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Psycho-cognitive factors and adherence to disease-modifying biologic therapies in patients with rheumatoid arthritis: A cross-sectional study

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Abstract

Introduction: Therapeutic adherence with biologic therapies is crucial for optimal treatment outcomes in rheumatoid arthritis (RA).

Materials and Methods: This single-center, cross-sectional study aimed to assess biotherapy adherence in Moroccan RA patients and investigate its relationship with psycho-cognitive factors, including depression, anxiety, pain catastrophizing, and fibromyalgia.

We evaluated 67 RA patients at Ayachi University Hospital – Salé, using the Girerd questionnaire for medication adherence, a French adaptation of the 6-item MMAS (Morisky Medication Adherence Scale), the Hospital Anxiety and Depression Scale (HAD) Pain Catastrophizing Scale (PCS), and Fibromyalgia Rapid Screening Tool (FIRST).

Results: The sample population was predominantly female (92.5%), with a mean age of 55.5 years ± 13.7 years. Most patients received Rituximab (52.2%), followed by anti-TNF drugs (35.9%) and anti-IL6 drugs (11.9%). Results revealed poor adherence in 71.6% of patients, with a high prevalence of psychological comorbidities: anxiety (100%), depression (98.5%), pain catastrophizing (53.7%), and fibromyalgia (19.4%).

In univariate analysis, poorer adherence was associated with a higher Health Assessment Questionnaire (HAQ) score (OR = 0.24; 95% CI [0.09 – 0.64]; p = 0.004) and a longer history of RA (OR = 0.92; 95% CI [0.85 – 0.99]; p = 0.043). Multi-medicated patients had poorer adherence (OR = 3.12; 95% CI [1.03 - 9.42]; p = 0.043), as did those with pain catastrophizing (OR = 3.61; 95% CI [1.16 - 11.18]; p = 0.02).

Surprisingly, anxiety, depression, and fibromyalgia did not significantly affect adherence.

Conclusion: This study reported a low rate of adherence to biotherapy (28.4%) in Moroccan RA patients, with key factors such as disease duration, HAQ index, polypharmacy and pain catastrophizing significantly affecting adherence.

These findings highlight the need for tailored therapeutic education and management strategies to improve biotherapy adherence in RA patients.

Keywords: Rheumatoid arthritis; Medication adherence; Biological disease-modifying antirheumatic drugs (bDMARDs); Girerd

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1. Introduction

Rheumatoid Arthritis (RA) is the most common chronic inflammatory rheumatic disease, with a global prevalence between 1980 and 2019 of 0.46%, with variations due to geographical location [1]. It is a potentially severe autoimmune condition characterized by bilateral and symmetrical joint involvement, progressing in flares and leading to joint deformation and destruction, along with extra-articular manifestations affecting such as pulmonary, cardiac, ocular, and cutaneous systems. [2].

In RA management, treatment guidelines recommend a "Treat to Target" approach, aiming for low disease activity or remission [2]. This approach relies on conventional (csDMARDs) and/or biological (bDMARDs) disease-modifying therapies to control symptoms, induce remission and prevent structural damage. Poor compliance and lack of persistence with prescribed medications result in increased morbidity, mortality, and higher healthcare costs [3].

Medication compliance is defined as "the extent to which a patient acts in accordance with the prescribed interval and dose of a dosing regimen". While medication adherence is defined as "the act of conforming to the recommendations made by the provider with respect to timing, dosage, and frequency of medication taking" [3]. The difference between the two terms lies in the existence, in medication adherence, of active and voluntary participation by the patient in applying medical recommendations, as well as doctor-patient collaboration in decision-making [4].

In RA specifically, non-adherence can lead to treatment failure, delayed recovery, accelerated disease progression and the need for more aggressive treatment [4].

The management of RA is further complicated by the complex nature of pain in these patients. Beyond inflammatory pain, some patients experience nociplastic pain associated with fibromyalgia or manifest psycho-cognitive disorders such as depression, anxiety and pain catastrophizing. In these cases, biological treatments alone may be insufficient for optimal pain control [5]. Understanding these psychological factors becomes crucial as they might influence treatment adherence and outcomes.

Several validated tools are available to assess medication adherence, including the Girerd questionnaire, a French adaptation of the 6-item MMAS (Morisky Medication Adherence Scale) [6].

