RESEARCH ARTICLE

Medication-related burden among Iraqi patients with rheumatoid arthritis: An observational study [version 1; peer review: awaiting peer review]

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Abstract

Background: Rheumatoid arthritis (RA) is a chronically progressing inflammatory disease having articular, extra-articular, and systemic manifestations of unclear origin. Medication-related burden (MRB) is a novel concept that focuses on unpleasant feelings associated with the therapeutic process. The purpose of this research was to examine MRB among Iraqi patients with rheumatoid arthritis from the patient’s viewpoint.

Methods: The present research was a cross-sectional study conducted on patients with rheumatoid arthritis who had previously been diagnosed and visited Baghdad Teaching Hospital/Medical City/Rheumatology department between December 2021 through March 2022. The Living with Medicines Questionnaire was used to assess MRB (LMQ).

Results: The study recruited 250 RA patients. The average age of the patients was 47.29± 12.72 years. The vast majority were women, 80.8%. The mean LMQ score was 113.78± 13.95. Most participants experienced a moderate degree of burden of 72.0%, followed by a minimum commitment of 24.4%, a high burden of 2.8%, and no burden of 0.8%, with no patient experiencing a high burden of 0 %. Women had significantly higher medication-related burdens (total LMQ). RA patients with more than five chronic medications had substantially higher MRB than those with fewer scheduled medications. Patients with chronic diseases (other than RA) had significantly higher MRB than those without other chronic diseases. The total LMQ score had a significant positive correlation with the Clinical Disease Activity Index (CDAI) value. In other words, when disease severity increases, the MRB increases.

Conclusion: A considerable proportion of the RA patients involved in the current study have experienced MRB. Female sex, polypharmacy,
comorbidities, and more severe disease are associated with more MRB.

Keywords
Rheumatoid arthritis, Medication-related burden, Living with Medicines Questionnaire, Clinical Disease Activity Index, Iraq

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Introduction
Rheumatoid arthritis (RA) is an unknown origin that stimulates the inflammatory process in the synovial tissue of joints, bone, cartilage, and, less commonly, extra-articular structures. The prevalence rate was from 0.5% to 1% of the population and had regional variation. The prevalence rate in Iraq is 1%. RA risk factors include genetics, smoking, sex (females show higher incidence), older age, and obesity. Morning stiffness, joint discomfort, and swelling are typical clinical manifestations of RA. Furthermore, RA patients frequently have nonspecific symptoms such as fever, malaise, and weariness. These are common symptoms of Xerostomia, dry eyes, subcutaneous rheumatoid nodules, numb hands and feet, and shortness of breath.

Rheumatoid arthritis is a debilitating disease associated with psychological and physical negative impacts, decreasing quality of life and negatively impacting the disease course. The therapeutic goals of treatment for RA are to reduce pain and inflammation of joints, improve joint function, and prevent joint destruction and deformity. RA management includes a combination of pharmacological treatment, rest, weight-bearing exercise, and patient education about the disease. Four main classes of pharmacological therapy are currently available: glucocorticoids, analgesics including non-steroidal anti-inflammatories (NSAIDs), and disease-modifying antirheumatic drugs (DMARDs), including both biologic and conventional non-biologic DMARDs. RA patients are frequently treated by combining these therapies.

Whereas disease burden depicts the effect of diseases on a patient, the relatives, and the healthcare system, treatment burden reflects the repercussions of individuals undergoing or participating in treatment, such as taking drugs, medical procedures, and so on. Medications are the most frequently used medical technology to treat different diseases. In addition to side effects, medication-related burden (MRB) includes difficulties in managing complex treatment regimes, practical problems (such as opening the package), psychosocial responsibilities, notably societal stigma, interruptions to daily life, and health system burdens related to frequent medication usage, the latter encompassing both information burden and patient-provider interactions. Recent research indicating that three-quarters of RA patients were dissatisfied with their therapy, despite most being treated with biologic DMARDs, highlighted the significance of knowing patients’ perspectives of MRB.

In the Western world, several studies analyzing MRB have been conducted, and there are no studies published considering MRB of RA in Iraqi individuals. Therefore, we performed research among RA patients in Iraq to better comprehend the MRB from the patients’ perspective.

