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Evaluation of Treatment Adherence in Iraqi Patients with Behçet's Disease

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Abstract

Behçet's disease (BD) is a multisystemic vasculitis with chronic relapsing course. Adherence to treatment plays important role in management of these patients, nonetheless, adherence to treatment among these patients has not been well studied, particularly among Iraqi patients, hence this study aimed to evaluate adherence to treatment in Iraqi patients with Behçet's disease & determine the factors associated with non-adherence to treatment in such patients. We conducted a cross-sectional study at the Rheumatology Unit of Baghdad Teaching Hospital in Medical City including 75 patients. We use the Compliance Questionnaire for Rheumatology (CQR5) and Beliefs about Medicines Questionnaire (BMQ) in evaluation of patients. We found that 65.3% of the patients were low adherent to treatment, factors associated with low adherence were, longer disease duration, using too many medications, high cost of treatment, fear of side effect, difficulty of oral intake and lack of family support While being married, higher level of educations, good belief in the necessity of medications and low disease activity associated with better level of adherence.

Keywords: Behçet's disease; Management, Adherence; Beliefs about medications; Compliance; Quality of life.

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1. INTRODUCTION

Behçet's disease (BD) is a multisystemic vasculitis characterized by frequent oro-genital aphthous ulcers, uveitis, and skin lesions with chronic relapsing course. Behçet's disease has the ability to affect almost all organ systems variably with significant organ-threatening morbidity and mortality (1,2).

The World Health Organization (WHO) describes treatment adherence as "the extent to which the persons' behavior corresponds with the recommendations from a healthcare provider (3). Medication adherence has been shown to improve health outcomes and decrease health care charges (4) Adherence is particularly challenging in chronic diseases including rheumatic diseases which usually requires prolonged periods of poly medication (5) Adherence can be assessed by indirect method (self-reporting, questionnaires) (6) Self-reported medication adherence was found to be low in BD patients (7). Efforts to develop management outcomes necessitate a good understanding of the specific fences to achieve good adherence to therapy (8).

2. METHODOLOGY

A cross-sectional study conducted at the Rheumatology Unit of Baghdad Teaching Hospital in Medical City. Ethical approval was taken from Iraqi board of medical specialties. A total of 75 patients with BD diagnosed according to the International Criteria for Bechet's Disease (ICBD) (2014) (9) and using at least one medication and being ≥18 years old at the time of the study were included. Patients with medications that have been changed more than once in the last 3 months were excluded from the study.

Data were collected using a questionnaires about socio-demographic characteristics, disease duration, medications used and other chronic diseases, lifestyle behaviors and the most common self-reported causes for non-adherence (10)

Medication adherence was evaluated using the Arabic translation of A 5 item version of the Compliance Questionnaire for Rheumatology (CQR5) (11).

The Beliefs about Medicines was evaluated by the Arabic Translation of the Beliefs about Medicines Questionnaire (BMQ) (12).

Respondents indicated their degree of concurrence with each individual statement on a 5-point Likert scale.

Disease activity was evaluated using Behcet's Syndrome Activity Score (BSAS, score =0–100) (13).

Statistical analysis performed using the statistical package or social sciences (SPSS) version 22. Statistical tests and correlation analysis performed accordingly using appropriate statistical methods at a level of significance of 0.05 or less to be significant correlation or difference.

3. RESULTS

The mean age was 38.5 ± 10.6 years . Males were dominant with a male to female ratio of almost 3.7 to 1 . Other socio-demographic characteristics are shown in (Table 1). Regarding the disease duration , the mean was 6.5 ± 2.3 years . Hypertension was the more frequent comorbidity reported in 24.0% of patients as shown in (Table 2). Regarding the clinical findings, oral ulcers, eye involvement, musculoskeletal and skin features were reported in more than 50 % of patients as shown in (Table 3).

Table 4 summarizes the medications used by the BD patients. Prednisolone, Colchicine and Azathioprine were the more frequently medications used. The total number used by a patient ranged 1-5 with a median was 3 medications and almost 80% of the patients used \geq 3 medications, (Table 4).

