

Medications' Adherence amongst a Sample of Patients with Ankylosing Spondylitis

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ABSTRACT:

BACKGROUND:

Ankylosing spondylitis is a chronic progressive inflammatory disease affecting spine and other joints leads to great disability and chronic pain, and has a notable adverse financial and social effect upon patients' life; for this, a good medicines adherence is demanded to achieve good daily activity and better quality of life.

AIM OF STUDY:

To explore adherence to medicines in Iraqi patients with Ankylosing spondylitis.

PATIENTS & METHODS:

A cross-sectional study enrolled 100 (96 males and 4 females) Iraqi patients with Ankylosing Spondylitis diagnosed according to ASAS criteria. Data collection was done using questionnaires and interview. Adherence quantified using Arabic version of 8-item Morisky Medication Adherence Scale (MMAS-8).

RESULTS:

High score of adherence to medicines in the study population was found, and the mean of the score was (6.8±1.6) with 83% of studied patients showing moderate to high adherence. A strong positive correlation found between the adherence & both the kind of treatment (Non-Steroidal Anti Inflammatory Drugs) and number of medicines taken.

CONCLUSION:

Most of the studied Ankylosing Spondylitis patients were adherent to their treatment.

KEYWORDS: Ankylosing spondylitis, Adherence to medications, Arabic version of 8-item Morisky Medication Adherence Scale (MMAS-8), spondyloarthropathies, Adherence to therapy.

1.INTRODUCTION:

1.1 Ankylosing spondylitis

Ankylosing spondylitis (AS) is one of seronegative spondyloarthropathies (SpA) and it is a chronic inflammatory disease affecting sacroiliac joints, axial skeleton, peripheral joints and some patients have extra articular involvement, such as enthesitis and uveitis⁽¹⁾. The inflammation of the sacroiliac (SI) joints and the spine might lead to bony ankyloses⁽²⁾. Ankylosing spondylitis involves people aged less than 40 years⁽³⁾. The prevalence of Ankylosing Spondylitis comprehensively runs parallel to the prevalence of *HLA-B27*⁽⁴⁾. The worldwide prevalence rates are 238 per 100,000 in Europe, 319 per 100,000 in North America, and 167 per 100,000 in Asia⁽⁵⁾.

In Iraq; the prevalence of Ankylosing Spondylitis was 0.9 %⁽⁶⁾. Spondyloarthritis is a complex interaction between genetic polymorphisms and environmental elements. For Ankylosing Spondylitis, heritability is estimated to be more than 90%, suggesting that environmental factors (immune response, microbial infection, and endocrinopathies) are omnipresent^(7,8).

The diagnosis of Ankylosing Spondylitis at an early phase of disease depends chiefly on a careful history and physical examination with using the classification criteria of Assessment in Spondyloarthritis International Society (ASAS) can be very helpful^(9,10). Ankylosing Spondylitis is a chronic disease that needs long term management & follow up, management divided in to two main types:

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Non-pharmacologic Therapy

The ASAS-EULAR guideline for AS/axSpA recommends exercise for all patients (11). Physical therapy improves outcomes in Ankylosing Spondylitis patients (11,12). In addition to formal physical therapy, patients should perform back exercises and stretching (11).

Pharmacologic Therapy

Non-steroidal anti-inflammatory drugs (NSAIDs) are the first-line medication therapy (11). Response to treatment is rapid and an assessment can be performed at 2 to 4 weeks after commencement (11). Second line medications are the TNF inhibitors (TNFi) with no particular TNFi recommended, but comorbidities and patient preferences may influence choice of agent (11). If failure of treatment with TNFi, it is endorsing to treat with IL-17 inhibitors secukinumab or ixekizumab (11). Traditional conventional synthetic DMARDs (csDMARDs) have been studied without demo of benefit in AS/axial disease (13, 14). There is no evidence that systemic glucocorticoids work well in AS/ axSpA, but local steroid injections may be considered (11).