Methods
Ethical approval
The ethical and scientific board reviewed and approved the research proposal presented to the College of Pharmacy, University of Baghdad, which outlined the current study’s objectives and anticipated data collecting methodologies (ethics board approval code: 2514) on March 16, 2021. Before distributing the questionnaire, the researcher described the purpose of the research to each respondent and acquired their verbal and written consent to participate in the study (before participation, each individual provided written informed consent, preceded by verbal permission). Patients were not provided any incentives.

Study design
The present research was observational, cross-sectional research of patients who had already been diagnosed with rheumatoid arthritis.

Setting
From December 2021 to March 2022, patients at Baghdad Teaching Hospital/Medical City/Rheumatology Department were enrolled in this study, which was performed in a single center.

Sample size
The number of participants was calculated using G*Power (RRID: SCR 013726) version 3.1.9.7 freeware. With a 95% confidence interval, 90% power, a two-tailed t-test with alpha value of 0.05, and an effect size of 0.23, the following were the output parameters: noncentral parameters = 3.62, critical t = 1.97, and Df = 233. The minimum sample size of 235 patients (f) was required to attain an actual power of 0.9503.

Eligibility criteria
The inclusion criteria of the study were:
1. Patients with RA were diagnosed using the rheumatoid arthritis diagnostic criteria released by the European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR) in 2010.15

2. Patients aged 18 years or more of either sex are accepted to participate in the study.

3. Patients have been treated for at least one year before this study.

**Exclusion criteria**

The exclusion criteria of the study were:

1. Patients did not consent to participate.

2. A patient with hearing, speech or cognitive deficits (physical or mental state) impairs understanding of the questions.

**Bias**

Throughout the selection of respondents, there may be selection bias. However, sampling error is less likely in this research. The ideal research population is well-defined, attainable, highly reliable, and representative to achieve the desired result. To eliminate bias, persons with limited subject awareness due to hearing, speech, or cognitive impairments were excluded from the sample of participants. To avoid misunderstanding, we also used popular terminology.

**The questionnaires**

The Arabic version16,17 of the living with medicines questionnaire (LMQ) was utilized to assess MRB in RA patients. On a 5-point Likert scale (from strongly agree to disagree strongly), respondents answered 41 items comprising the LMQ.16 The LMQ shall consist of eight domains: Practicalities, Efficacy, Relationships with Health Professionals, Information, Attitudes, Adverse Effects, Impacts, and Control. Total LMQ scores varied from 41 to 205, with higher values implying greater MRB scores.18 In addition, the Clinical Disease Activity Index (CDAI) was used to evaluate the disease activity score of RA.19

**Administration of questionnaires**

When RA patients were identified with the Rheumatology Department, they were asked whether they would be willing to participate in the current research; if they accepted, they were provided with an explanation of the study’s aims and allowed 20 to 30 minutes to finish the questionnaire.

**Statistical analysis**

Descriptive statistics (means, standard deviation, frequencies, and percentages) were conducted for all study items. Data were analyzed using Statistical Package for the Social Sciences (SPSS) software version 25. Pearson correlation was used to measure the correlation between Medication-Related Burden (LMQ) and disease severity measures (DAS28 and CDAI Scores). Additionally, Pearson correlation was used to measure the correlations between the LMQ domains and clinical disease measures (DAS28 and CDAI Scores). Independent T-tests and one-way ANOVA tests were used to measure the influence of patient’s demographic and clinical characteristics on medication burden measures (LMQ). A P-value of less than 0.05 was considered statistically significant.

**Results**

The study recruited 250 patients with RA. More than three-quarters of the patients (80.8%) were women and married (78.4%). The patients were adults with an average age of 47.3 (±12.7). The majority had either primary school (29.2%) or secondary school (30.8%) degrees. Most patients lived in urban areas (90.4%), and more than two-thirds (68%) were from the Baghdad governorate. Approximately one-quarter (24.8%) were smokers, and (4.8%) were alcohol drinkers. The majority (82.8%) relied on private and governmental sources to obtain their medications (Table 1).

The mean disease duration was 7.87 ± 6.42 years, the mean of DAS28 was 4.75 ± 1.18, CDAI was 18.59 ± 8.99, no. of chronic medications was 3.81 ± 1.71, no. of other chronic diseases was 0.53 ± 0.73 (Table 2).