The main reported side effects are summarized in (Table 5), where increased blood sugar was the most frequently reported (37.3%), followed by increased blood pressure , headache , osteoporosis. The total mean score of the responses of BD patients towards the items of CQR5 was 18.57±3.7 with 34.7% of the patients took their medicines correctly as prescribed. (cutoff point 80%). The main reasons of non-adherence reported by the patients shown in (Table 6).

The total mean scores of the responses of BD patients towards General belief domains (Harm & Over-use) were 9.25±2.8 & 13.53±4 respectively. The total mean score of the responses towards the specific belief items (Necessity & Concern) were 17.92±2.1 & 14.83±3.9 respectively.

A significant correlation was found between adherence and each of marital status (married patients had higher adherence score) and higher level of education (the adherence score increased with increasing of level of education), (P. value < 0.05), (Table 7). No significant association was found with comorbidities (in all correlations P. value > 0.05). Regarding the correlation with clinical findings, no selected finding was significantly associated with adherence score. Despite none of individual medication used by BD patients showed a significant correlation with adherence, the larger number of medication used by the patients had adverse effect on their adherence, where a negative (inverse) correlation was reported between the total number of medication used and adherence score, (r = -0.242, P. value < 0.05), (Table 8).

The correlation analysis between individual reasons of non-adherence and the overall mean adherence score revealed in (Table 9). Results of pairwise bivariate analysis for the correlation between adherence, , necessity, concerns and BSAS scores of BD patients revealed a direct (positive) correlation between Necessity and adherence scores, (r = 0.245, P = 0.034). A significant inverse correlation between adherence score and BSAS-score (r = -0.235, P = 0.043), (Table 10). Results of Analysis of variances (ANOVA) testing revealed a highly significant results where the adherence score reduced with longer duration (Figure 3)

Table 1. Demographic characteristics of the studied group (N=75)

