

Factors Associated with Medications Adherence among Patients with Rheumatoid Arthritis

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DOI: <https://doi.org/10.5281/zenodo.14558188>

Published Date: 26-December-2024

Abstract: Background: Rheumatoid arthritis is a progressive systemic inflammatory autoimmune disease that initially affects the joints, manifesting as pain, stiffness, and synovitis leading to the destruction of cartilage and bone, functional limitation, and disability also accompanied by extra-articular organ involvement. Although this inflammatory process is reversible, it may progress into irreversible damage of articular structures if left untreated and may lead to loss of function. DMARDs remain the first-line treatment of RA. The aim of RA treatment is to achieve remission, or low disease activity, avoid joint damage and disability, maintaining the quality of life, and controlling extra-articular manifestations. Therapeutic success depends on both drug's efficacy and medications adherence. Objective: To identify factors associated with medications adherence among patients with rheumatoid arthritis. Setting: The study was conducted at the Rheumatology Outpatient Clinic in the Alexandria Main University Hospital. Subjects: A convenience samples of 120 adult patients with rheumatoid arthritis from both sexes were selected from the above-mentioned settings. Tools: three tools were used for data collection. Tool I: Socio-demographic, Clinical Data, and Patient's Knowledge Structured Interview Schedule, Tool II: Korean Version of the Hill-Bone Medication Adherence Subscale (HBMA-K), Tool III: Factors Associated with Medications Adherence among Patients with Rheumatoid Arthritis Structured Interview Schedule. Results: the study revealed that more than half (55%) of the studied patients had poor knowledge, while more than one third (36.7%) had fair knowledge and only (8.3%) had good knowledge. Whereas, it was found that more than half (53.4%) of the studied patients had moderate adherence to medications, while more than one third (38.3%) of them had highly adherence and only 8.3 of them had poor adherence to medication. There was no statistical significant relationship between studied patients knowledge and their level of medications adherence as ($P = 0.360$). Whereas there were statistically significance relation between the Therapy related factors, condition-related factors, patient related factors, educational, social and economic factors, and health care system factors and adherence level to medications as ($p < 0.001$). Conclusion: study revealed that most of the studied patients with RA were adherent to their medications, and more than half of them had poor knowledge related to RA disease. Recommendations: Develop and implement health teaching program to improve patients' knowledge regarding the rheumatoid arthritis disease and its treatment.

Keywords: Adherence, Factors affecting, Medications, Rheumatoid Arthritis.

I. INTRODUCTION

Rheumatoid arthritis (RA) is a progressive systemic inflammatory autoimmune disease that initially affects the joints, manifesting as pain, stiffness, and synovitis eventually leading to cartilage and bone loss, functional limitation, and impairment (Chimenti et al., 2019; Wabe et al., 2019). It is the most common autoimmune inflammatory arthritis among the adults patients (Liu, 2018).

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It can also attack other organs and cause extra-articular manifestations as vasculitis, pulmonary involvement, and rheumatic nodules (Qorban et al., 2018). The disease's hallmark is symmetric chronic synovitis, which usually affects small peripheral joints. However, any joint with a synovial membrane may be affected. Although this inflammatory process is reversible, if left untreated, it may lead to irreversible damage of articular structures and loss of function (Angelotti et al., 2017).

Rheumatoid arthritis affects around 0.24% to 1% of the world's population (England & Mikuls, 2020). Studies carried out amongst American Indians show a higher prevalence ranging between 5.3 % (Pima Indians) and 6.3 % (Chippewa Indians) in contrast, many population studies from Africa and Asia show lower prevalence rates for RA in the range of 0.2–0.4% with a female predominance of 2–3 times more than men (Cho, Bhattacharyya, & Helfgott, 2019; Fauci & Langford, 2013; Xu & Lin, 2017).

Rates are higher in monozygotic twins (12–15%) than in dizygotic twins (3%). It can occur at any age, the peak onset is between the fourth and fifth decades of life (Innes, 2016; Sierakowska et al., 2016). In Egypt, the prevalence of the disease reaches 0.3% of all population (Usenbo, Kramer, Young, & Musekiwa, 2015). A range of poor long-term outcomes can potentially occur, but these have been reduced to some degree with the use of more aggressive treatment strategies and more effective drug therapies. However, RA's financial burden on society remains substantial (England & Mikuls, 2020).

Although the exact pathogenesis of RA is uncertain (Firestein & McInnes, 2017), several factors can interfere in genetically susceptible hosts, including genetic predisposition and epigenetic factors, and multiple genetic risk factors have been established. The shared epitope, referring to a specific sequence at the Human leukocyte antigen (HLA-DRB1) locus which is involved with antigen presentation, has been one of the most studied along with environmental exposures that result in the systemic inflammatory process include cigarette smoking has been identified as a significant risk factor. Periodontal disease also is associated with the development of RA. Silica is an example of an associated occupational exposure, as well as lifestyle-related factors, such as diet and obesity (Alam, Jantan, & Bukhari, 2017; Wisłowska, 2018).