The mean LMQ score was 113.78 ± 13.95. Range: was 65-147. The findings showed that the majority of the participants experienced a moderate degree of burden of 72.0%, followed by a minimum burden of 24.4%, a high burden of 2.8%, and no burden of 0.8%, with no patient experiencing an extremely high burden 0.0 % as illustrated in Table 3.
### Table 1. The sociodemographic characteristics of the patients.

| Subcategory         | Frequency (N) | %    |
|---------------------|---------------|------|
| **Sex**             |               |      |
| Male                | 48            | 19.2 |
| Female              | 202           | 80.8 |
| **Education level** |               |      |
| Illiterate          | 34            | 13.6 |
| Primary school      | 73            | 29.2 |
| Secondary school    | 77            | 30.8 |
| College degree      | 66            | 26.4 |
| **Social status**   |               |      |
| Single              | 24            | 9.6  |
| Married             | 196           | 78.4 |
| Divorced            | 6             | 2.4  |
| Widowed             | 24            | 9.6  |
| **Living place**    |               |      |
| Urban               | 226           | 90.4 |
| Rural               | 24            | 9.6  |
| **Governorate**     |               |      |
| Baghdad             | 170           | 68.0 |
| others              | 79            | 32.0 |
| **Cigarette smokers** |             |      |
| Yes                 | 62            | 24.8 |
| No                  | 188           | 75.2 |
| **Alcohol drinker** |               |      |
| Yes                 | 12            | 4.8  |
| No                  | 238           | 95.2 |
| **Source of medications** |     |      |
| Public sector       | 14            | 5.6  |
| Private sector      | 29            | 11.6 |
| Both                | 207           | 82.8 |
| **Age (years)**     | 18            | 87   |
| Minimum             | 47.29         |
| Maximum             | 12.723        |

### Table 2. Disease characteristics of the patients.

| Variables                              | Mean (SD)       |
|----------------------------------------|-----------------|
| Disease duration (years) (mean ± SD)   | 7.87 (6.42)     |
| Number of chronic medications (mean ± SD) | 3.81 (1.71)   |
| Number of other chronic diseases (mean ± SD) | 0.53 (0.73) |
| DAS28-value (mean ± SD)                | 4.75 (1.18)     |
| CDAI-value (mean ± SD)                 | 18.59 (8.99)    |

CDAI: Clinical Disease Activity Index; DAS28: Disease Activity Score of 28 joints.

### Table 3. The overall LMQ score and frequency of patients at each medication burden level.

| Medication burden | Actual range | Mean | Std. deviation |
|-------------------|--------------|------|----------------|
| Total LMQ-score   | (65-147)     | 113.78| 13.95          |
| No burden         | (41-73)      | 2    | 0.8            |
| Minimum           | (74-106)     | 61   | 24.4           |
| Moderate          | (107-139)    | 180  | 72.0           |
| High              | (140-172)    | 7    | 2.8            |
| Extremely high    | (173-205)    | -    | -              |

LMQ: Living with Medicines Questionnaire.
Five LMQ domains had the lowest mean of burden scores (below the average): domain 1 (relationships with HCPs), domain 2 (practical difficulties in using medicines), domain 4 (side effects of drugs), domain 5 (effectiveness of prescribed medications) and domain 6 (concerns about treatments use). On the other hand, three domains had the highest mean of burden scores: domain 3 (cost-related burden), domain 7 (impact of using medicines on daily life), and domain 8 (autonomy to vary regimen) (Table 4).

The total LMQ score was significantly P-value <0.05 different according to patient sex. Women had a considerably higher medication-related burden (total LMQ) (Table 5).

The total LMQ score was significantly (P-value <0.05) different according to the number of chronic medications and having a chronic disease. RA patients with regular medicines of more than five had significantly higher medication-related burdens (total LMQ score) compared to those with a lower number of scheduled medications. Patients with chronic diseases (other than RA) had significantly higher medication-related burdens (total LMQ scores) than those without chronic diseases (Table 6).

The total LMQ score had a significant positive correlation with the CDAI value. In other words, when disease severity increases, the medication-related burden increases (Table 7).