Medication adherence to bDMARDs in RA patients, as well as the specific factors affecting biotherapy adherence, particularly in relation to psycho-cognitive disorders and fibromyalgia, have not been previously investigated in our population. Therefore, given the potential impact of psychological factors on treatment success, this study aims to measure adherence to biotherapy in Moroccan RA patients using the Girerd questionnaire, and to investigate whether adherence is influenced by psycho-cognitive disorders or the presence of associated fibromyalgia.

2. Material and methods

2.1. Study Design and Setting

This cross-sectional study was conducted at the Rheumatology Department B of El Ayachi Hospital, Salé, Morocco between March and June 2024. El Ayachi Hospital serves as a national reference center for rheumatic diseases.

2.2. Study Population

2.2.1. Eligibility Criteria

Eligible participants were adults (≥18 years) diagnosed with RA according to the 2010 American College of Rheumatology/ European League Against Rheumatism (ACR-EULAR 2010) classification criteria. According to the inclusion criteria, participants had to be receiving biological treatment for at least 3 months. The date of recruitment served as the index date.

2.2.2. Recruitment

Patients receiving biological treatment with regular hospital follow-up and meeting eligibility criteria were consecutively enrolled. Patients who declined participation or were lost to follow-up were excluded.

2.3. Data Collection

Patients were evaluated by a rheumatologist during scheduled visits, which were coordinated with their treatment schedule: on the day of infusion for patients receiving intravenous bDMARDs, and during regular consultation visits every three months for those on subcutaneous bDMARDs. These visits served as index dates for data collection.

At each scheduled visit, comprehensive clinical assessments were conducted, including detailed physical examination focusing on joint tenderness and clinical synovitis, along with collection of anamnestic and paraclinical data. Evaluations of biotherapy adherence, psycho-cognitive factors, and fibromyalgia scores were systematically performed at the end of each appointment. For patients unable to complete in-person assessments, follow-up was conducted via telephone consultation with their attending rheumatologist. Questionnaire completion implied consent for data use, and all information was analyzed anonymously.

All patients undergoing biological treatment have a data file, in both paper and electronic form, documenting medical history, current treatments, clinical progression and biological markers under treatment, as well as any side effects.

Socio-demographic data included age, gender, marital status, employment status, residential environment, educational level, monthly income, and health insurance coverage.

Clinical data were directly collected from patients, including the number of painful and swollen joints, the visual analogue pain scale scores and the HAQ (Health Assessment Questionnaire) answers. Comorbidities such as diabetes, hypertension, thyroid disorders, pulmonary and cardiovascular conditions, gastric and hepatic pathologies, renal failure, neoplasia and stroke were also recorded.

We measured disease activity using the Disease Activity Score (DAS28) based on erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP).

For subcutaneous bDMARDs, patients received initial nurse-supervised training in self-injection techniques. At a follow-up appointment, patients performed self-injections under nurse guidance. Depending on preference, subsequent injections were self-administered under supervision, received at local health centers, or administered by the hospital staff. Patients on intravenous bDMARDs were monitored on infusion days, which served as the reference date for data collection.

2.4. Endpoint Measures

2.4.1. Primary Endpoint

The primary endpoint of the study is the prevalence of RA patients with good biotherapy adherence, assessed using the modified Girerd questionnaire. Modifications included adapting questions 1/3/6 to better reflect biotherapy administration.

2.4.2. Modified Items

- Item 1: “Did you forget to take your medication this past month?” We replaced “this morning” with “this past month”.
- Item 3: “Have you ever taken your treatment later than the usual date? “Time” is replaced with “date”, which was more in line with biotherapy treatment.
- Item 6: “Do you think you have too many medications to take?” was also modified by replacing “tablet” with “medications”.
- A “Yes” response is scored 1 point, a “No” response 0 points. Scores range from 0-6, with 0 indicating “good therapeutic adherence” and ≥1 indicating “therapeutic adherence problems”.

2.4.3. Secondary Endpoints

Secondary endpoints included prevalence of psycho-cognitive factors—depression, anxiety, pain catastrophizing —and fibromyalgia, as well as their influence on biotherapy adherence.

To evaluate depression and anxiety disorders, we applied the Hospital Anxiety and Depression Scale (HAD) which includes two subscales -one for anxiety and one for depression- each consisting of seven items scored from 0 to 3. According to HAD criteria, patients scoring 7 or lower show no anxiety or depressive symptoms, scores between 8 and

10 indicate possible symptoms, and a score of 11 confirms the presence of symptoms [7]. For this study, we included only patients with definite symptomatology (Score ⩾ 11).

