

Medication Adherence in Patients with Rheumatoid Arthritis and Juvenile Idiopathic Arthritis: A Comparative study

Yasser A Abdelhameed, Sahar S. Ganeb, Waleed A. Salah Eldin, Faten M. Abdeltawab*

Department Rheumatology, Rehabilitation, and Physical Medicine, Faculty of Medicine, Benha University, Egypt

*Corresponding author: Faten M. Abdeltawab, Mobile: (+20) 1122254083, E-Mail: faten.abdeltawab@yahoo.com

ABSTRACT

Background: In chronic illnesses requiring long-term therapy, such as Rheumatoid Arthritis (RA) and Juvenile Idiopathic Arthritis (JIA), medication non-adherence is a major issue that drives up expenses globally. Adherence is crucial to achieving desired results but is frequently poor during treatments.

Objective: Our study aimed to evaluate compliance to DMARDS between Rheumatoid Arthritis patients and Juvenile Idiopathic Arthritis patients by Compliance Questionnaire of Rheumatology (CQR) and factors potentially affecting it.

Subjects and methods: This comparative study included two groups: Group (1): 120 rheumatoid arthritis and group (2): 60 juvenile idiopathic arthritis patients. All patients were subjected to: Complete history taking, clinical examination, disease activity assessment, quality of life, anxiety and depression, socioeconomic status and adherence to treatment by Standardized questionnaires. **Results:** Our study revealed that medication non-adherence was higher in RA group than JIA group with highly significant difference between both groups. Fear of drug side effect was the first cause of disease-modifying antirheumatic drugs (DMARDs) non-adherence in both groups. Also our study found that there was significant difference as regards steroid administration in JIA group and DMARD non adherence. There was significant value regarding depression and DMARD non-adherence in RA group. As regards socioeconomic status and DMARD non-adherence, there was significant difference among RA group.

Conclusion: RA group had a greater rate of DMARDS non-adherence than JIA group. Non-adherence is a complex issue that is impacted by a number of variables. These variables may be separated into five categories: Social and economic variables, treatment-related factors, disease-related factors, patient-related factors, and factors associated to the health care system.

Keywords: RA, JIA, KMARD, Quality of life.

INTRODUCTION

The chronic inflammatory illness rheumatoid arthritis (RA) is characterised by ongoing synovitis in the joints and systemic inflammatory reactions that may result in permanent impairment ^(1, 2). RA is seen as a multistep illness. The immune system becomes activated outside the joint compartment, primarily in the mucosal surfaces, during the preclinical stage of the illness as a result of genetic predisposition and environmental stimuli ⁽³⁾. In children, JIA is the most prevalent chronic rheumatic condition. Currently, all types of chronic arthritis with an uncertain aetiology that begin before the age of 16 are included under the general label "JIA" ⁽⁴⁾. There are seven distinct subtypes of JIA according to the International League of Associations for Rheumatology (ILAR) ⁽⁵⁾. Notably, oligoarticular JIA (oJIA) is more prevalent in European nations, whereas polyarticular JIA (pJIA), enthesitis-related arthritis (ErA), and systemic JIA (sJIA), are most prevalent in Asia, India, Australia, New Zealand, Costa Rica, and South Africa ⁽⁶⁾.

There are two types of medical non-adherence: purposeful and inadvertent. It may be divided into purposeful sources for non-adherence, such as cases when a patient decided to stop taking medicine or skip a dose on their own initiative without contacting a doctor ⁽⁷⁾.

SUBJECTS AND METHODS

This study involved two groups:

- **Group (I):** 120 RA patients diagnosed according to the American College of

Rheumatology/European League Against Rheumatism (ACR/EULAR) 2010 classification criteria for diagnosis of RA ⁽⁸⁾.

- **Group (II):** 60 JIA patients diagnosed according to ILAR classification criteria of JIA ⁽⁹⁾.

All patients were recruited from those attending the Outpatient's Clinic and Inpatient's Unit of Rheumatology, Rehabilitation and Physical Medicine Department of Benha University Hospitals.

Exclusion criteria:

- a. Additional autoimmune disorders: Vasculitis, SLE, rheumatic fever, dermatomyositis, polymyositis, enteropathic arthritis, Behcet illness, Sjogren's syndrome, and mixed connective disorders that are some examples of connective diseases.
- b. Acute illness or septic arthritis.
- c. Metabolic disorders.
- d. Endocrine conditions.
- e. Neuropathic illnesses.
- f. A hereditary bone condition.
- g. Neoplastic illnesses, such as leukaemia.
- h. Psychogenic rheumatic disease.
- i. Sarcoidosis.
- j. Familial Mediterranean fever.
- k. Soft tissue rheumatic disease.