| Male 59 78.7 Female 16 21.3 Residence Urban 61 81.3 Rural 14 18.7 Married 59 78.7 Unmarried 16 21.3 Crowded 42 56.0 Not crowded 33 44.0 Mormal 36 48.0 BMI category Overweight 22 29.3 Obese 17 22.7 Illiterate 12 16.4 Read and write 18 24.7 Primary school 0 0.0 Secondary school 19 26.0 Institute 4 5.5 University 16 21.9 Higher Education 4 5.5 Working 19 25.3 Employee 32 42.7 Retired 4 5.3 Income Fair 40 53.3 Poor | Variable | | No. | % |
|---|----------------------|------------------|-----|------|
| Age (year)* 41 - 50 | | 21 - 30 | 12 | 16.0 |
| Main (SD) 38.5 ± 10.6 | A = 0 (1 1 2 2 1) * | 31 - 40 | 38 | 50.7 |
| Mean (SD) 38.5 ± 10.6 Gender Male 59 78.7 Employment Mare (SD) Male 59 78.7 Married 59 78.7 Married 59 78.7 Unmarried 16 21.3 Crowded 42 56.0 Normal 36 48.0 Moly and price of the price of | Age (year) | 41 - 50 | 15 | 20.0 |
| Male 59 78.7 Female 16 21.3 Residence Urban 61 81.3 Rural 14 18.7 Married 59 78.7 Unmarried 16 21.3 Crowded 42 56.0 Not crowded 33 44.0 Mormal 36 48.0 BMI category Overweight 22 29.3 Obese 17 22.7 Illiterate 12 16.4 Read and write 18 24.7 Primary school 0 0.0 Secondary school 19 26.0 Institute 4 5.5 University 16 21.9 Higher Education 4 5.5 Working 19 25.3 Employee 32 42.7 Retired 4 5.3 Income Fair 40 53.3 Poor | | > 50 | 10 | 13.3 |
| Gender Female 16 21.3 Residence Urban 61 81.3 Rural 14 18.7 Married 59 78.7 Marital status Unmarried 16 21.3 Crowded 42 56.0 Not crowded 33 44.0 Mormal 36 48.0 BMI category Overweight 22 29.3 Obese 17 22.7 Read and write 18 24.7 Primary school 0 0.0 Institute 4 5.5 University 16 21.9 Higher Education 4 5.5 Working 19 25.3 Employee 32 42.7 Retired 4 5.3 Income Fair 40 5.3 Poor 35 46.7 Smoker 19 25.3 | Mean (SD) | 38.5 ± 10.6 | | |
| Female | Condor | Male | 59 | 78.7 |
| Residence Rural 14 18.7 Married 59 78.7 Unmarried 16 21.3 Crowded 42 56.0 Not crowded 33 44.0 BMI category Normal 36 48.0 BMI category Overweight 22 29.3 Obese 17 22.7 Read and write 18 24.7 Primary school 0 0.0 Secondary school 19 26.0 Institute 4 5.5 University 16 21.9 Higher Education 4 5.5 Working 20 26.7 Working 19 25.3 Employee 32 42.7 Retired 4 5.3 Fair 40 53.3 Income Poor 35 46.7 Smoker 19 25.3 | Gender | Female | 16 | 21.3 |
| Married 14 18.7 Married 59 78.7 Unmarried 16 21.3 Crowded 42 56.0 Not crowded 33 44.0 Mormal 36 48.0 Mose 17 22.7 Read and write 12 16.4 Read and write 18 24.7 Primary school 0 0.0 Institute 4 5.5 University 16 21.9 Higher Education 4 5.5 Working 19 25.3 Employee 32 42.7 Retired 4 5.3 Income 7 7 Poor 35 46.7 <tr< td=""><td>Pasidanca</td><td>Urban</td><td>61</td><td>81.3</td></tr<> | Pasidanca | Urban | 61 | 81.3 |
| Marital status Unmarried 16 21.3 Crowded 42 56.0 Not crowded 33 44.0 BMI category Overweight 22 29.3 Obese 17 22.7 Illiterate 12 16.4 Read and write 18 24.7 Primary school 0 0.0 Institute 4 5.5 University 16 21.9 Higher Education 4 5.5 Working 19 25.3 Employee 32 42.7 Retired 4 5.3 Income Fair 40 53.3 Income Poor 35 46.7 Smoker 19 25.3 | Residence | Rural | 14 | 18.7 |
| Unmarried 16 21.3 Crowded 42 56.0 Not crowded 33 44.0 BMI category Normal 36 48.0 BMI category Overweight 22 29.3 Obese 17 22.7 Illiterate 12 16.4 Read and write 18 24.7 Primary school 0 0.0 Secondary school 19 26.0 Institute 4 5.5 University 16 21.9 Higher Education 4 5.5 Working 20 26.7 Working 19 25.3 Employment 32 42.7 Retired 4 5.3 Retired 4 5.3 Income 7 53.3 Poor 35 46.7 | Marital status | Married | 59 | 78.7 |
| Crowding index Not crowded 33 44.0 Anomal 36 48.0 BMI category Overweight 22 29.3 Obese 17 22.7 Illiterate 12 16.4 Read and write 18 24.7 Primary school 0 0.0 Institute 4 5.5 University 16 21.9 Higher Education 4 5.5 Not working 20 26.7 Working 19 25.3 Employee 32 42.7 Retired 4 5.3 Income Fair 40 53.3 Poor 35 46.7 Smoker 19 25.3 | Maritai Status | Unmarried | 16 | 21.3 |
| Not crowded 33 44.0 | Consuling index | Crowded | 42 | 56.0 |
| Overweight 22 29.3 | Crowaing index | Not crowded | 33 | 44.0 |
| Obese 17 22.7 Illiterate 12 16.4 Read and write 18 24.7 Primary school 0 0.0 Secondary school 19 26.0 Institute 4 5.5 University 16 21.9 Higher Education 4 5.5 Working 20 26.7 Working 19 25.3 Employee 32 42.7 Retired 4 5.3 Income Fair 40 53.3 Poor 35 46.7 Smoker 19 25.3 | | Normal | 36 | 48.0 |
| Illiterate | BMI category | Overweight | 22 | 29.3 |
| Read and write 18 24.7 Primary school 0 0.0 Secondary school 19 26.0 Institute 4 5.5 University 16 21.9 Higher Education 4 5.5 Not working 20 26.7 Working 19 25.3 Employee 32 42.7 Retired 4 5.3 Income Fair 40 53.3 Poor 35 46.7 Smoker 19 25.3 | | Obese | 17 | 22.7 |
| Education Primary school 0 0.0 Secondary school 19 26.0 Institute 4 5.5 University 16 21.9 Higher Education 4 5.5 Not working 20 26.7 Working 19 25.3 Employee 32 42.7 Retired 4 5.3 Income Fair 40 53.3 Poor 35 46.7 Smoker 19 25.3 | | Illiterate | 12 | 16.4 |
| Education Secondary school 19 26.0 Institute 4 5.5 University 16 21.9 Higher Education 4 5.5 Not working 20 26.7 Working 19 25.3 Employee 32 42.7 Retired 4 5.3 Income Fair 40 53.3 Poor 35 46.7 Smoker 19 25.3 | | Read and write | 18 | 24.7 |
| Institute | | Primary school | 0 | 0.0 |
| University 16 21.9 Higher Education 4 5.5 Not working 20 26.7 Working 19 25.3 Employee 32 42.7 Retired 4 5.3 Income Fair 40 53.3 Poor 35 46.7 Smoker 19 25.3 | Education | Secondary school | 19 | 26.0 |
| Higher Education 4 5.5 Not working 20 26.7 Working 19 25.3 Employee 32 42.7 Retired 4 5.3 Income Fair 40 53.3 Poor 35 46.7 Smoker 19 25.3 | | Institute | 4 | 5.5 |
| Not working 20 26.7 Working 19 25.3 Employee 32 42.7 Retired 4 5.3 Income Fair 40 53.3 Poor 35 46.7 Smoker 19 25.3 | | University | 16 | 21.9 |
| Working 19 25.3 Employee 32 42.7 Retired 4 5.3 Income Fair 40 53.3 Poor 35 46.7 Smoker 19 25.3 | | Higher Education | 4 | 5.5 |
| Employment Employee 32 42.7 Retired 4 5.3 Income Fair 40 53.3 Poor 35 46.7 Smoker 19 25.3 | Employment | Not working | 20 | 26.7 |
| Employee 32 42.7 Retired 4 5.3 Income Fair 40 53.3 Poor 35 46.7 Smoker 19 25.3 | | Working | 19 | 25.3 |
| Fair 40 53.3 Poor 35 46.7 Smoker 19 25.3 | | Employee | 32 | 42.7 |
| Poor 35 46.7 Smoker 19 25.3 | | Retired | 4 | 5.3 |
| Poor 35 46.7 Smoker 19 25.3 | la como | Fair | 40 | 53.3 |
| | income | Poor | 35 | 46.7 |
| Alcohol consumer 4 5.3 | Smoker | | 19 | 25.3 |
| | Alcohol consumer | | 4 | 5.3 |