| LMQ domains                      | Minimum | Maximum | Mean of burden scores | Std. Deviation |
|----------------------------------|---------|---------|-----------------------|----------------|
| LMQ domain 1 (Relationships with HCPs) | 5.00    | 20.00   | 9.42                  | 2.47           |
| LMQ domain 2 (Practical Difficulties in Using Medicines) | 9.00    | 72.00   | 25.91                 | 4.77           |
| LMQ domain 3 (Cost Related Burden) | 3.00    | 15.00   | 12.25                 | 3.07           |
| LMQ domain 4 (Side Effects of Medicines) | 4.00    | 20.00   | 11.81                 | 3.07           |
| LMQ domain 5 (Effectiveness of prescribed medications) | 6.00    | 20.00   | 10.39                 | 2.57           |
| LMQ domain 6 (Concerns about Medicines Use) | 14.00   | 59.00   | 25.13                 | 5.15           |
| LMQ domain 7 (Impact of Using Medicines on Daily Life) | 7.00    | 28.00   | 17.93                 | 3.90           |
| LMQ domain 8 (Autonomy to Vary Regimen) | 3.00    | 15.00   | 10.17                 | 3.34           |

LMQ: Living with Medicines Questionnaire.

| Medication burden               | N   | Mean  | Std. Deviation | P-value  |
|---------------------------------|-----|-------|----------------|----------|
| Total-score-LMQ                 |     |       |                |          |
| Sex                             |     |       |                |          |
| Male                            | 48  | 104.21| 14.84          | 0.0001*  |
| Female                          | 202 | 116.05| 12.74          |          |
| Social status                   |     |       |                |          |
| Without spouse                  | 54  | 114.52| 14.58          | 0.659    |
| Married                         | 196 | 113.57| 13.80          |          |
| Address                         |     |       |                |          |
| Urban                           | 226 | 113.37| 14.07          | 0.157    |
| Rural                           | 24  | 117.61| 12.35          |          |
| Governorate                     |     |       |                |          |
| Baghdad                         | 170 | 112.78| 14.49          | 0.099    |
| Others                          | 80  | 115.90| 12.54          |          |

*Significant P-value <0.05 according to Independent T-test. LMQ: Living with Medicines Questionnaire.
Discussion

This is the first research in Iraq to look at MRB in people with rheumatoid arthritis. Women made up more than three-quarters of the patients (80.8%). As previously stated, RA is two to three times more common in women than in men.20

Our study indicated that all the participants suffered varying degrees of burden related to their medication. The majority of therapeutic approaches for patients with rheumatoid arthritis are pharmacological, and therapeutic effectiveness is crucial for reducing complaints, impaired functioning, and joints abnormalities.21 Consequently, RA patients need several DMARDs, glucocorticoids, and analgesics. In addition, most RA patients suffer complications attributable to the condition’s persistent inflammatory process. Consequently, overtreatment is more widespread among RA patients than among other patient populations,22 and patients may have several problems during therapy,22 so people may have several problems during therapy. Three domains had the highest mean of burden scores: cost-related burden, the impact of using medicines on daily life, and autonomy to vary regimen. In other words, the patients had difficulty with medicine costs, could not change their regimen, and their medicines impacted their daily life.

The financial burden of medications has a detrimental impact on some people’s well-being due to a disrupted family and social life. This resulted in internal conflict and unpleasant sensations in certain circumstances.10,23 Furthermore, many patients indicated that medication regimens interfered with personal and social life beyond their capacity to cope and were a significant obstacle to engaging in practical medication usage.24–30 On the other hand, five LMQ domains had the lowest mean of burden scores: relationships with HCPs, practical difficulties in using medicines, side effects of drugs, the effectiveness of prescribed medications, and concerns about medicine use. Prior research of Iraqi RA patients found that the vast majority of participants (88%) firmly believed in the need for therapy (specific necessity score greater than specific-concern score).31

Women had significantly higher medication-related burdens (total LMQ). Smokers had substantially lower medication-related burdens than non-smokers, and alcohol drinkers had significantly lower medication-related burdens than non-drinkers. Sex appears to be a key antecedent of treatment burden because women and men experience different treatment burdens. Women experienced a higher treatment burden than men. Additionally, women reported more caregiver burden when their children were sick, possibly due to their traditional homemaker roles.32–34

Rheumatoid arthritis patients with more than five chronic medications had significantly higher medication-related burdens than those with a lower number of scheduled drugs. Patients with chronic diseases (other than RA) had a substantially higher medication-related responsibility than those without other chronic diseases. As expected, polypharmacy was associated with higher LMQ scores. The possible explanation for this could be that as people with the disease utilize medicines on a regular basis, they expend as much feelings, energy, time, and money on prescription practice management35,36 (e.g., medicine selection, medicine collocation perversion, medicine-related precautionary measures, medicine

| Total-LMQ-score | N   | Mean | Std. Deviation | P-value |
|-----------------|-----|------|----------------|---------|
| Chronic medications | ≤ 5 | 211  | 112.97         | 14.26   | 0.034* |
|                  | > 5 | 39   | 118.12         | 11.26   |         |
| Chronic diseases | No  | 152  | 111.61         | 13.97   | 0.002* |
|                  | Yes | 98   | 117.14         | 13.28   |         |
| Disease duration | ≤ 5 years | 124 | 114.07         | 12.63   | 0.746   |
|                  | > 5 years | 126 | 113.49         | 15.17   |         |