Every Rheumatoid Arthritis participant in this research underwent:

A) Complete history taking, which included information on age, sex, smoking, drinking, the duration

of the condition, if morning stiffness is present how long it has persisted, and medicines.

B) Clinical examination.

C) Assessment of disease activity by DAS28 score⁽¹⁰⁾.

D) Standardized questionnaires:

- **Assessment of quality of life:** by 36 item form health survey (SF-36) questionnaire⁽¹¹⁾.
- **Assessment of anxiety and depression:** by Hospital anxiety depression scale (HADS)⁽¹²⁾.
- **Assessment of socioeconomic status of patients.**
- **Assessment of adherence to treatment:** by Compliance Questionnaire of Rheumatology (CQR) and factors potentially affecting it. The CQR comprises 19 statements on medicine intake, and the patient rates their level of agreement with each one using a Likert scale with a maximum of four points⁽¹³⁾. A CQR score of less than 80% was used to determine non-adherence.

Each and every JIA patient involved in this research underwent:

A) Complete history taking, including age, sex, smoking, drinking, the length of the condition, the presence of morning stiffness and how long it has persisted, and drugs.

B) Clinical examination.

C) Assessment of disease activity by validated score JADAS-27 (JAD Activity Score-27)⁽¹⁴⁾.

D) Standardized questionnaires:

- **Assessment of functional ability and quality of life by Juvenile Arthritis Multidimensional Assessment Report (JAMAR questionnaire) FOR JIA patients⁽¹⁵⁾.**
- **Assessment of anxiety and depression in children by PECK (personal experience checklist) questionnaire⁽¹⁶⁾.**

- **Assessment of socioeconomic status of parents of children.**

- **Assessment of adherence to treatment by Compliance Questionnaire of Rheumatology (CQR) and factors potentially affecting it⁽¹³⁾.**

Ethical approval: Benha University's Ethics Committee gave this experiment its approved. Adult rheumatoid arthritis patients and JIA children Parents' written informed consents were obtained after being informed of the purpose of the study, and the data collected at the personal level was held in absolute confidence.

Statistical Analysis

An "Investigation report form" was used to capture the information. Using the software SPSS version 26, these data were tabulated, coded, and then analysed. The data were transformed into descriptive statistics in the form of mean, standard deviation (SD), number, and percent. To compare the means of two sets of numerical (parametric) data, the Student's t-test was employed to determine the significance of the difference. Inter-group comparison of continuous non-parametric data was carried out using the Mann-Whitney U-test, while categorical data was compared across groups using the chi square test (X²-value) or fisher exact test, and various parameters were correlated using the Pearson correlation coefficient (r) test. Which of these elements was regarded as a significant predictor was determined using certain examined parameters incorporated into a logistic regression model. Statistical significance (S) was defined as P ≤ 0.05.

RESULTS

There was no significant difference between RA and JIA groups as regards medication adherence and demographic data (Table 1).

Table (1): Medication adherence among study groups regarding demographic data

Characteristics	RA (n=120)				Test of sig.	P-value	JIA (n=60)				Test of sig.	P-value	
	Non-adherent (n=61)		Adherent (n=59)				Non-adherent (n=11)		Adherent (n=49)				
Age/years mean ± SD)	47.05	12.56	49.63	12.32	1.1	0.3	11.27	4.61	9.17	3.03	1.4	0.2	
Sex No. (%)	Female	52	85.2%	49	83.1%	0.1	0.7	6	54.5%	36	73.5%	1.5	0.2
	Male	9	14.8%	10	16.9%			5	45.5%	13	26.5%		
BMI (mean ± SD) (kg/m ²)	27.13	4.11	27.14	3.98	0.1	0.9	16.77	2.66	17.04	3.19	0.3	0.2	
Disease duration (mean ± SD)	10.38	7.42	8.22	7.17	1.6	0.1	3.95	3.75	2.75	2.13	1.1	0.3	

There was high significance (P<0.001) regarding fear of drug side effect, poor income and lack of response to drug as causes of non-adherence to medications among RA group. There was significant (P<0.05) difference regarding psychological, poor patient education, and disease remission as causes of non-adherence to medications among RA group. There was high significance (P<0.001) regarding fear of drug side effect and lack of response to drug as causes of non-adherence to medications among JIA group. There was significant (P<0.03) difference regarding poor parent education and disease remission as causes of non-adherence to medications among JIA group (Table 2).