Rheumatoid arthritis is a lifelong disease process that has no known cure and requires long term treatment with multiple medications (Lamb et al., 2015; J. Smolen, Aletaha, & McInnes, 2016). Disease-modifying anti-rheumatic drugs (DMARDs) are the mainstay of RA therapy (Alhefny, Abd El-Rahman, Abd El-Moteleb, Sakr, & Hassan, 2016). RA treatment aims to achieve remission, or low disease activity, avoid joint damage and disability, maintaining the quality of life, and controlling extra-articular manifestations (Nam, 2016).

Medication adherence and drug effectiveness are two important factors of therapeutic success. As a result, drug adherence is critical for achieving desired clinical outcomes (Suh et al., 2018). Medication adherence is described as “the degree or extent of conformity to the instructions regarding day-to-day treatment by the health care provider concerning the timing, dosage, and frequency (Heidari, Cross, & Crawford, 2018). Adherent patients have more favorable outcomes, including better disease control, higher remission rates, improved physical function, slower disease progression, and lower risk of therapy escalation to more aggressive treatment (Berner, Erlacher, Fenzl, & Dorner, 2019; Oh, Park, & Moon, 2019).

Non-adherence to medications decrease the efficacy of drugs, delays the recovery from symptoms, allows the progression of the disease, and necessitates the addition of new interventions and medications to maintain optimal control of the symptoms with the risk of triggering pharmacological interactions and adverse events, as well as a rise in costs also, it affects the quality of life and generates an increase in the number of disease flares, disability, and mortality (Costa et al., 2015; Harnett et al., 2016; Xia et al., 2016).

Non-adherence to treatment can be classified into unintentional and intentional. The unintentional non-adherence occurs when the patient has the intention to take the prescribed treatment but cannot do it due to different circumstances, such as forgetting to take the medication, lack of understanding of the recommendations given during the prescription, or inability to pay for pharmacological treatment (Marengoni et al., 2016). The intentional non-adherence is determined by the patient's decision to discontinue treatment or by the modification of the dosage regimen that had been prescribed by the health professional. This type of non-adherence may be influenced by the beliefs of the patients about the effectiveness of the recommendations of health professionals, their knowledge about the disease, and their ability to achieve health goals (Marengo & Suarez-Almazor, 2015).

Medication adherence is a multifactorial problem that can be influenced by various factors. The World Health Organization 2003 classified the factors that associated with patients' medication adherence into main five domains including social and economic related factors such as cost of medication, healthcare team and system-related factors as lack of knowledge and training of healthcare

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providers, disease-related factors including disease-related disability, therapy-related factors as medication regimen complexity and patient-related factors including perceptions and expectations of the patient (Kalogianni, 2011; Mathes, Jaschinski, & Pieper, 2014).

According to this, the nurse has an important role in performing an assessment to identify barriers that prevent rheumatoid arthritis patients from adhering to their medications and provide appropriate intervention. As they are responsible for helping patients gain knowledge, skills, and change attitude necessary to maintain adherence to medications. Therefore, this study aimed to identify factors associated with medication adherence among patients with rheumatoid arthritis.

II. BODY OF ARTICLE

I- MATERIALS AND METHOD

MATERIALS

Research Design:

A descriptive research design was utilized for this study.

Setting:

The study was conducted at the Rheumatology Outpatient Clinic of Alexandria Main University Hospital.

Subjects:

A convenience sample of 120 adult patients with rheumatoid arthritis will comprise the subjects of this study.

The study sample size was estimated based on the Epi info program using the following parameters:

- Population size is 400/year
- Expected frequency is 50%,
- Margin of errors is 10%,
- Confidence coefficient is 99%,
- Minimum sample size is 120

Inclusion criteria: Subjects were considered eligible to participate in the study if they met the following criteria:

- Adult patients diagnosed with RA aged from 20 to 60 years.
- On disease-modifying anti-rheumatic drugs
- Alert, able to communicate

Study Tools:

Three tools were used for data collection:

Tool I:

Socio-demographic Characteristics, Clinical Data, and Patient's Knowledge Structured Interview Schedule: This tool consisted of two parts:

Part I: This part was developed by the researcher after reviewing of the recent related literature (Esmail, 2019) to elicit the socio-demographic Characteristics and clinical data of RA patients.

Part II: "Rheumatoid Arthritis Patients' Knowledge Structured Interview Schedule:" This tool was developed by the researcher based on a review of related literature (Esmail, 2019) to assess rheumatoid arthritis patients knowledge. It included questions about RA definition, signs and symptoms, risk factors, affected joints, the diagnostic procedure needed for rheumatoid arthritis diagnosis, management modalities and complications.

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Scoring System: The patients' knowledge answers were scored on 3 points Likert Scale; a score of (2) points was given to "correct and complete answer" while score (1) point was given to "correct and incomplete answer" and score (0) was given to "the wrong answer or do not know". This score was converted to percent. Patients who had a knowledge score of less than 50 % were categorized as having "poor knowledge level", while those who knew score 50 to less than 75% were categorized as having "fair knowledge", while those knew score 75% and more were categorized as having "good knowledge level".