The Pain Catastrophizing Scale (PCS) was designed to evaluate pain catastrophizing trait. It is a questionnaire with 13 items, each rated by the patient from 0 to 4, based on their agreement with specific thoughts or emotions occurrence when experiencing pain. A PCS score of 30 out of 52 was defined as clinically relevant [8].

Fibromyalgia diagnosis was made using the FiRST (Fibromyalgia Rapid Screening Tool) questionnaire where a score above 4 out of 6 suggests fibromyalgia, with a sensitivity of 90.5% and specificity of 85.7% [9].

2.5. Statistical analysis

The data were input and analyzed, and a descriptive analysis of the validated data was performed subsequently. Qualitative variables were described in terms of numbers and percentages, and quantitative variables were presented as means and standard deviations, and medians with interquartile ranges, as appropriate.

For comparisons between groups, qualitative variables were analyzed using the Chi-square test, while quantitative variables were compared using Student's t-test if the normality of distribution and homogeneity of variances were met. When the distribution was not normal, a Mann-Whitney test was applied. If necessary, variables were transformed.

We performed univariate analysis using logistic regression. The results for each variable were reported as odds ratios with corresponding confidence intervals.

All statistical analyses were performed using JAMOVI 2.3.18 software.

3. Results

3.1. Socio-demographic, clinical and biological characteristics

Out of the 92 initial patients, 67 were included in the final analysis. Among the 25 excluded patients, 16 could not be reached by telephone to complete their interviews, 5 were lost to follow-up, 3 encountered medical coverage issues preventing treatment access, and 1 relocated to another town.

The study population was predominantly female (92.5%) and resided in urban areas (88.1%). The mean age was 55.5 ± 13.7 years. Most patients were unemployed (76.1%), illiterate (43.3%) and had no income (73.1%). Only 14.9% lived alone (Table 1).

Table 1 Socio-Demographic characteristics of study respondents

Gender: Female*	62 (92.5)
Age (years) **	55.5 ± 13.7
Residence area, Urban*	59 (88.1)
Marital Status*	
Single	15 (22.4)
Married	39 (58.2)
Divorced	7 (10.4)
Widowed	6 (9.0)
Educational Level*	
Illiterate	29 (43.3)
Primary	14 (20.9)
Middle school	2 (3.0)
High school	8 (11.9)

University	14 (20.9)
Work*	
Active	7 (10.4)
Unemployed	51 (76.1)
Retired	9 (13.4)
Monthly Income*	
< SMIG	8 (11.9)
≥ SMIG (approximately equivalent to 290 €)	10 (14.9)
No income	49 (73.1)
Lifestyle*	
Alone	10 (14.9)
Lives with family	57 (85.1)
Medical care*	
No medical cover	0
Compulsory health insurance	40 (59.7)
CNSS/CNOPS	27 (40.3)
Private	0

* Expressed as n (%); ** Expressed as mean and standard deviation.

In addition to RA, patients were being monitored for various comorbidities, with 56.7% of patients taking multiple medications. The most prevalent comorbidities were arterial hypertension (59.7%), followed by diabetes (54.8%), thyroid disorders (26.2%), and liver disease (23.8%).

The majority of patients had seropositive (65.7%) and erosive (83.6%) RA, with a median disease duration of 12 years (8-19.5). Laboratory findings indicated a median ESR of 25 mm (12- 40) in the first hour, and CRP levels were not elevated [5 mg/L (2.35- 13.9)].

Disease activity assessment based on DAS28 (CRP) placed 22 patients (32.8%) in remission, with others showing low (9%), moderate (34.3%) or high (23.9%) disease activity. The HAQ functional score indicated mild to moderate difficulties 0.87 (0.25- 1.50); and patients reported mild pain levels [VAS 4 (2- 5)] (Table 2).