Table (2): Medication adherence among study groups regarding cause of non-adherence

	RA (n=120)				X ²	p-value	JIA (n=60)				X ²	p-value
	Non-adherent (n=61)		Adherent (n=59)				Non-adherent (n=11)		Adherent (n=49)			
	No.	%	No.	%			No.	%	No.	%		
Fear of drug side effect	17	27.9%	1	1.7%	16.1	<0.001*	6	54.5%	0	0.0%	23.9	<0.001*
Poor income	15	24.6%	0	0.0%	16.6	<0.001*	---	---	---	---	---	---
Poor patient/parents' education	10	16.4%	0	0.0%	8.5	0.004*	2	18.2%	0	0.0%	4.4	0.03*
Lack of response to drug	16	26.2%	0	0.0%	17.9	<0.001*	4	36.4%	0	0.0%	13.7	<0.001*
Psychological	9	14.8%	0	0.0%	7.4	0.002*	2	18.2%	1	2.0%	2.1	0.1
Disease remission (feeling well)	7	11.5%	0	0.0%	5.3	0.007*	2	18.2%	0	0.0%	4.4	0.03*
Child refusal	---	---	---	---	---	---	1	9.1%	0	0.0%	0.6	0.2

There was significant (p =0.04) value as regards depression and medication non-adherence in RA group. ^a The scale is applicable only on 45 cases of JIA, 15 patients were under age of [Spence children's Anxiety scale and Birlleson Depression Self-Rating Scale for Children (DSRS-C)] (Table 3).

Table (3): Medication adherence among study groups regarding Anxiety

	RA (n=120)				X ²	p-value	JIA (n=45) ^a				X ²	p-value
	Non-adherent (n=61)		Adherent (n=59)				Non-adherent (n=8)		Adherent (n=37)			
	No.	%	No.	%			No.	%	No.	%		
Depression	34	55.7%	22	37.3%	4.1	0.04*	3	37.5%	4	10.8%	1.8	0.09
Degree	Mild	16	26.2%	10	16.9%	1.5	0.2					
	Moderate	12	19.7%	9	15.3%	0.4	0.5					
	Severe	6	9.8%	3	5.1%	0.4	0.3					
Anxiety	33	54.1%	25	42.4%	1.7	0.2	2	25.0%	6	16.2%	0.3	0.5
Degree	Mild	17	27.9%	12	20.3%	0.9	0.3					
	Moderate	12	19.7%	8	13.6%	0.8	0.4					
	Severe	5	8.2%	4	6.8%	0.1	0.5					

There was very high significant (P<0.001) value as regards middle socioeconomic status and medication adherence in RA group. There was significant (P=0.004) value as regards very low socioeconomic status and medication non-adherence in RA group. There was no significant (p value > 0.05) difference as regards socioeconomic status and medication adherence in JIA group (Table 4).

Table (4): Medication adherence among study groups regarding socioeconomic status

	RA (n=120)				X ²	p-value	JIA (n=60)				X ²	p-value
	Non-adherent (n=61)		Adherent (n=59)				Non-adherent (n=11)		Adherent (n=49)			
	No.	%	No.	%			No.	%	No.	%		
Very low	16	26.2%	4	6.8%	8.2	0.004*	2	18.2%	6	12.2%	0.3	0.5
Low	21	35.0%	13	22.0%	2.5	0.1	4	36.4%	25	51.0%	0.8	0.4
Middle	20	32.8%	38	64.4%	12.1	<0.001*	5	45.5%	18	36.7%	0.3	0.4
High	3	4.9%	4	6.8%	0.2	0.5	---	---	---	---	---	---

Table (5) showed that univariate logistic regression analysis revealed that educational level, socioeconomic status, disease activity, total number of pills and family member support were significant predictors for non-adherence in RA cases, while in multivariate logistic regression only socioeconomic status and disease activity was significant predictors for it.