1.2 Adherence: definition, clinical application

Adherence is defined by the World Health Organization (WHO) as "the degree to which the person's behavior—taking medication, following a diet and/or executing lifestyle changes— corresponds with the agreed recommendations from a healthcare provider" (15). Adherence is the most substantial factor that affects treatment outcomes. Also, poor adherence carries an important economic burden on healthcare costs worldwide (16). There is no gold standard method for monitoring patients' compliance with drug programs. Direct techniques such as the measurement of drug level in blood, serum or urine are very costly, and indirect methods such as the analysis of administrative databases (prescriptions, rate of prescription restocks); pill counts; electronic medication monitors; and self-reported measures by the patient (questionnaires, diaries, interviews) may not be possible on an everyday basis (17,18). Poor medication adherence is quite common. Studies in chronic conditions have shown consistently that twenty to thirty percent of medicine prescriptions are never occupied and that, approximately, fifty percent of chronic diseases' prescriptions are not taken; much higher rates in developing countries (16).

Medication adherence can be influenced by the disease (chronic, asymptomatic, requiring different strategies to reach the goal); cost of medicines and information about their hurt (syndrome of leaflet), dosage scheme and raising skills with administration; plan of treatment (polypharmacotherapy, treatment of acute and chronic phase), experience and skills of personages (motor activity, good vision, cognitive characteristics, etc.); and patient-physician relationship (19). For AS, medication adherence has been more with older age, illness awareness, white race, beliefs about medicines, Quality of Life, choice of drugs and route of administration (20).

2. PATIENTS AND METHODS:

2.1 PATIENTS:

A total of 100 (96 males and 4 females) Iraqi patients with Ankylosing Spondylitis enrolled in the study.

2.1.1 Inclusion criteria

- 1- Patients with Ankylosing Spondylitis as defined by ASAS Classification Criteria for Axial Spondyloarthritis 2016 (11).
- 2- More than 18 years old, both genders who accepted participating in the study.
- 3- Disease duration (after diagnosis) >2 months.
- 4- Current treatment with NSAIDs and/or DMARDs (including methotrexate and sulfasalazine) with or without concomitant administration of biologic agents and if using steroid.
- 5- Patients have not changed their medication in the last three months.

2.1.2 Exclusion criteria

- 1- Patients who had a cognitive deficits or psychological diseases.
- 2- If they were receiving no medication.
- 3- Disease duration (after diagnosis) < 2 months.
- 4- Pregnant and lactating ladies.

2.2 METHODS:

2.2.1 The questionnaire

The data were collected using a sheet containing questionnaire for the patients that include general Socio-demographics data: age, gender, marital status, educational level, smoking, disease duration, type of drug treatment for Ankylosing Spondylitis (classified as use of NSAIDs, steroids, DMARDs, or biologics) & Presence of major organ comorbidities. Adherence was measured using Arabic version of 8-item Morisky Medication Adherence Scale (MMAS-8) which

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consisted of 8 questions, answers to questions 1–7 will be presented as 'yes/no'. Question 8 will be presented in 5-point Likert scale (never scored 1, other responses scored 0). Scores on the Morisky Medication Adherence Scale range from 0 to 8, scores < 6 will consider to be low adherence, scores $\geq 6 < 8$ represent medium adherence, and scores = 8 signify a high adherence (2).

2.2.2 Study design and settings

A cross-sectional study was conducted at outpatient clinics in Baghdad Teaching Hospital/Medical City Complex, during the period from December 2019 to September 2020, after approval of the study protocol by Iraqi Board for Medical Specialties.

2.2.3 Statistical analysis

Analysis of data was carried out using the available statistical package of SPSS-26 (Statistical Packages for Social Sciences- version 26). Data were offered in simple measures of frequency,

percentage, mean, standard deviation, and range (minimum-maximum values).

The significance of difference of different percentages (qualitative data) was tested using Pearson Chi-square test (χ^2 -test) with application of Yate's correction or Fisher Exact test whenever applicable. Statistical significance was considered whenever the P value was less than 0.05.