SD: standard deviation of the mean,

Table 2. Distribution of comorbidities reported among the studied group (N=75)

| Comorbidities | No. | % |
|------------------------|-----|------|
| Hypertension | 18 | 24.0 |
| Diabetes Mellitus | 10 | 13.3 |
| Peptic ulcer | 6 | 8.0 |
| Ischemic heart disease | 2 | 2.7 |
| Asthma | 4 | 5.3 |
| Migraine | 2 | 2.7 |

Table 3. Clinical findings of the studied group (N=75)

| Clinical findings | No. | % |
|---------------------------|-----|------|
| Oral ulcers | 51 | 68.0 |
| Eye involvement | 47 | 62.7 |
| Musculoskeletal features | 45 | 60.0 |
| Skin features | 41 | 54.7 |
| Neurological features | 30 | 40.0 |
| Gastrointestinal features | 28 | 37.3 |
| Genital ulcers | 24 | 32.0 |
| Pathergy test | 23 | 30.7 |
| Vascular involvement | 18 | 24.0 |

Table 4. Distribution of total number of medications used among the studied group (N=75)

| Medication | No. | % |
|------------------|-----|------|
| Prednisolone | 59 | 78.7 |
| Colchicine | 56 | 74.7 |
| Azathioprine | 43 | 57.3 |
| NSAIDs | 10 | 13.3 |
| Cyclosporine | 8 | 10.7 |
| Biologics | 8 | 10.7 |
| Sulfasalazine | 6 | 8.0 |
| Methotrexate | 4 | 5.3 |
| Cyclophosphamide | 2 | 2.7 |
| Others | 31 | 41.3 |