Tool II: Korean Version of the Hill-Bone Medication Adherence Subscale (HBMA-K):

This subscale was adapted by the researcher from the original Hill-Bone Compliance Scale which was developed by Kim, et al 2000 (Culig & Leppe, 2014). It was used to assess patients' adherence to rheumatoid arthritis medications. It consists of nine categories which are: 1) how often does he/she forgets taking the prescribed medication, 2) how often does he/she decide not to take prescribed medication, 3) how often does he/she forgets to get prescriptions filled, 4) how often does he/she run out of prescribed medication, 5) how often does he/she omit his/her prescribed medication, 6) how often does he/she miss taking prescribed medication when he feels better, 7) how often does he/she miss taking prescribed medication when he/she feels sick, 8) how often does he/she miss taking prescribed medication when he/she is not caring of dose, 9) how often does he/she takes alternative else's prescribed medication.

Scoring System: HBMA-K consisted of nine categories; each category was rated on four points Likert Scale; 1 indicated "never", 2 indicated "some of the time", 3 indicated "most of the time", 4 indicated "all of the time". The total score ranged from 9 to 36, higher scores (36) reflected "poorer adherence to rheumatoid arthritis medication" and lower scores (9) reflected "highly adherence."

Tool III: Factors Associated with Medications Adherence among Patients with Rheumatoid Arthritis Structured Interview Schedule:

This tool was developed by the researcher after reviewing the recent related literature (Bae et al., 2016;). It was used to identify factors associated with medications adherence among patients with rheumatoid arthritis. It included five main factors:

- (a) Educational, social and economic factors which included 12 items.
- (b) Health care system factors which included 10 items.
- (c) Condition-related factors which included 4 items.
- (d) Therapy-related factors which included 8 items.
- (e) Patient related factors which included 18 items divided into physical factors were 5 items and the psychological/behavioral were factors 13 items.

The tool covered 52 statements with "Yes" or "No" answers. It was represented statistically as numbers and a percent.

Method

The study was accomplished as follows:

- Written approval:

Written approval to carry out the study was obtained from the Ethical Committee of the Faculty of Nursing, Alexandria University. Also, an official letter was submitted from the Faculty of Nursing, Alexandria University, to the head of out-patient clinics of Alexandria Main University Hospital to obtain their approval for conducting the study, after explaining the aim of the study.

- Tool development:

Tool I: Socio-demographic characteristics, clinical data, and patients' knowledge structured interview schedule was developed by the researcher based on a review of the recent related literature (Esmail, 2019; Hennell et al., 2004; Mäkeläinen et al., 2009). Tool II: Korean Version of the Hill-bone medication adherence subscale was adapted by the

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researcher (Culig & Leppe, 2014). Tool III: factors associated with medications adherence among patients with rheumatoid arthritis was developed by the researcher based on a review of the relevant literature (Bae et al., 2016; Behnood-Rod et al., 2016; World Health Organization, 2003). The three tools were translated into the Arabic language by the researcher after reviewing of relevant literature and according to the jury.

- Testing of content validity:

The three tools were submitted to jury members of five experts in the field of Medical-Surgical Nursing, to assure the content validity, completeness, and clarity of items and appropriateness of translations. Every jury member was informed about the aim and method of the study. Comments and suggestions of the jury were considered, and the tools were modified accordingly.

- Reliability testing:

Tool I – part II rheumatoid arthritis patients' knowledge was tested on a sample of 12 subjects using Cronbach's Alpha statistical test for internal consistency of tool items. The data was analyzed; the correlation coefficient was (0.92).

Tool II: Korean Version of the Hill-bone medication adherence subscale was tested on a sample of 12 subjects using Cronbach's Alpha statistical test for internal consistency of tool items. The data were analyzed; the correlation coefficient was (0.88).

Tool III: Factors associated with medications adherence among patients with rheumatoid arthritis was tested on a sample of 12 subjects using Cronbach's Alpha statistical test for internal consistency of tool items. The data were analyzed; the correlation coefficient was (0.82).

- Pilot study:

Before embarking on the actual study, a pilot study was carried out on 12 patients with RA to ascertain the clarity and applicability of the study tools and to identify obstacles that may be faced during data collection and then necessary modifications were done. These patients were excluded from the actual study subjects.

- Data collection:

- Data collection started after securing the administrative approval.
- The final drafts of the developed tools were used to collect data to achieve the objective of this study.
- Data were collected during the morning shift on Sunday, Tuesday, and Thursday from each week at the Rheumatoid Arthritis Outpatient Clinic.
- The patients were interviewed individually for 20-30 minutes after explaining the purpose of the study.
- Data were collected throughout three months from the beginning of December 2020 to the end of February 2021.

- INDENTATIONS AND EQUATIONS

- Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp).
- Qualitative data were described using number and percent.
- Quantitative data were described using range (minimum and maximum), mean, and standard deviation.
- Significance of the obtained results was judged at the 5% level.