Table 2 Clinical and Paraclinical characteristics of the population

Comorbidities*	40 (59.7)
Hypertension	23 (54.8)
Diabetes	11 (26.2)
Thyroid disease	10 (23.8)
Hepatic disease	2 (4.8)
Gastric disease	4 (9.5)
Cardiovascular disease	2 (4.8)
Pulmonary pathology	4 (5.9)
Neoplasia	0
Renal failure	0

Stroke	0
Other	4 (9.5)
Polypharmacy*	38 (56.7)
Disease duration (years)*	12 (8- 19.5)
Presence of rheumatoid factor and/or anti-CCP antibodies*	44 (65.7)
Structural damage*	56 (83.6)
ESR (mm/h),**	25 (12- 40)
Reactive-C-Protein (mg/L)**	5 (2.35- 13.9)
DAS28 (CRP)*	
Remission ≤ 2.6	22 (32.8)
2.6 < Low activity ≤ 3.2	6 (9.0)
3.2 < Moderate activity ≤ 5.1	23 (34.3)
> 5.1 High activity	16 (23.9)
Pain (VAS 0-10)**	4 (2- 5)
HAQ**	0.87 (0.25- 1.50)

* Expressed as n (%); ** Expressed as median with interquartile ranges

3.2. Treatment

Among the 67 treated patients, only 4.5% received bDMARD monotherapy, while the majority (95.5%) were on combination therapy with bDMARDs and csDMARDs. Methotrexate was the most commonly prescribed csDMARD (55.2%), administered either orally (67.6%), or subcutaneously (32.4%); followed by Leflunomide (29.9%) and Sulfasalazine (12.1 %). No patient was taking hydroxychloroquine.

Regarding symptomatic treatments, 25.4% of patients were taking non-steroidal anti-inflammatory drugs (NSAIDs), and 86.6% remained on corticosteroids.

Out of the 35 patients taking biotherapy, Rituximab was most frequently prescribed (52.2%), followed by anti-TNF agents (Infliximab 14.9%, Etanercept 7.5%, Certolizumab pegol 6%, Golimumab 4.5%, and Adalimumab 3%). A small proportion of patients received Tocilizumab (11.9%).

Most patients (89.6%) received their injections at the hospital, while 3% received them at health centers by a health professional, and 7.5% self-injected at home.

All patients had previously received at least one csDMARD prior to their current biological therapy. Additionally, 40.3% patients were on first line biotherapy, while 59.7% had previously received at least one bDMARD prior to their current treatment (Table 3).

Table 3 Treatment features in the population

NSAIDs (nonsteroidal anti-inflammatory drugs)*	17 (25.4)
Methotrexate (MTX)*	37 (55.2)
Route of administration of MTX*	
By injection	12 (32.4)
Oral route	25 (67.6)
Sulfasalazine*	8 (12.1)
Leflunomide*	20 (29.9)

Hydroxychloroquine*	0
Corticosteroid*	58 (86.6)
bDMARDs as monotherapy vs. in association*	
Monotherapy	3 (4.5)
in association with csDMARDs	64 (95.5)
Type of bDMARDs*	
Rituximab	35 (52.2)
Infliximab	10 (14.9)
Adalimumab	2 (3)
Golimumab	3 (4.5)
Etanercept	5 (7.5)
Certolizumab Pegol	4 (6)
Tocilizumab	8 (11.9)
Type of Health care facility*	
Injection at home	5 (7.5)
Injection in a health center by a health professional	2 (3)
Injection at the hospital	60 (89.6)
First line biotherapy*	27 (40.3)
Prior Biotherapy*	40 (59.7)

* Expressed as n (%).

3.3. Adherence to biologics, prevalence of psycho-cognitive factors and factors associated with good or poor adherence

A majority of patients (71.6%) had poor adherence to biotherapy (Girerd score⩾1). Depression was nearly universal (98.5%) and anxiety disorders were present in all patients (100%). Pain catastrophizing was observed in 53.7% of patients, while 19.4% had FiRST scores indicating associated fibromyalgia (Table 4).

Table 4 Adherence to biologics and Prevalence of psycho-cognitive factors in the population

Girerd questionnaire*	
Good adherence	19 (28.4)
Low adherence	48 (71.6)
HAD*	
HAD D	66 (98.5)
HAD A	67 (100)
FIRST*	13 (19.4)
Pain Catastrophizing PCS*	36 (53.7)

* Expressed as n (%).

Table 5 demonstrates significant associations between adherence and RA duration, HAQ index, pain levels, and polypharmacy.

However, socio-demographic factors, autoantibody status, structural damage, comorbidities, disease activity, and inflammatory markers did not influence biotherapy adherence.