3. RESULTS:

3.1 Demographic and clinical characteristics of the study population

The current study included 100 Ankylosing Spondylitis members; the majority of them were male (96%). The mean age of respondents was 39.5 ± 9.4 years with a range of (20 - 58 years). The mean BMI was (28.2 ± 5.1), Majority of patients 87% were married, 98% living with family, and 11% had illiterate education level, and 80% live in urban areas.

Other baseline characteristic of AS patients was shown in table 1

Table 1: The socio-demographic and disease characteristics of Ankylosing Spondylitis patients included in the study.

	No.	%	
Age (years)	20---29	13	13.0
	30---39	38	38.0
	40---49	30	30.0
	50---59	19	19.0
	Mean \pm SD (Range)	39.5 \pm 9.4 (20-58)	
Gender	Male	96	96.0
	Female	4	4.0
BMI (Kg/m2)	Underweight (<18.5)	2	2.0
	Normal (18.5-24.9)	29	29.0
	Overweight (25-29.9)	36	36.0
	Obese I (30-34.9)	21	21.0
	Obese II (≥ 35)	12	12.0
	Mean \pm SD (Range)	28.2 \pm 5.1 (17.3-40.6)	
Education level	Illiterate	11	11.0
	Primary	43	43.0
	Secondary	21	21.0
	College	24	24.0
	Higher education	1	1.0
Occupation	Not working	23	23.0
	Retired	5	5.0
	Working	72	72.0
Smoking	Not smoker	44	44.0
	Ex-smoker	13	13.0
	Current smoker	43	43.0

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Alcohol	Yes	4	4.0
	No	96	96.0
Residency	Urban	80	80.0
	Rural	20	20.0
Living situation	With family	98	98.0
	Alone	2	2.0
Marital status	Single	12	12.0
	Married	87	87.0
	Widow	-	-
	Divorced	1	1.0
Number of comorbidities	No	84	84.0
	One	12	12.0
	Two	3	3.0
	Three & more	1	1.0
NSAIDs		33	33.0
Steroids		4	4.0
DMARDs		7	7.0
Biologics		99	99.0
Mixed		37	37.0
Number of drugs	None	-	-
	Single	63	63.0
	Multiple	37	37.0

BMI: body mass index, Ankylosing spondylitis, NSAIDs: Non-steroidal anti-inflammatory drugs, DMARDs: Disease modifying anti rheumatic drugs. SD: standard deviation

Table 2: The Disease duration and disease activity of Ankylosing Spondylitis patients included in the study.

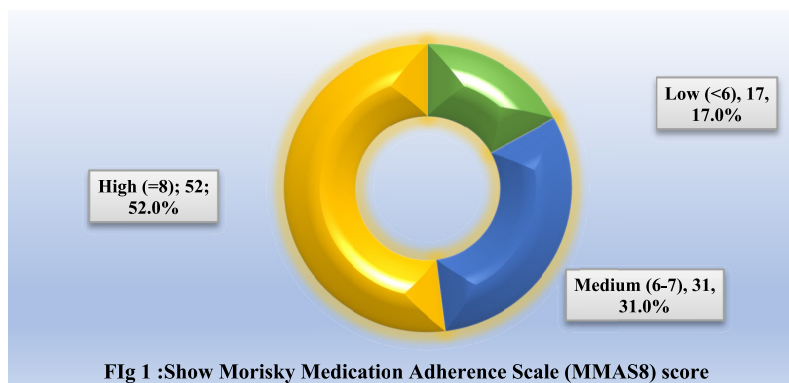
Variables	values(n(%) or mean±SD (range))		
Disease duration (years)	1---9	60	60.0
	10---19	27	27.0
	=>20 years	13	13.0
	Mean±SD (Range)	9.3±7.7 (1-39)	
Disease activity	Active	91	91.0
	Inactive	9	9.0
	Poor (<4)	73	73.0
BASDAI (Bath AS Disease Activity Index)	Suboptimal control (= >4)	27	27.0
	Mean±SD (Range)	3.1±1.6 (0.2-7.6)	
	Inactive (<1.3)	13	13.0
ASDAS (AS Disease Activity Score)	Low activity (1.3-2.0)	30	30.0
	High activity (2.1-3.4)	47	47.0
	Very high activity (= >3.5)	10	10.0
	Mean±SD (Range)	2.3±0.9 (0.2-4.5)	
BASFI (Bath AS Functional Index)	No limitation (<1.5)	15	15.0
	Functional limitation (= >1.5)	85	85.0
	Mean±SD (Range)	2.9±1.6 (0-7)	