The used tests were

1 - Chi-square test

For categorical variables, to compare between different groups

2 - Monte Carlo correction

Correction for chi-square when more than 20% of the cells have expected count

3 - F-test (ANOVA)

For normally distributed quantitative variables, to compare between more than two groups

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III. RESULTS

Table 1: it was noticed that more than one-third of the studied patients (38.3%) were within the age group 40 to less than 50 years, while more than one-quarter (26.7%) were in the age group of 20 to less than 30 years and lower percent (16.7, 18.3% respectively) was noticed within the age group of 30> 40 and 50-60 years. the majority of the studied patients (85.0%) were female. it was found that more than two-third (68.3%) of them were married. it was found that nearly half of the studied patients (48.3%) had a secondary education, while nearly one-quarter (23.3%) of them had a university education.

Concerning the area of residence, it was found that two-third (66.7%) of the studied patients were living in urban areas, nearly half (46.8%) of the studied patients were housewives and more than one-quarter (28.3%) of them had professional work.

As regards the monthly income from a patients' point of view, more than half (60.0%) of the studied patients had an insufficient income. Regarding the type of treatment, it was noticed that more than two-third (70.0%) of the studied patients were treated on the expense of the country (State expense), while (23.3%) of them were treated by their health insurance.

In relation to the body mass index, it was noticed that more than one-third (43.4%) of the studied patients had overweight while one-quarter (25%) of them had normal weight and (18.3, 10 % respectively) of them obese and extremely obese.

Table (1): The Frequency Distribution of the Studied Patients according to their Socio-demographic Characteristics (n=120)

Socio-demographic characteristics	No.	%
Gender		
- Male	18	15.0
- Female	102	85.0
Age in years		
- 20> 30	32	26.7
- 30> 40	20	16.7
- 40> 50	46	38.3
- 50≥ 60	22	18.3
Marital status		
- Single	24	20.0
- Married	82	68.3
- Widow	6	5.0
- Divorced	8	6.7
Level of education		
- Illiterate	14	11.7
- Read & write	14	11.7
- Primary education	4	3.3
- Preparatory education	2	1.7
- Secondary education	58	48.3
- University education	28	23.3
Residence area		
- Rural	40	33.3
- Urban	80	66.7
Monthly income (from patient's point of view)		
- Enough	48	40.0
- Not enough	72	60.0
Occupation		
- Professional work	34	28.3

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- Manual work	10	8.3
- Housewife	56	46.8
- Retired	4	3.3
- Not work	16	13.3
Treatment payment system		
- Health insurance	28	23.3
- Patient expense	8	6.7
- State expense	84	70.0
Body mass index kg/m2		
- Under weight	4	3.3
- Normal weight	30	25.0
- Over weight	52	43.4
- Obese	22	18.3
- Extremely obese	12	10.0

Table II: Shows the frequency distribution of the studied patients according to their clinical data and family history of rheumatoid arthritis. the table showed that more than one-third (36.7%) of the studied patients had a medical history for chronic disease. In relation to the RA duration, it was noticed that nearly two-third (60%) of the studied patients had RA from five years and more.

the study reveals that the majority (95%) of the studied patients discovered the disease by suffering from symptoms. Concerning the discovering symptoms it was noticed that 30% of the studied patients were suffering from joints pain and 25% of them were suffering from early morning joints stiffness, while 41% of the studied patients were suffering from joints pain, early morning joints stiffness, and joint swelling. It was noticed that more than half (58.3%) of the studied patients were not previously hospitalized. Concerning current treatment methods, the table showed that more than two-third (71.7%) of the studied patients were subject to treatment with medication only while more than one-quarter (28.3%) of them subject to physiotherapy and medication.

Table (II): The Frequency Distribution of the Studied Patients according to their Clinical Data and Family History of Rheumatoid Arthritis (n=120)

Clinical Data	No.	%
Medical history for chronic disease		
- Yes	44	36.7
- No	76	63.3
Types of chronic diseases (n=44)*		
- Cardiovascular diseases	10	22.7
- Endocrine diseases	8	18.2
- Hypertensions	32	72.7
- Kidney diseases	4	9.1
- Diabetes mellitus	12	27.3
Disease duration(RA)		
-6 month < 1 year	4	3.3
-1 < 3 years	30	25.0
-3 < 5 years	14	11.7
-> 5 years	72	60.0
disease discovery (RA)		
- Periodic check	4	3.3
- Suffering from signs and symptoms	114	95.0
- Accidentally	2	1.7
Discovery signs and symptoms (RA)		
-Joints pain	36	30.0

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-Joints swelling	4	3.3
-Early morning joints stiffness	30	25.0
-All of the above	50	41.7
Previous hospitalization		
-Yes	50	41.7
-No	70	58.3
Current treatment methods		
-Medications	86	71.7
-Physiotherapy and Medications	34	28.3
Family history of rheumatoid arthritis		
-Yes	40	33.3
-No	80	66.7

Table III: Concerning knowledge of studied patients about RA, it was found that more than half (55%) of them had poor knowledge about RA disease, while more than one third (36.7%) had fair knowledge and only 8.3% had good knowledge