Median number of medications used = 3 (Range: 1-5)

Table 5. Distribution of the more frequently reported side effect

| Common Side Effect | No. | % |
|-------------------------|-----|------|
| Increase blood sugar | 28 | 37.3 |
| Increase blood pressure | 17 | 22.7 |
| Headache | 11 | 14.7 |
| Osteoporosis | 11 | 14.7 |
| Infections | 9 | 12.0 |
| Increase body weight | 8 | 10.7 |
| Rash | 4 | 5.3 |
| Cataract | 4 | 5.3 |
| Peptic ulcer | 3 | 4.0 |

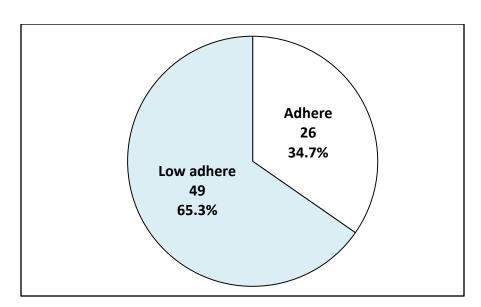


Figure 1. Adherence levels of the studied group

Table 6. Reasons of non-adherence to treatment reported by BD patients

| Reason of non-adherence | No. | % |
|---|-----|------|
| Too many medications | 51 | 68.0 |
| Fear of side effects | 49 | 65.3 |
| Forgetfulness | 48 | 64.0 |
| Lack of symptoms | 48 | 64.0 |
| Cost | 45 | 60.0 |
| Misunderstanding/ Complexity of regimen | 45 | 60.0 |
| Lack of availability | 43 | 57.3 |
| Lack of family support | 28 | 37.3 |
| Problems with access to hospital | 17 | 22.7 |
| Lack of improvement | 9 | 12.0 |
| Difficulty regarding oral intake | 8 | 10.7 |
| Difficulty regarding IV/SC intake | 6 | 8.0 |

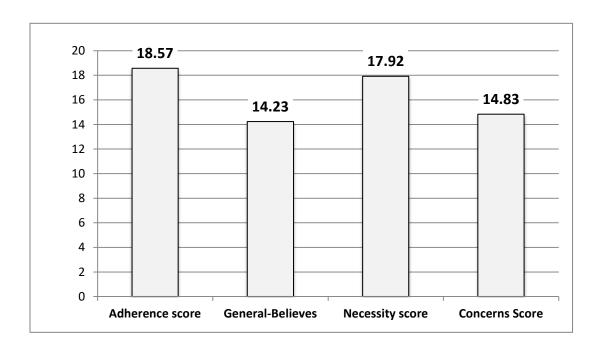


Figure 2. Descriptive statistics of total adherence, general believes, necessity and concerns scores of the studied group

Table 7. Results of bivariate analysis for the correlation between adherence score and demographic characteristics of BD patients

| Characteristic | R | P. value |
|----------------------|--------|----------|
| Age (year) | 0.152 | 0.193 |
| Age at disease onset | 0.182 | 0.119 |
| Gender | 0.029 | 0.808 |
| Residence | -0.093 | 0.425 |
| Marital status | 0.295 | 0.010* |
| Crowding index | 0.018 | 0.876 |
| BMI category | -0.011 | 0.925 |
| Education | 0.243 | 0.038* |
| Employment | 0.107 | 0.361 |
| Income | -0.180 | 0.122 |
| Smoking | 0.117 | 0.316 |
| Alcohol | 0.128 | 0.426 |
| | | |

R: Correlation coefficient, * significant correlation,

Table 8. Results of bivariate analysis for the correlation between adherence score and medications used by BD patients

| Medication | R | P. value |
|----------------------------------|--------|----------|
| Prednisolone | -0.154 | 0.187 |
| Colchicine | -0.034 | 0.770 |
| Azathioprine | 0.074 | 0.529 |
| Methotrexate | -0.174 | 0.136 |
| Cyclophosphamide | -0.065 | 0.582 |
| Cyclosporine | -0.105 | 0.368 |
| Sulfasalazine | 0.019 | 0.870 |
| NSAIDs | 0.168 | 0.150 |
| Biologics | -0.063 | 0.590 |
| Others | 0.139 | 0.235 |
| Side effect | 0.127 | 0.191 |
| Total number of medications used | -0.242 | 0.037* |