Table 5 Comparison of sociodemographic, clinical, and paraclinical characteristics between adherence groups

	Low adherence	**Good adherence**	***p***
Gender: Female*	45 (72.6)	17 (27.4)	0.54
Age (years)**	56 ± 14.2	54.4 ± 12.6	0.68
Residence area*			
Urban	44 (74.6)	15 (25.4)	0.14
Rural	4 (50)	4 (50)	
Marital Status*			
Single	11 (73.3)	4 (26.7)	0.34
Married	26 (66.7)	13 (33.3)	
Divorced	7 (100)	0 (0)	
Widowed	4 (66.7)	2 (33.3)	
Educational Level*			
Illiterate	19 (65.5)	10 (34.5)	0.67
Primary	11 (78.6)	3 (21.4)	
Middle school	2 (100)	0 (0)	
High school	5 (62.5)	3 (37.5)	
University	11 (78.6)	3 (21.4)	
Work*			
Active	3 (42.9)	4 (57.1)	0.12
Unemployed	37 (72.5)	14 (27.5)	
Retired	8 (88.9)	1 (11.1)	
Monthly Income*			
< SMIC	4 (50)	4 (50)	0.17
≥ SMIC	9 (90)	1 (10)	
No income	35 (71.4)	14 (28.6)	
Lifestyle*			
Alone	9 (90)	1 (10)	0.16
Lives with family	39 (68.4)	18 (31.6)	
Comorbidities*	30 (75.0)	10 (25.0)	0.45
Polypharmacy*	31 (81.6)	7 (18.4)	**0.039**
Disease duration (years) ***	15 (9.5 – 20.0)	11 (6.00- 12.00)	**0.022**
Presence of rheumatoid factor and/or anti-CCP antibodies*	32 (72.7)	12 (27.3)	0.78
Structural Damage	40 (71.4)	16 (28.6)	0.93
ESR (mm/h), ***	28.0 (10.5- 41.5)	20 (15.5- 37.5)	0.63
Reactive-C-Protein (mg/L),***	6.45 (2.88- 13.5)	3 (1.55- 12.5)	0.08
DAS28 (CRP) *			

Remission ≤ 2.6	14 (63.6)	8 (36.4)	0.31
2.6 < Low activity ≤ 3.2	3 (50.0)	3 (50.0)	
3.2 < Moderate activity ≤ 5.1	19 (82.6)	4 (17.4)	
> 5.1 High activity	12 (75.0)	4 (25.0)	
Pain (VAS 0-10)***	4.00 (2.00- 6.00)	2 (1.00- 4.50)	**0.04**
HAQ***	1 (0.57 – 1.90)	0.25 (0.00- 0.75)	**0.001**

* Expressed as n (%); ** Expressed as mean and standard deviation; *** Expressed as median with interquartile ranges

The concurrent use of csDMARDs, glucocorticoids, NSAIDs, type of bDMARDs and type of health care facility did not influence biotherapy adherence (Table 6).

Table 6 Comparison of treatments between adherence groups

	Low adherence	**Good adherence**	***p***
NSAIDs*	15 (88.2)	2 (11.8)	0.07
Corticosteroid*	44 (75.9)	14 (24.1)	0.052
Methotrexate (MTX)*	26 (70.3)	11 (29.7)	0.78
Route of administration of MTX*			
By injection	10 (83.3)	2 (16.7)	0.22
Oral route	16 (64.0)	9 (36.0)	
Sulfasalazine*	5 (62.5)	3 (37.5)	0.48
Leflunomide*	17 (85.0)	3 (15.0)	0.11
bDMARDs as monotherapy vs. in association*			
Monotherapy	1 (33.3)	2 (66.7)	0.13
in association with csDMARDs	47 (73.4)	17 (26.6)	
Type of bDMARDs*			
Rituximab	23 (65.7)	12 (34.3)	0.85
Infliximab	8 (80.0)	2 (20.0)	
Adalimumab	1 (50.0)	1 (50.0)	
Golimumab	4 (80.0)	1 (20.0)	
Etanercept	2 (66.7)	1 (33.3)	
Certolizumab Pegol	3 (75.0)	1 (25.0)	
Tocilizumab	7 (87.5)	1 (12.5)	
Type of Health care facility*			
Injection at home	3 (60.0)	2 (40.0)	0.57
Injection in a health center by a health professional	2 (100.0)	0 (0.0)	
Injection at the hospital	43 (71.7)	17 (28.3)	

* Expressed as n (%).

Among psycho-cognitive factors, only pain catastrophizing showed a significant association with treatment adherence (p=0.022) (Table 7).