Table (III): The Frequency Distribution of the Studied Patients according to their Levels and Scores of Knowledge about the Rheumatoid Arthritis Disease (120)

Rheumatoid arthritis Patient's Knowledge levels and scores	No.	%
Poor knowledge <50%	66	55.0
Fair knowledge 50-<75%	44	36.7
Good knowledge ≥75%	10	8.3
Total score		
Min. – Max.	4.0 – 16.0	
Mean ± SD.	9.58 ± 2.88	
% score		
Min. – Max.	20.0 – 80.0	
Mean ± SD.	47.92 ± 14.42	

Table IV: Regarding the adherence to medications, the study finding revealed that more than half (53.4%) of the studied patients had moderate adherence to medications, while more than one-third (38.3%) of them had highly adherence and only 8.3 of them had poor adherence to medication.

Table (IV): The Frequency Distribution of the Studied Patients according to their Levels and the Total Scores of Adherence of Rheumatoid Arthritis Medications (n = 120)

Levels and scores of medications adherence	No.	%
Poor Adherence<50%	10	8.3
Moderate Adherence 50-<75%	64	53.4
Highly Adherence≥75%	46	38.3
Total score		
Min. – Max.	22.0 – 36.0	
Mean ± SD.	28.60 ± 3.20	
% score		
Min. – Max.	48.15 – 100.0	
Mean ± SD.	72.59 ± 11.84	

Table V: Shows ranking of factors associated with medications adherence. Regarding ranking of factors associated with medications adherence, the table revealed that the therapy related factors rated the highest factors with high main score (58.33 ± 22.76) followed by condition-related factors, educational, social and economic factors, patient-related factors and health care system factors respectively with mean score (57.08 ± 18.39, 50.14 ± 19.95, 48.61 ± 13.50, 48.61 ± 13.50).

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Table (V): The Ranking of Factors Associated with Medications Adherence among Patients with Rheumatoid Arthritis (n=120).

Rank	Factors associated with Medications Adherence	Min. – Max.	Mean ± SD.
1-	Therapy-related factors	12.50 – 100.0	58.33 ± 22.76
2-	Condition-related factors	0.0 – 75.0	57.08 ± 18.39
3-	Educational, social and economic factors	8.33 – 83.33	50.14 ± 19.95
4-	Patient-related factors	22.22 – 94.44	48.61 ± 13.50
5-	Health care system factors	0.0 – 70.0	48.61 ± 13.50

Table (VI): Demonstrates the relationship between the overall medications adherence levels and socio-demographic characteristics of the studied patients

The table showed that the highest percentage of the studied patients who had high adherence level to medications were between age from 20 to less than 30 years, females, married, housewives, university educated, over weighted and had enough income (34.8%, 91.3%, 60.9%, 43.5%, 43.6%, 39.2%, 52.2%) respectively.

There were statistical significant relations between age, level of education, income, occupation and body mass index and overall adherence level of the studied patients to medications. (MCP=0.017, MCP=<0.001, P= 0.008, MCP=0.033, MCP=0.001) respectively.

It was found that, there were no statistical significant relationships between adherence level to medications and some of socio-demographic characteristics of the studied patients as regards gender, marital status, residence area, and treatment payment system as P-values were > 0.05.

Table (VI): The relationship between overall medications adherence levels and socio -demographic characteristics of the studied patients (n=120).

Socio-demographic characteristics	Overall medications adherence levels						χ ²	P
	Poor Adherence< 50% (n = 10)		Moderate Adherence 50-<75% (n = 64)		Highly Adherence≥75 % (n = 46)			
	No.	%	No.	%	No.	%		
Gender								
Male	2	20.0	12	18.7	4	8.7	2.336	0.311
Female	8	80.0	52	81.3	42	91.3		
Age (years)							14.293 *	MCP= 0.017*
20> 30	2	20.0	14	21.9	16	34.8		
30> 40	4	40.0	8	12.5	8	17.4		
40> 50	4	40.0	32	50.0	10	21.7		
50≥60	0	0.0	10	15.6	12	26.1		
Marital status							9.884	MCP= 0.087
Single	2	20.0	8	12.5	14	30.4		
Married	8	80.0	46	71.9	28	60.9		
Widow	0	0.0	6	9.4	0	0.0		
Divorced	0	0.0	4	6.2	4	8.7		
Level of education							26.363 *	MCP
Illiterate	0	0.0	8	12.5	6	13.0		
Read & write	4	40.0	8	12.5	2	4.3		