R: Correlation coefficient, *significant

Table 9. Results of bivariate analysis for the correlation between adherence score and reasons of non-adherence reported by BD patients

| Reasons | R | P. value |
|---|--------|----------|
| Fear of side effects | -0.211 | 0.031 |
| Lack of availability | -0.054 | 0.646 |
| Cost | -0.269 | 0.021* |
| Misunderstanding/ Complexity of regimen | 0.106 | 0.364 |
| Too many medications | -0.496 | <0.001* |
| Lack of family support | -0.327 | 0.004* |
| Difficulty regarding oral intake | -0.230 | 0.047* |
| Difficulty regarding IV/SC intake | 0.092 | 0.682 |
| Forgetfulness | 0.033 | 0.782 |
| Lack of symptoms | -0.15 | 0.198 |
| Problems with access to hospital | 0.062 | 0.599 |
| Lack of improvement | 0.191 | 0.101 |

R: Correlation coefficient, *significant

Table 10. Results of pairwise bivariate analysis for the correlation between adherence, necessity, concerns and BSAS scores of BD patients

| Score | Correlation | Adherence | Necessity | Concerns | General believes |
|---|-------------|-----------|-----------|----------|------------------|
| | parameter | score | score | Score | General Delleves |
| Necessity | R | 0.245 | | | |
| Score | P. value | 0.034* | | | |
| Concerns | R | 0.116 | 0.188 | | |
| Score | P. value | 0.322 | 0.107 | | |
| General | R | 0.154 | 0.192 | 0.083 | |
| believes | P. value | 0.188 | 0.104 | 0.485 | |
| BSAS-score | R | -0.225 | 0.165 | 0.018 | 0.124 |
| | P. value | 0.043* | 0.157 | 0.878 | 0.291 |
| R: Correlation coefficients, *significant at $P < 0.05$ | | | | | |

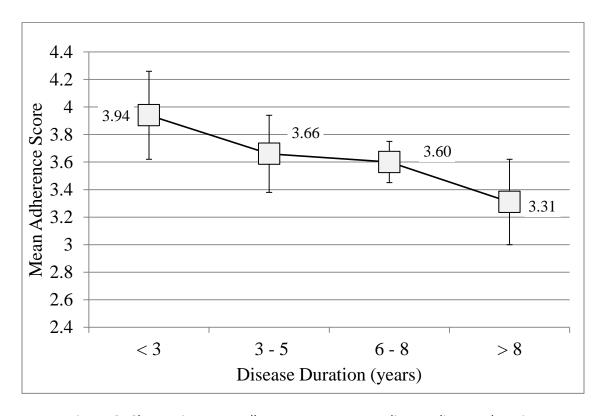


Figure 3. Change in mean adherence score according to disease duration

4. DISCUSSION

Behçet's disease is a complex autoimmune disease in which adherence to treatment, if unmet, could lead to poor outcomes. BD mimic to other chronic disorders where more unnecessary visits, frequent hospitalization and extra medication payments are thought to stem from lack of adherence to medications. The current study showed no specific range of ages to have a certain level of adherence to treatment confirming previous results observed in similar studies assessing treatment adherence in BD patients done in Turkey and Egypt (5,14). The ages of the patients and correlations with extent of adherence among patients with rheumatic disease is a matter of debate between researchers. The study sound with other researchers who neglect the role of gender difference in contribution to certain level of adherence among patients with BD (5,14) while Khabbazi et al. (15). reach that non-adherence was significantly more common in men.