SD: standard deviation

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3.2. Total adherence of medications among Ankylosing Spondylitis patients High adherence to medications in the study group was found,

and the mean of the score was 6.8 ± 1.6 . The total scores with their sub-scores of patient's adherences showed in figure 1.



3.3 impact of baseline characteristics on adherence level.

Demographic data of the studied group revealed no significant difference according to Morisky Medication Adherence Scale (MMAS8) while there is strong positive correlation with P value

less than 0.05 between the adherence & both the type of treatment (NSAID) and number of drugs as shown in tables 3 and 4.

Table 3: Impact of baseline characteristics on adherence level.

		Morisky Medication Adherence Scale (MMAS8)				P value
		Low (<6)		Med-High (>=6)		
		No	%	No	%	
Age (years)	20---29	2	15.4	11	84.6	0.368
	30---39	4	10.5	34	89.5	
	40---49	8	26.7	22	73.3	
	50---59	3	15.8	16	84.2	
Gender	Male	17	17.7	79	82.3	0.356
	Female	-	-	4	100.0	
BMI (Kg/m2)	Underweight (<18.5)	-	-	2	100.0	0.557
	Normal (18.5-24.9)	4	13.8	25	86.2	
	Overweight (25-29.9)	9	25.0	27	75.0	
	Obese I (30-34.9)	3	14.3	18	85.7	
	Obese II (>=35)	1	8.3	11	91.7	
Education level	Illiterate	1	9.1	10	90.9	0.169
	Primary	12	27.9	31	72.1	
	Secondary	2	9.5	19	90.5	
	College	2	8.3	22	91.7	
	Higher education	-	-	1	100.0	
Occupation	Not working	2	8.7	21	91.3	0.235
	Retired	-	-	5	100.0	
	Working	15	20.8	57	79.2	
Smoking	Not smoker	6	13.6	38	86.4	0.680
	Ex-smoker	3	23.1	10	76.9	
	Current smoker	8	18.6	35	81.4	

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Alcohol	Yes	1	25.0	3	75.0	0.664
	No	16	16.7	80	83.3	
Residency	Urban	11	13.8	69	86.3	0.084
	Rural	6	30.0	14	70.0	
Living situation	With family	17	17.3	81	82.7	0.518
	Alone	-	-	2	100.0	
Marital status	Single	1	8.3	11	91.7	0.618
	Married	16	18.4	71	81.6	
	Widow	-	-	-	-	
	Divorced	-	-	1	100.0	
Disease duration (years)	1---9	10	16.7	50	83.3	0.516
	10---19	6	22.2	21	77.8	
	=>20 years	1	7.7	12	92.3	

*Significant difference between proportions using Pearson Chi-square test at 0.05 level.

BMI: body mass index.

Table 4 : Impact of disease activity and medications used on adherence level.