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Primary education	0	0.0	2	3.1	2	4.3		<0.001
Preparatory Education	0	0.0	2	3.1	0	0.0		*
Secondary education	4	40.0	38	59.4	16	34.8		
University Education	2	20.0	6	9.4	20	43.6		
Residence area								
Rural	2	20.0	26	40.6	12	26.1	3.418	0.181
Urban	8	80.0	38	59.4	34	73.9		
Income (from patients' view point)								
Enough	0	0.0	24	37.5	24	52.2	9.674*	0.008*
Not enough	10	100.0	40	62.5	22	47.8		
Occupation								
Professional work	0	0.0	18	28.1	16	34.8	14.936	MCp=
Manual work	2	20.0	8	12.5	0	0.0	*	0.033*
Housewife	6	60.0	30	46.9	20	43.5		
Retired	0	0.0	2	3.1	2	4.3		
Not work	2	20.0	6	9.4	8	17.4		
Treatment payment system								
Health insurance	1	10.0	19	29.7	8	17.4	4.961	MCp=
Patient expense	0	0.0	6	9.4	2	4.3		0.256
State expense	9	90.0	39	60.9	36	78.3		
Body mass index kg/m2								
Under weight	0	0.0	2	3.1	2	4.3	22.327	MCp=
Normal weight	0	0.0	22	34.4	8	17.4	*	0.001*
Over weight	8	80.0	26	40.6	18	39.2		
Obese	0	0.0	6	9.4	16	34.8		
Extremely obese	2	20.0	8	12.5	2	4.3		

Table (VII): Demonstrates the relationship between the overall medications adherence levels and clinical data of the studied patients. The table showed that the studied patients who had high adherence level to medications had no medical history for chronic disease, RA duration five years and more, and had family history of rheumatoid arthritis (56.5%, 43.5%, 30.4%) respectively.

The table also showed that there were a statistically significant relationship between RA disease duration and family history for RA and overall adherence level of the studied patients to medications (MCp= 0.003, P= 0.035) respectively.

It was found that, there were no statistically significant relations between medical history for chronic disease and current treatment method and overall adherence level of the studied patients to medications as P-values were >0.05

Table (VII): The Relationship between the Overall Medications Adherence Levels and Clinical Data of the Studied Patients (n = 120).

Clinical Data	Overall medications adherence levels						χ^2	P
	Poor Adherence<50% (n = 10)		Moderate Adherence 50-<75% (n = 64)		Highly Adherence≥75% (n = 46)			
	No.	%	No.	%	No.	%		
Medical history for chronic disease								
Yes	6	60.0	18	28.1	20	43.5	5.274	0.072
No	4	40.0	46	71.9	26	56.5		

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Disease duration(RA)								
6 month < 1 year	0	0.0	0	0.0	4	8.7	17.109*	MCp= 0.003*
1 < 3 years	0	0.0	12	18.8	18	39.1		
3 < 5 years	2	20.0	8	12.5	4	8.7		
≥ 5 years	8	80.0	44	68.7	20	43.5		
Current treatment methods								
Medications	8	80.0	46	71.9	32	69.6	0.443	0.801
Physiotherapy and Medications	2	20.0	18	28.1	14	30.4		
Family history of rheumatoid arthritis								
Yes	0	0.0	26	40.6	14	30.4	6.705*	0.035*
No	10	100.0	38	59.4	32	69.6		

Table (VIII): Shows the relationship between the studied patients' overall knowledge related to rheumatoid arthritis disease and their level of adherence to medications. Regarding relationship between the studied patients' knowledge and their level of medications adherence, the study finding revealed that, there was no statistical significant relationship between the studied patients' knowledge and their level of medications adherence as P-values was > 0.05.

The table showed that good knowledge level was more prevalent among studied patients with moderate adherence level 60% compared to those with highly adherence level 20% only.

Table (VIII): The Relationship between the Studied Patients' Overall Knowledge related to Rheumatoid Arthritis Disease and their Level of Adherence to Medications (n = 120)

Adherence level	Knowledge level						χ ²	MCp
	Poor (n = 66)		Fair (n = 44)		Good (n = 10)			
	No.	%	No.	%	No.	%		
Poor Adherence <50%	6	9.1	2	4.5	2	20.0	4.180	0.360
Moderate Adherence 50-<75%	36	54.5	22	50.0	6	60.0		
High Adherence ≥75%	24	36.4	20	45.5	2	20.0		

Table (IX): Shows the relationship between overall medications adherence level and factors associated with medications adherence among studied patients

Concerning the relationship between factors and medications adherence level, the study finding revealed that there were a statistically significant relation between the all factors (Therapy-related factors, condition-related factors, patient-related factors, educational, social and economic factors, and health care system factors) associated with medications adherence among studied patients and their adherence level to medications as p-value <0.001.

Table (IX): The Relationship between Overall Medications Adherence Level and Factors Associated with Medications Adherence among Studied Patients (n = 120)

Factors associated with medications adherence	Overall medications adherence level			F	p
	Poor Adherence <50% (n = 10)	Moderate Adherence 50-<75% (n = 64)	High Adherence ≥75% (n = 64)		
Therapy-related factors	85.0 ± 12.91	57.42 ± 23.33	53.80 ± 19.87	8.856*	<0.001*
Condition-related factors	70.0 ± 10.54	60.16 ± 16.50	50.0 ± 19.72	7.517*	0.001*
Patient- related factors	67.78 ± 21.40	45.31 ± 11.30	49.03 ± 10.69	14.802*	<0.001*
Educational, social and economic factors	63.33 ± 22.64	54.17 ± 17.94	41.67 ± 19.08	8.618*	<0.001*
Health care system factors	60.0 ± 9.43	38.13 ± 15.21	43.91 ± 11.83	11.786*	<0.001*

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IV. DISCUSSION

Rheumatoid arthritis is an autoimmune systematic inflammatory disease primarily characterized by synovitis which is accompanied by extra-articular organ involvement. Although this inflammatory process is reversible, it may progress into irreversible damage of articular structures if left untreated and may lead to loss of function. Disease-modifying anti-rheumatic drugs remain the first line treatment of RA. RA treatment aims to achieve remission, or low disease activity, avoid joint damage and disability, maintaining the quality of life, and controlling extra-articular manifestations (Oh, Park, & Moon, 2019; Tanaka, 2020).