Married patients and those with higher levels of education were found to be significantly more adherent. Married patients usually get psychological support from their partner who also may help them to take their medication properly, while Khabbazi et al. (15) observed the contrary finding. Several other studies found no significant role for this variable to affect degree of adherence (5,14,16). Patients with higher level of education were more adherent likely due to better understanding of the instructions given to them by their physicians and they may have easy access to other sources to knew more . However, this positive association of high level of education was not seen to affect adherence significantly in similar studies assessing treatment adherence in BD (5,14,16) The current study showed no significant role for monthly income on level of adherence, contradicted the result obtained by other researchers in this issue (15). This may be explained partly by the relatively inexpensive medications that is usually prescribed for BD patients and partly by the profound role of the governmental health institute in Iraq that freely confer most of the medications that used for such patients. There was no remarkable effect of employment status on adherence state observed, coping with that observed by Cinar et .al (2016) and H. S Zayed et .al (2019) (5,14) but Khabbazi A. et.al (2018) concluded that being employed is risk factor for non-adherence (15) Employment may be associated with frequent missing of morning doses of medications, possible losing appointment visits for hospitals and added stress on the cognitive and physical functions of the patients. The present study didn't link certain BMI category to a specific level of adherence. However, some physicians viewed that patients with higher BMI are less likely to be adherent to medications and may not receive guideline-recommended care (17). Among other variables; the disease duration shows an inverse relation to the level of adherence. This finding is discordant with previous observations in BD that showed no similar relations between the adherence and disease duration (5,14,16), but their finding may not fit with the common sense which is supported by many other studies assessed adherence in other chronic diseases which consider the long disease duration as a grieving contributor to the degree of adherence (6,18) The study showed no selected clinical feature correlated well with level of adherence while Khabbazi A. et.al (2018) (15) found that musculoskeletal involvement and erythema nodosum were significantly more

common in non-adherent patients with BD (15). Mumcu et al. (19) found that higher medication adherence was observed in patients with eye involvement. The drug profile have substantial effects on long term adherence of the current study patients to treatment reflected by the fear of the patients from side effects in about 65 % of patients. Of note almost 80% of the patients used 3 or more medications, so they may face some degree of confusions or boring on long terms with possible increasing costs. In one Iranian study, only NSAID use associated with poor adherence to the chronic medications (15) this study didn't find such correlation possibly due to low usage of such medications which is reported only in 16.3 % of patients. Utilizing 5 items version of CQR scoring system , the current study showed that overall mean score of adherence is 74.2% and only 34.7 % of patients took their medications correctly as prescribed and achieved 80 % or more of adherence according to this score. Similar study assessing adherence among patients with BD done in Egypt (2019) using CQR19 version showed the score of adherence was 69.2 ± 11.79 % with only 22% of the patients scoring > 80% (5). Cinar et al. (2016) found a mean CQR (66.48 ± 13.49) among Turkish patients with BD (14). A total of 49.3% of the patients with BD were adherent to treatment in another study done in Iran where the adherence to treatment was evaluated by the consideration of adherence to medication and appointment- keeping behavior (15) A Turkish study published in (2013) using Morisky scale for evaluation of medication adherence reporting low adherence is observed in BD patients (7). The difference between the results of these studies may be attributed to using different ways of assessing adherence like other group of questionnaires, variables, scaling or differences in the size of study sample. Also there is no consensus about the definition of adherence between these studies . The role of different cultures , attitudes , levels of education and facilities in each nations should be kept in mind when discussing the differences between levels of adherence in different regions of the world .Regarding the common reasons of non-adherence, about 2/3rd of the patients feels that they have too many medications, may fear from side effects. Prescription of too many medications and side effects of them are well known causes of non-adherence among a wide number of patients worldwide . In the present study , they were significantly affected level of adherence to treatment in agreement with similar two previous studies in BD populations

(5,7). About 60 % of the patients report their suffering from cost of medications and had significantly affecting level of adherence among them in spite of the relatively low price for most of the medications used in treatment of BD in Iraq, especially for those with poor income or living far from the specialized hospitals where they usually received medications freely. In Iran, although the effect of cost of treatment on adherence among patients with BD was not significant; side effects of medications and high cost of treatment were the most frequent causes of non-adherence (15). In Egypt, health care sources were the only sociodemographic factor presenting meaningfully different CQR scores, with the lowermost score belonging to self-funded patients with BD (5). Lack of family support also appear significantly affected level of adherence in a negative manner among the current study. Support (from family and community) was shown to have an encouraging impact on adherence. This is valid for other diseases and shows the importance of providing an ideal level of collaboration and provision that patients need in order to adhere to their treatments (16). Although reported less frequently, difficulty regarding oral intake found to affects level of adherence among the studied patients. This is especially reported in patients with BD. Traditional treatments using topical medications and colchicine may not eliminate oral ulcer activity. Therefore, this condition may be a barrier to medication adherence (19).