Table 7 Comparison of psycho-cognitive factors and fibromyalgia between adherence groups

	Low adherence	**Good adherence**	**p**
HAD D*	48 (72.7)	18 (27.3)	0.10
FIRST*	9 (69.2)	4 (30.8)	0.83
Pain Catastrophizing PCS*	30 (83.3)	6 (16.7)	0.022

* Expressed as n (%).

3.4. Univariate analysis

In univariate analysis (Table 8), poorer adherence was associated with a higher Health Assessment Questionnaire (HAQ) score (OR = 0.24; 95% CI [0.09 – 0.64]; p = 0.004) and a longer history of RA (OR = 0.92; 95% CI [0.85 – 0.99]; p = 0.043).

Multi-medicated patients had poorer adherence (OR = 3.12; 95% CI [1.03 - 9.42]; p = 0.043), as did those with pain catastrophizing (OR = 3.61; 95% CI [1.16 - 11.18]; p = 0.02). Anxiety, depression and fibromyalgia, however, did not affect adherence.

Table 8 Univariate Analysis

	Univariate analysis	
	OR	**95% CI**
Age	0.99	0.95 – 1.03
Gender	1.76	0.27 – 11.49
Residence area	2.93	0.65- 13.20
FIRST score	0.86	0.23 – 3.24
HAD D	N/A	0.00 – infinity
PCS score	3.61	1.16 – 11.18
Monthly Income	0.4	0.08- 1.83
Marital status	1.37	0.17 – 10.65
Educational Level	0.51	0.11 – 2.30
Work	0.09	0.007- 1.21
Lifestyle	4.15	0.48- 35.30
Disease duration	0.92	0.85 – 0.99
Presence of rheumatoid factor and/or	1.16	0.38 – 3.53
anti-CCP antibodies		
HAQ	0.24	0.09 – 0.64
Structural damage	0.93	0.22 – 3.98
comorbidities	1.50	0.51 – 4.38
polypharmacy	3.12	1.03 – 9.42
ESR	0.99	0.96 – 1.01
CRP DAS28(CRP)	0.97 1.71	0.94 – 1.01 0.41 - 7.14
Pain (VAS 0-10)	0.76	0.58 – 1.00

NSAID	3.86	0.79 – 18.89
Corticosteroid	3.92	0.92 – 16.67
Methotrexate	0.86	0.29 – 2.51
Route of administration of MTX	2.81	0.50 – 15.76
Sulfasalazine	0.58	0.12 – 2.73
Leflunomide	2.92	0.74 – 11.48
Biotherapy in monotherapy vs in association	0.18	0.01 – 2.12
Type of bDMARDs	0.47	0.08 – 2.62
Healthcare facilities	0.59	0.09 – 3.87

4. Discussion

Multiple methods exist for assessing treatment adherence, including self-reporting, pill counting, pharmacy dispensing records, electronic pillbox monitoring, laboratory analyses, physician assessment, and graded questionnaires; however, each approach has inherent strengths and limitations, with no universally accepted standard [10].

Our study used the Girerd Questionnaire, a French adaptation of the MMAS-6 item questionnaire. While originally developed for assessing drug adherence in hypertensive patients, the MMAS has been widely adopted across various patient populations [11], including those with chronic pain conditions [12].

In the absence of a standard reference method, we opted for the Girerd score, chosen for its simplicity and brevity. Given that, other questionnaires were used to assess psycho-cognitive factors, the selection of a concise adherence tool particularly suitable for our Moroccan population was essential.

This study revealed poor adherence to biological treatments among 71.6% of patients, which aligns with findings by Mohsen et al. who reported poor adherence in 90.7% of 140 RA patients using the MMAS-8 [13].

In contrast, other studies have reported higher adherence rates among RA patients [6, 14, 15]. For instance, Natalia Mena-Vazquez et al. found an 88.8% adherence with biotherapy in a sample of 178 patients, measured over a 6-month retrospective period using the Medication Possession Ratio (MPR) [14]. The MPR is calculated by dividing the number of days of medication possession based on prescription redemption and refills by therapeutic days [16].

This variability across studies may reflect differences in adherence assessment tools or population-specific factors influencing adherence. For example, Clélia Monchablon et al, employing several tools including the Girerd questionnaire and MPR in their study of 183 patients to assess adherence to RA treatments, revealed that only 7% of patients were poorly adherent according to Girerd scores, while MPR calculations for 84 patients showed 23% poor adherence [6].