Therapeutic success depends on both drug efficacy and medication adherence. Therefore, medication adherence is essential for desired clinical outcomes. Non-adherence to the medications leads to poor disease control, increased morbidity, and recurrent hospitalization with consecutively increased utilization of health resources (Oh et al., 2019). As regarding the socio-economic status, it was one of the most important factors affecting medications adherence and the overall health of rheumatoid arthritis patients, this study revealed that more than half of the patients had insufficient income. It could be due to the high cost of treatment, the financial burden of follow-up and some of the studied patients were unemployed. This finding was in line with (Li et al., 2020) who mentioned that the majority of their studied patients had insufficient income which was mainly due to the financial burden of RA treatment.

Concerning the family history of RA, the present study revealed that one-third of the studied patients had a positive family history of RA. This finding can be interpreted by the fact that the family history of RA is considered as a risk factor for developing RA in relatives. This finding is supported by (Murata et al., 2020) who stated that family history is an indicator for an individual's genetic and environmental risk of developing RA, and family history of RA is one of the strongest risk factors for disease onset, with a threefold to fivefold increase in risk. Regarding patients' knowledge about RA medications, the present study revealed that more than two-thirds of studied patients know the name of their medications. These findings may be related to the fact that most of the studied patients have a high level of education between secondary and university levels. These results were congruent with (Mäkeläinen, Vehviläinen-Julkunen, & Pietilä, 2009) who stated that three-quarters of their studied patients knew the names of medications they are taking.

Regarding the type and action of prescribed medications, the present study found that the majority of the studied patients know the types of medication they were taking but nearly two-thirds of them did not know the action. This finding may be related to the fact that the patients take many medications per day which makes them confused about action of each medication. This is consistent with (Kamruzzaman et al., 2019) who stated that two third of their studied patients didn't know the action of medication they were taking. Moreover if medications cause side effects, the present study revealed that more than one-third of studied patients continuing to take it as prescribed, while one-quarter of them reduce the dose by themselves. This finding may be related to the fact that the benefit of medication exceeds its side effects. This finding was in line with (Bernier, Erlacher, Fenzl, & Dorner, 2019) who stated that nearly one-quarter of their studied patient took fewer drugs than prescribed when they experienced side effects.

Concerning measures that the studied patients adopted when they forget to take medication on time the study found that half of them were taking it when they remember while nearly half of them skip the dose and take another on time. This may be related to the burden medication schedule per day. This result is in accordance with (Ubaka et al., 2021) who pointed that fifty percent of their studied patient if forget the dose of their medications take it when they remember and the others skip it. Furthermore the present study finding revealed that more than one-third of studied patients were taking medications for another chronic disease as hypertension, diabetes mellitus, and cardiovascular disease and more than two-third of them were taking more than one drug at the same time.

It could be related to the fact that the patients are afraid of forgetting some dose of their medications also burden medication schedule per day and other medication for associated comorbidity all of this makes the patients taking more than one drug at the same time. This finding is supported by (Bharthi et al., 2019) who stated that more than one-third of their studied patients receiving medications for another chronic disease and three-quarters of them take more than one drug at the same time due to the polypharmacy.

Concerning the knowledge of studied patients about RA disease, it was found that more than half of them had poor knowledge. Although the most of studied patients had a high educational level, their knowledge level related to the disease was low. In the fact, the patients had general information about the disease and the specific point as, laboratory investigation,

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treatment modalities, extraarticular complications, and so on the most of patients unfamiliar with it. On the other hand, the patients were reported that they did not like to read more about the disease to avoid frustration. This finding is in line with (El Saman, Mohamed, Khalifa, Meghezal, & Radwan, 2020) who reported that half of their studied patients had bad knowledge levels about RA disease. While half of the studied patients had moderate adherence to medications, while more than one-third of them had high adherence and a small percent of them had poor medication adherence. This high adherence rate may be related to patients perceive the benefit of medications and fear from recurrent disease flares as most of them experienced disease flares previously. This result agrees with (Kim et al., 2018) who found that the majority of their studied patients were adherent and a low percentage of them were poor adherent.