Table (5): Univariate and Multivariate logistic regression analyses of various variables for prediction of non-adherence in RA patients

	Univariate analysis				Multivariate analysis			
	p-value	OR	95%CI		p-value	OR	95%CI	
Age	0.17	0.98	0.95	1.01				
Sex	0.503	0.71	0.27	1.92				
BMI	0.65	0.98	0.90	1.07				
Disease duration	0.051	1.05	1.00	1.11				
Educational level	0.004*	0.77	0.65	0.92	0.47	0.92	0.74	1.15
Socioeconomic status	<0.001*	0.40	0.24	0.66	0.01*	0.42	0.22	0.81
Income	0.19	0.75	0.49	1.15				
Disease activity	<0.001*	1.85	1.30	2.62	0.003*	1.83	1.23	2.71
Number of medications	0.10	1.39	0.93	2.07				
Total number of pills	0.01*	1.36	1.08	1.70	0.32	0.67	0.31	1.47
Family member support	0.02*	0.34	0.14	0.82	0.054	1.52	0.99	2.33

Table (6) showed that univariate logistic regression analysis revealed that none of the factors was significant predictor for non-adherence in JIA cases.

Table (6): Univariate logistic regression analyses of various variables for prediction of non-adherence in JIA patients

	Univariate analysis			
	p-value	OR	95%CI	
Age	0.07	1.21	0.98	1.49
Sex	0.22	2.31	0.60	8.86
BMI	0.79	0.97	0.77	1.22
Disease duration	0.16	1.19	0.93	1.52
Educational level	0.62	0.91	0.64	1.31
Socioeconomic status	0.90	1.06	0.40	2.82
Income	0.64	1.26	0.48	3.30
Disease activity	0.19	1.59	0.80	3.16

DISCUSSION

In our study, there was significant (P=0.005) value as regards low income (borrow) and medication non-adherence in RA group and this completely agrees with **Sharma et al.** (17) where they discovered that non-adherence to the therapy was statistically significant and caused by poor income (P < 0.0001).

In the study by **Beretta et al.** (18), 100 JIA patients were engaged. School absences were recorded more frequently in JIA with uveitis than in JIA alone without uveitis (32.7% vs 10.8%, p0.0211). **Our study** revealed that 26 JIA patients were regular attendants to school 22 (84.6%) were adherent to their medications and 4 (15.4%) were non-adherent to their medications also our study showed that 34 JIA patients were non-regular attendants to school 27 (79.4.6%) were adherent to their medications and 7 (20.6) were non adherent to their medications. In **Abdul-Sattar et al.** (19) Egyptian study addressing JIA sufferers' participation in school, 52 JIA patients who had been ill for at least a year straight and were under 7 years old were examined. 69% of the sample missed three or more weeks of school during the previous academic year. 12.5% of school days were lost on average, which is equal to 25 missed days. 46% of the patients had subpar school performance.

In our study, 59 RA patients (49.2%) were adherent to their medications. demographic data including Age, sex, BMI and disease duration were not significantly associated with medication adherence. However, there were significant difference (p = 0.02) between educational level (primary school) attendance and medication non-adherence. Also, there were significant difference (p = 0.005) between very low income (borrow) and medication non-adherence. In addition, there was significant difference (p = 0.001) regarding not active disease and medication adherence. All of these results partially agree with **Ko et al.** study (20). The participants in this study were 207 RA patients. 68 individuals (33.3%) who received a CQR cutoff score of 80% or higher were determined to be adherent. Age, sex, marital status, level of education, drinking habits, occupation, family income, comorbidities, the existence of negative side effects, the presence of disease activity, and laboratory results were not significantly linked with medication adherence.

In our study, 52 (43.3%) were treated with methotrexate, while 10.8% were treated with biologic DMARDs. Medication adherence and non-adherence patients did not differ with regard to types of DMARDs or methotrexate However there was significant negative

correlation between CQR19 % and total number of pills (p value = 0 .013). Regarding **Ko et al.** ⁽²⁰⁾ study, less than 10% of patients received treatment with biologic DMARDs, while the majority of participants (75%) received methotrexate. Patients with and without medication adherence did not differ in terms of the total number of tablets prescribed, the number of DMARDs prescribed, the categories of DMARDs, or the amount of methotrexate. **Alongi et al.** study ⁽²¹⁾ enrolling 2251 JIA sufferers, when disease activity is low, this significantly affects school activity and medicine adherence. Specific adverse drug reactions, particularly nausea, had the strongest influence on treatment adherence (p <0.001) and was the only AE directly connected to drug rejection, and this partially agrees with our study, which revealed that adverse effects of medication was the first cause of medication non-adherence among JIA group (p-value <0.001), but disease activity did not significantly affect medication adherence.

CONCLUSION

RA group had a greater rate of DMARDs non-adherence than JIA group. Educational attainment, socioeconomic standing, disease activity, and the total number of tablets taken were all significant predictors of non-adherence in instances of RA, while none of these variables were significant predictors of non-adherence in cases of JIA.

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