Similarly, Le Zhang et al. study examined adherence in 252 patients with rheumatic conditions (RA, ankylosing spondylitis and systemic lupus erythematosus) using both the Compliance Questionnaire for Rheumatology (CQR) and an interview-based self-report finding that 41.7% of patients demonstrated good treatment adherence [17].

These differences underscore the challenge of comparing adherence rates across studies with varying measurement tools and patient populations.

Literature has identified several factors associated with good medication adherence, including the use of reminder tools such as pillboxes and/or preparation of drugs by a patient's relative [6, 17], presence of diabetes as comorbidity [6], young patient age, general satisfaction, on-time medication renewal rate and disease activity [13].

Factors negatively affecting adherence included low levels of education [18], drug side effects [17, 18], employment status, use of alternative therapies [17], disease activity [13, 14] and subcutaneous administration route of bDMARDs [14].

Concerning the factors influencing adherence in our study, duration of RA was found to be significantly associated with adherence in Mohsen et al; and HAQ index as reported by Natalia et al. One possible reason for the link between HAQ index and poor adherence in our population could be that long-term poor adherence is responsible for structural progression of the disease, which may explain the disability found in these patients.

Regarding secondary endpoints, the psychological assessment in our study revealed high rates of anxiety (100%) and depression (98.5%) in the population – substantially exceeding those reported in a systematic review and meta-analysis of 72 studies, where depression prevalence averaged 14.8% among 13189 RA patients. In that analysis, 30 studies used the HAD scale with a threshold of 11, consistent with the threshold applied in our study [19].

Similarly, a systemic review of 47 studies (n = 11,085 participants), with a wide variability of anxiety prevalence in RA patients ranging from 2.4% to 77%, using the HAD scale [20].

This discrepancy may reflect cultural or regional differences in psycho-cognitive responses, suggesting a need for further studies in diverse populations.

While our study found no correlation between fibromyalgia or depression and bDMARDs adherence in RA patients, pain catastrophizing, which was present in 53.7% of our patients, emerged as a significant factor affecting treatment adherence (p=0.022). Although this association has not been widely explored in RA adherence studies, Hilde B Hammer et al. observed that high levels of pain catastrophizing reduced the likelihood of achieving a composite score remission [21].

Conversely, our study found a 19.4% prevalence of fibromyalgia, consistent with Sizheng Steven Zhao's findings of 18-24% in RA patients. However, this result warrants cautious interpretation given the lack of validated Fibromyalgia criteria for inflammatory arthritis patients [22].

This study has several limitations. First, all participants were recruited from a single center which may be more prone to publication bias and may have lower methodological quality than multicenter trials [23].

Second, our use of the Girerd score for treatment adherence assessment, though concise and suitable for the local context, is a subjective tool.

Additionally, the final question of the Girerd score questionnaire, “Do you think you have too many medications to take?” was problematic for many patients. In fact, most of our RA patients were elderly and were frequently on a combination of csDMARD and biological treatments, along with additional medications for comorbidities. As a result, responses to this question may have led to higher perceived non-adherence rates.

5. Conclusion

This cross-sectional study investigated biotherapy adherence among Moroccan rheumatoid arthritis patients, uncovering a concerning low adherence rate of 28.4%. Our analysis revealed significant associations between adherence and several clinical factors, including disease duration, HAQ index, and polypharmacy. Most importantly, we found that pain catastrophizing trait is a key factor significantly associated with biotherapy adherence.

The study identified remarkably high prevalence rates of depression and anxiety, alongside significant presence of pain catastrophizing traits and fibromyalgia. These findings underscore the substantial psychological burden in this population and point to the potential value of a comprehensive approach, incorporating psychological support and pain management strategies in the context of biotherapy treatment.

While our study's focused examination of a specific patient population and comprehensive assessment of various factors represent important strengths, limitations such as the single-center design, subjective nature of adherence measurement tool and cross-sectional nature limit our ability to draw causal inferences. Furthermore, our findings suggest that current assessment tools would benefit from transcultural adaptation to better reflect the Moroccan context.

Future multicenter longitudinal studies could help establish causal relationships and enhance our understanding of biotherapy adherence patterns in Moroccan RA patients, particularly regarding the influence of psychological factors on treatment adherence.

Compliance with ethical standards

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Disclosure of conflict of interest

The authors have declared no conflict of interest.

Author's contributions

All authors have read and agreed to the final version of this manuscript and have equally contributed to its content and to the management of the manuscript.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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