Forgetfulness may be caused by chronic disease status with its associated anxiety and possible low sleep quality, CNS involvement by disease itself or some medications can cause memory weakness. The study results exhibit that forgetfulness is frequently reported which are in accordance with the possible reasons for nonadherence seen by Mumcu et al. (2013) (19). This can be improved through frequent patients training, giving obvious information and fixed times for medications according to hourly intervals (e.g., every 8 h) or times per day (e.g., twice or thrice daily) and providing an easy and understandable instructions on labels will aid patients use complex medication regimens safely and improves medication adherence. Lack of symptoms as a reason of poor adherence has been described particularly in long term settings. This often happens when patient have few or no symptoms (10). A similar number had a difficulties with understanding the instructions of their clinicians either because of their low level of

educations, compromised cognitive functions, or the short time of the interview and problems with privacy issue or noise from surroundings especially in crowded clinics. This problem can be managed by few steps including broadening the time of the interview with the patients and providing a peaceful rooms with keeping a degree of privacy and be sure that message gotten by the patients by testing his ability to remember the instructions before discharge home. Belief about medications was assessed using the Arabic Translation of the Beliefs about Medicines Questionnaire (BMQ) (12) The BMQ-specific assessed beliefs about the necessity of prescribed medication and concerns about prescribed medication based on beliefs about the danger of dependence and long-term toxicity and the disruptive effects of medication. The BMQ-General assessed beliefs that medicines are hurtful, addictive, poisons which must not be taken unceasingly (General-Harm) and that medicines are overused by doctors (General-Overuse) . In this study, patients confessed beliefs that medications are necessary for their health more than reported concerns about taking medications . The analysis showed significant positive association between adherence and specific-necessity. In this respect, Cinar et al. (2016) reported that specific necessity scores were significantly higher in BD patients with high/ medium adherence compared to those with low adherence (14).

In Egyptian study (2019) , beliefs about the necessity of medications showed a positive correlation with the CQR score whereas the concerns score and the beliefs about medications' harm showed a significant negative correlation (5). Therefore, health care providers should realize the importance of assessment of medication beliefs and be attentive of these concerns and directly educate patients to reduce such concerns and hence minimize non-adherence. Studies reported different values for specific-necessity and concerns when BMQ was used in different types of chronic diseases suggesting that the impact of medication belief on adherence may depend on the nature of the disease (20) Lastly , the disease activity measured during time of questionnaires show that adherent patients are more likely to have low disease activity and found that BSAS was significantly correlated with adherence in contradictory to that noticed by Khabbazi et al.(2018) and Zayed et al.(2019) who found that disease activity were not related to adherence (5,15). However, Mumcu, et al. found the adherence score was lower in

patients with major organ involvement (7). The main limitation of this study lies in the limited number of patients. Furthermore , using a questionnaire have restricted value because they are subjective and the results may be distorted by the patients. Further studies are needed to confirm the validity of both adherence and beliefs scales among Iraqi patients. Also there is no generalized agreement about the definitions of adherence to treatments as well as the methods that used to assess adherence . On the other hand , the study may have some strong points . The study is the first in Iraq that assess treatment adherence and medications belief in BD and the first study benefits from utilizing the CQR5 to assess adherence , and highlighting the factors that affects medications adherence and addressing the possible reasons of non-adherence to treatment in BD.

5. CONCLUSIONS

The majority of Iraqi patients with BD were low adherent to treatment. Different factors appeared to be associated with low adherence including longer duration of disease, having too many medications, high medications cost, fear of side effects, difficulty of oral intake and lack of family support. Hence we recommend. Being married patients, highly educated, higher belief in the necessity of medications and lower disease activity were associated with better adherence. We recommend further studies with larger sample size, more validation of scales used in assessments with possible use of software applications in data entry, using other more precise method to assess adherence like measuring levels of drugs in the body fluids, utilization of electronic devices and pick-up/refill checkers may be of value in following the extent of patients adherence.

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Ethical Clearance:

All ethical issues were approved by the authors. Data collection was in accordance with Declaration of Helsinki of the World Medical Association, 2013, the ethical principles of research involving human subjects.

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