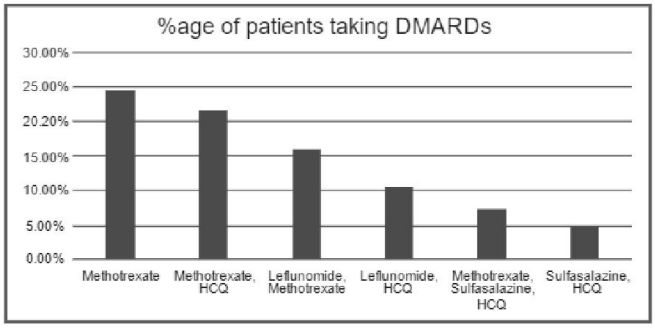
Results:

The demographics of participants are shown in the Table 1. The mean age for 163 patients included in this study, was 43.11±12.11 years. The study included 31(19%) male and 132 (81%) female patients with mean disease period of 7.43 ± 2.94 years. Forty-four (27%) participants had attained primary level of education, whereas, 46(28.2%) achieved secondary level of education. Moreover, 21(12.9%) and 10(6.1%) patients had attended college and university respectively. An overwhelming number (n = 42; 25-%) of patients in the study was illiterate.

A very high number of participants were housewives (n = 106; 65%), followed by the occupation of tailor and welder (n = 24; 14.7%). Majority of participants had a reason other than RA for not working (n=99; 60.7%). However, 60 (36.8%) were unable to work due to RA at present. The most widely used DMARD by participants was Methotrexate (n = 40; 24.5%), followed by a combination of Methotrexate and HCQ (n = 35; 21.5%), Leflunomide and Methotrexate (n= 26; 16%), Leflunomide and HCQ (n= 17; 10.4-%), Methotrexate, Sulfasalazine and HCQ (n = 12; 7.4%), Sulfasalazine and HCQ (n= 8; 4.9%).

Table 1: *Demographic data*

Age (years)	43.11+ 12.1	
Duration of Disease (years)	7.43 + 2.94	
Gender	Male	31(19%)
	Female	132(81%)
Level of Education	Primary	44(27%)
	Secondary	46(28.2%)
	College	21(12.9%)
	University	10(6.1%)
	Not Educated	42(25.8%)
Occupation	Housewife	106(65%)
	Shopkeeper	18(11%)
	Driver	3(1.8%)
	Farmer	4(2.5%)
	Hospital staff	4(2.5%)
	Teacher	4(2.5%)
	Tailor, welder and Others	24(14.7%)
If currently not working then	Not working due to RA	60(36.8%)
	Retired	4(2.5%)
	Not working for other reason	99(60.7%)
Which DMARDs are you taking	Methotrexate	40(24.5%)
	Methotrexate, HCQ	35(21.5%)
	Leflunomide, Methotrexate	26(16%)
	Leflunomide, HCQ	17(10.4%)
	Methotrexate, Sulfasalazine, HCQ	12(7.4%)
	Sulfasalazine, HCQ	8(4.9%)



The BMQ score, SIMS score and IPQ score were compared with demographic data, as shown in the Table 2. The specific concern (p=0.00<0.05), and general harms scores (p=0.00< 0.05) were significantly higher in males than females. This suggests negative orientation among males towards medicine in general. However, negative point of views of male population is also indicated against DMARDS specifically.

The factors of specific concern (p=0.00<0.05) and general overuse (p=0.00< 0.05) also showed significant difference among genders, but their scores were less as compared to other BMQ characteristics.

According to SIMS scores, SIMS action and usage were higher (n = 36 and 38) as compared to SIMs potential problems (n = 22 and 24). However, statistically significant difference was evident among genders on the basis of SIMS score (p = 0.006 and p = 0.00 < 0.05).

According to IPQ scoring, only emotional representation (p= 0.01<0.05) showed significant difference on the basis of gender.

Table 2: *BMQ, SIMS, IPQ Score Median according to gender of patient*

Variables	Male	Female	p value
BMQ			
Specific Necessity	6 (5-8)	5 (5-8)	0.021*
Specific Concern	10(7-12)	8 (6-12)	0.00*
General overuse	5 (4-6)	4 (3-6)	0.00*
General Harm	10	8 (5-10)	0.00*
SIMS			
SIMs Action and Usage	36(29-40)	38 (27-41)	0.006*
SIMs Potential Problem	22 (19-23)	24 (13-24)	0.00*
IPQ			
Cyclical Timeline	20(14-25)	14 (11-20)	0.180
Consequence	20(16-24)	20 (14-24)	0.239
Personal control	20(9-22)	20 (13-24)	0.910
Treatment control	18(9-22)	18(13-24)	0.965
Illness coherence	16(11-21)	16 (12-22)	0.68
Emotional representation	21(11-26)	22 (12-25)	0.010*

* Statistically significant (p<0.05)

The distribution of MARS score in accordance with demographic data is shown in Table 3. Females had higher MARS scores as compared to males with statistical significance. The MARS score for educational levels of primary and college education were higher as compared to secondary and university education. However, no statistical significance was evident on the basis of educational levels(p = 0.98). Similarly statistical significance was not found for unemployed participants (p = 0.6).