		Morisky Medication Adherence Scale (MMAS8)				P value
		Low (<6)		Med-High (=>6)		
		No.	%	No.	%	
Disease activity	Active	16	17.6	75	82.4	0.622
	Inactive	1	11.1	8	88.9	
BASDAI (Bath AS Disease Activity Index)	Poor (<4)	12	16.4	61	83.6	0.806
	Suboptimal control (=>4)	5	18.5	22	81.5	
ASDAS (AS Disease Activity Score)	Inactive (<1.3)	1	7.7	12	92.3	0.122
	Low activity (1.3-2.0)	9	30.0	21	70.0	
	High activity (2.1-3.4)	5	10.6	42	89.4	
BASFI (Bath AS Functional Index)	Very high activity (=>3.5)	2	20.0	8	80.0	0.682
	No limitation (<1.5)	2	13.3	13	86.7	
	Functional limitation (1.5-2.5)	15	17.6	70	82.4	
Number of Co-morbidities	No	16	19.0	68	81.0	0.635
	One	1	8.3	11	91.7	
	Two	-	-	3	100.0	
	Three & more	-	-	1	100.0	
NSAIDS	Present	10	30.3	23	69.7	0.013*
	Absent	7	10.4	60	89.6	
Steroids	Present	1	25.0	3	75.0	0.664
	Absent	16	16.7	80	83.3	
DMARDs	Present	2	28.6	5	71.4	0.398
	Absent	15	16.1	78	83.9	
Biologics	Present	17	17.2	82	82.8	0.649
	Absent	-	-	1	100.0	
Mixed	Present	10	27.0	27	73.0	0.041*
	Absent	7	11.1	56	88.9	
Number of drugs	None	-	-	-	-	0.041*
	Single	7	11.1	56	88.9	
	Multiple	10	27.0	27	73.0	

*Significant difference between proportions using Pearson Chi-square test at 0.05 level.

AS: Ankylosing spondylitis, NSAIDs: Non-steroidal anti-inflammatory drugs, DMARDs: Disease modifying anti rheumatic drugs.

4. DISCUSSION:

Medication adherence is a core concern in the management of chronic inflammatory rheumatic diseases ⁽²¹⁾, such as Ankylosing Spondylitis which is a chronic disease that leads to great disability and chronic pain, and has a notable adverse economic and social effect upon patients' life. Adherence is a dynamic process that changes with time and is influenced by many different factors. The WHO published outlines of adherence issues and endorsed a hand model for improving treatment adherence in a variety of conditions demanding long-term therapies. There were five domains, including patient, therapy, mental health, health system, and socioeconomic-related factors ⁽²³⁾.

In this study, MMAS-8 was used to measure the scope of adherence to medication and found (83%) of studied patients were adherent and (13%) of them were non-adherent.

This highlighted a significant association between treatment adherence and both the type of treatment (NSAID) and number of drugs, and this can be explained by as polypharmacy led to less adherence, alongside that many patients were wrongly misbelieved that NSAID are merely painkillers and cannot hold the disease progression. A study done in Turkey by Sena Tolu, et al. showed there were no significant differences between the adherent and non-adherent groups in terms of demographic and clinical characteristics, and only disease duration was significantly longer in the non-adherent group. The proportion of non-adherence in younger patients (aged ≤ 40 years; 69.4%) was nearly the same as that recorded in patients aged >40 years (60%) ⁽²⁴⁾. On other hand, a multi-country study done By Josef S Smolen, et al. showed lower adherence in Ankylosing Spondylitis patients in comparison to Rheumatoid arthritis and Psoriatic arthritis patients ⁽¹⁹⁾.

Also, this study revealed that the increment in beliefs score conveyed significant direct correlation with adherence score which means that concerns over medication, medicines overused and harmful scores were higher in low-adherent patients which is very similar to what is found by Pierre Michetti, et al. in multi-country, cross-sectional, self-administered survey study ⁽²⁵⁾.

Limitations of the study

This study was with many limitations. The patients were incorporated from only one tertiary center.

The adherence was measured using self-report method. The present study was a cross-sectional study rather than prospective which allows studying the effect of adherence to medication and belief about medications on patients' outcome, and lastly, this study was done during the peak of **COVID-19** crisis with many fears by patients and doctors of getting infected.

5. CONCLUSION:

According to our results in this study, most of the studied AS patients were adherent to their treatment with no significant impact of baseline characteristics on adherence level to medications apart from the type of treatment (NSAID) and number of drugs. It is important to include all health care professionals in medications adherence. Primarily the rheumatologists and all other healthcare providers including nurses. Pharmacists should more and more be involved as well. Advice by pharmacists on drug management has been shown to promote drug adherence, both in rheumatology and in other chronic disease settings. Patient education on the disease's pathophysiology and the mechanism of action of therapeutics may provide a good strategy to improve treatment adherence of with low concerns.

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