Regarding the educational, social, and economic factors, the findings of the current study showed that three-quarters of the studied patients could read and understand the medical guidelines. It could be related to the fact that most of the studied patients had a higher educational level, and this makes them aware of their disease and its complications and the importance of its treatment, which is considered an important factor for medication adherence. This result is supported by (Joplin, van der Zwan, Joshua, & Wong, 2015) who illustrated that medication non-adherence may be affected by low levels of health literacy and patient educational level. Furthermore, more than half of the studied patients reported that their family members were helping them to take medication regularly. In the fact social support play an important role in the life of RA patients as the patients sometimes suffering from disease flares and can not be bringing their medications by themselves also may forget some doses and family member reminded them. This is consistent with (Bharthi et al., 2019; Feldman, Lii, Gopalakrishnan, Franklin, & Kim, 2018; Mora et al., 2021) who stated that strong family support is vital for the management of chronic conditions like RA. Patients who had little or no family support were noted to be poorly adherent to medications.

Regarding the condition-related factors, the study finding revealed that the most of studied patients were thinking that RA is a chronic disease and can not be cured and cause psychological problems as depression. The long-term therapy needed for rheumatoid arthritis restricts the patient to change their lifestyle and make the patients more stressed and liable for a psychological problem that can negatively affect adherence level. This is in line with (Ismail et al., 2017) who reported that chronic diseases as rheumatic disorders can often be complex and require that the patient take multiple medications at various times throughout the day for the rest of life, this effect on psychological status which was considered as sources of non-adherence among patients with rheumatic disorders.

Regarding symptoms, the majority of the studied patients were suffering from symptoms that affect daily life activities, and more than two-thirds of them have symptoms despite taking their medication. These symptoms may be related to disease activity which indicates that patients are not taking their medications exactly as prescribed by the doctor, overtime patients cannot tolerate pain and have to adhere to treatment. This finding is supported by (Wabe et al., 2017) who stated that non-adherence was associated with increasing disease activity. Medications side effects that affecting their daily life activities. The long-term therapy of RA with multiple medications' was associated with a serious side effect in the long run and may lead to poor adherence. This result is in line with (Jack, McCutchan, Maier, & Schirmer, 2020) who reported that polytherapy is common and considerable in RA patients and makes them at risk for medication side effects, also it had a negative impact on health-related quality of life.

Regarding patient-related factors, it included two subcategories; physical factors and psychological and behavioral factors. Concerning physical factors, the study finding revealed that half of the studied patients had vision problems. The vision problem may affect the patient's ability to read medication related instructions. This finding is congruent with (Ismail et al., 2017) who stated that visual impairment was the most notified physical factor that affects the adherence level of their studied patients.

Concerning psychological and behavioral factors, the present study revealed that the majority of the studied patients had information about RA disease, knew the severity of the disease and its complications, knew the need for the medication, and knew the importance of taking the medication regularly. In addition to nearly two-thirds of them were expecting that the treatment was beneficial and had a positive result for the disease. In fact, if the patients perceived the importance of adherence and the benefit of medication and its positive effect on disease this makes them more adherent to medications. This result is supported by (Alhefny, Abd El-Rahman, et al., 2016) who reported that an important factor contributing to non-adherence in patients with RA in our study was the patient's lack of belief in the benefit of treatment, and patients seem to have better adherence when the treatment regimen makes sense to them: when the treatment seems effective, the benefits seem to exceed the risks/costs, and when they feel they have the ability to succeed at the regimen.

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Concerning the relationship between overall medications adherence levels and RA disease duration, the current study found that there was a statistically significant relationship between the disease duration and overall adherence level to medications in which patients who had longer disease duration more adherence than those who had shorter disease duration. This can be justified by the most of the studied patients may be suffering from high disease activity. This finding were supported by (Berner et al., 2019) who found significant relation between longer disease duration, disease flares and medications adherence among their studied patient .

V. CONCLUSION

In conclusion, this study revealed that most of the studied patients with RA were adherent to their medications, and more than half of them had poor knowledge related to RA disease. In addition to it was found no statistically significant relationship between studied patients knowledge related to RA disease and their level of medications adherence.

VI. RECOMMENDATIONS

Based on the findings of the present study the following recommendation are derived and suggested:

Recommendations for patients:

- Develop and apply an educational sessions in order to improve patients knowledge regarding the rheumatoid arthritis disease and its treatment.
- Colored illustrated booklet should be available and distributed for each patient with rheumatoid arthritis about the complication of rheumatoid arthritis and medications instructions.
- Prepare simplified illustrated and comprehensive videos to be presented to patients with rheumatoid arthritis to improve their knowledge and self-efficacy.

Recommendations for nurses:

- Manual guideline for nurses working with rheumatoid arthritis patients about recent update in rheumatoid arthritis disease and its treatment.
- Regular scientific meetings for both physicians and nurses those provide direct care for patients with rheumatoid arthritis must be conducted to discuss patients' problems and to detect barriers of adherence to the medication regimen.

Recommendations for further Studies:

- Effect of medication adherence on disease activity among patients with rheumatoid arthritis
- Impact of medication adherence on quality of life among patients with rheumatoid arthritis
- Study the impact of health teaching program increasing patients' knowledge and improve their adherence to the therapeutic regimen
- Replication of the same study on a larger sample of rheumatoid arthritis patients at different geographical areas for evidence of the results and generalization.

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