The low disease activity groups had the lowest MARS means score. Statistically significant difference was evident among remission, moderate and higher activity group with p value of 0.045 (p < 0.05).

Table 3: *Demographic data with Median MARS Score*

Categorical Variables		Median of MARS score	p value
Gender	**Male**	7 (6-18)	**0.05***
	Female	12 (7-24)	
Level of education	**Primary**	12 (6-18)	0.98
	Secondary	13 (6-21)	
	College	12 (11-24)	
	University	11 (6-18)	
	Not Educated	11 (6-20)	
If currently not working then	**Not working due to RA**	12.5 (12-24)	0.6
	Retired	12	
	Now working for other reason	9 (6-18)	
Disease activity level	**Remission**	11.06 + 3.64	
	Low	10.90 + 3.82	**0.045***
	Moderate	11.27± 3.25	

* Statistically significant (p<0.05)

The correlation analysis between SIMS and BMQ along with SIMS and BMQ is shown in the Table 4. According to which, the general overuse and general harm factor of BMQ has statistically significant correlation with features of action and usage, prospective problems of SIMS (p < 0.05). On the other hand, the factors of personal control, illness coherence and treatment control of IPQ are significantly correlated with action and usage of SIMS (p < 0.05), whereas, personal control, treatment coherence and cyclical timeline are significantly correlated with potential problem factor of SIMS (p <0.05)

Table 4: *Correlation analysis*

Correlation between SIMS and BMQ			
Action and Usage	p value	Potential Problem	p value
Specific Necessity	0.483	Specific Necessity	0.733
Specific Concern	0.473	Specific Concern	0.339
General overuse	0.001*	General overuse	0.021*
General Harm	0.001*	General Harm	0.001*
Correlation between SIMS and IPQ			
Action and Usage	p value	Potential Problem	p value
Personal control	0.001*	Personal control	0.001*
Illness coherence	0.001*	Illness coherence	0.535
Treatment control	0.013*	Treatment control	0.001*
		Cyclical Timeline	0.001*

* Statistically significant ($p<0.05$)

Discussion:

Measuring adherence is vital to most researchers and practitioners. Imprecise assessment of medication adherence leads to numerous difficulties, which have the potential to be expensive and hazardous in our setting. The present study enabled to observe the way in which cDMARDs adherence can be affected by variation in demographics.

In the present study, about 32-40% patients did not adhere to their cDMARDs prescriptions. The previous researches done by Kelly et al., and McCulley et al., have pointed out that patients have serious concerns about possible effects of DMARDs (19, 20). Same is true for present study, in which 18 (11%) individuals indicated specific concerns about medication. However, the patients with lower adherence we-re found more disappointed ($p < 0.01$, Spearman correlation for SIMS action). This factor can be the outcome of negative beliefs regarding DMARDs. The negative point of views of Asian patients can also be attributed to their specific culture[6]. The findings of present study suggest a significant difference between MARS score, BMQ, SIMS and gender. The emotional representation factor of IPQ was also found to have a statistically significant difference with respect to gender.

A previous study found that deep confidence in the necessity for treatment and beliefs regarding safety of medicines were affirmative in nature. Surprisingly, higher self-reported adherence was mainly found in white patients. Moreover, no relation between medication beliefs, self-reported adherence to RA and socio-demographic characteristics were found [21]. However, in present study a negative association has been indicated in education level and self-adherence score. The female patients had a higher score as compared to males ($p = 0.046$). On the other hand, positive association was depicted between gender and adherent score.

The procedure used in this study to assess adherence was conferred with patient's representatives that proposed a self-report strategy. No previous research work has utilized variety of questionnaires (MARS, SIMS, BMQ, IPQ). Moreover, the previous qualitative works were affected as perceptions of patients regarding disease, medications and desired outcome were under the influence of health beliefs[21].

There were certain limitations of our study. Firstly, all the patients were taken from only one center. Secondly all the responses recorded by the patients had potential for decreased recall and a response bias.

Conclusion:

The results of this study imply that all factors of BMQ and SIMS and feature of emotional representtation from IPQ show significant difference with regard to gender. It can be concluded that female rheumatoid arthritis patients had significantly higher adherence scores than males, whereas low diseases activity groups had significantly lower MARS scores

than other disease activity groups. The scales of SIMS, BMQ and IPQ show various determinants for adherence to DMARDs. This includes factors such as general overuse, general harm of BMQ and personal control, illness coherence, treatment control and cyclical timeline of IPQ linked with potential problems and action and usage of SIMS.

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