*Significant (P-value <0.05) according to Independent T-test. LMQ: Living with Medicines Questionnaire.

| Total-score-LMQ | Pearson Correlation | CDAI-value |
|-----------------|---------------------|------------|
|                 | 0.181               | 0.004*     |

*Significant (P-value <0.05) according to Pearson correlation. LMQ: Living with Medicines Questionnaire.
reserve, and medicine purchase), which increases their prescription burden. As expected, the presence of comorbidity was associated with an increased load. Some comorbidities, mainly psychological diseases such as depression or anxiety, were associated with a high degree of treatment burden. Chronic diseases such as diabetes mellitus and schizophrenia were associated with a higher treatment burden.

The total LMQ score had a significant positive correlation with the CDAI value. In other words, when disease severity increases, the MRB increases. Sav et al. analyzed studies on treatment burden released between 2000 and 2011. They asserted that various factors such as disease severity, sex, age, disease duration, treatment characteristics such as the prescription number and dosing frequency, and level of family support could all contribute to chronic disease treatment burden. Furthermore, Sav et al. bring attention to the dynamical aspect of treatment burden, implying that a person’s overall impression of treatment burden might alter during their sickness, depending on the severity and effect of the disease.

Limitations
The present research has certain limitations that should be noted. First, although a convenient sample of patients was used, but was drawn from just a single institution. More research is needed to determine if and to what extent they can reflect the overall number of RA patients in Iraq. As a consequence, the present findings may be restricted in their generalizability. Secondly, recollection and desirability biases may influence the self-reported medication-related burden. Finally, the sample size was limited in this case. Future research should include multi-center and high sample size investigations from different parts of Iraq to see whether the findings can be validated in other RA patients.

Conclusion
A considerable proportion of RA patients experienced MRB, which was affected by many factors including sex, comorbidities, number of medications taken by the patients, or disease severity. Therefore, Iraqi health care providers should focus on MRB and adopt suitable interventions to reduce such burden.

Data availability
Underlying data
Zenodo: Demographic information, as well as questionnaire answers. https://doi.org/10.5281/zenodo.7041030.

This project contains the following underlying data:
- Article’s data.xlsx (Demographic information, as well as questionnaire answers)

Data are available under the terms of the Creative Commons Attribution 4.0 International license (CC-BY 4.0).

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References
1. Scherer HU, Häupl T, Burmester GR: The etiology of rheumatoid arthritis. J. Autoimmun. 2020; 110: 102400. Publisher Full Text
2. Guo Q, Wang Y, Xu D, et al.: Rheumatoid arthritis: pathological mechanisms and modern pharmacologic therapies. Bone Res. 2018; 6(1): 1-14. Publisher Full Text
3. Al-Rawi ZS, Alazzawi AJ, Alajili FM, et al.: Rheumatoid arthritis in population samples in Iraq. Ann. Rheum. Dis. 1978; 37(1): 73-75. PubMed Abstract | Publisher Full Text | Free Full Text
4. Shams S, Martinez JM, Dawson JRD, et al.: The therapeutic landscape of rheumatoid arthritis: current state and future directions. Front. Pharmacol. 2021; 12: 68043. PubMed Abstract | Publisher Full Text
5. Tanaka Y: Rheumatoid arthritis. Inflamm. Regen. 2020; 40(1): 20. PubMed Abstract | Publisher Full Text
6. Bertin P, Fagnani F, Duburcq A, et al.: Impact of rheumatoid arthritis on career progression, productivity, and employability: the PRET study. Joint Bone Spine. 2016; 83(1): 47-52. PubMed Abstract | Publisher Full Text
7. Malm K, Bergman S, Andersson MLE, et al.: Quality of life in patients with established rheumatoid arthritis: a phenomenographic study. SAGE Open Med. 2017; 5: 205031211771364. Publisher Full Text
8. Bullock J, Rizvi SAA, Saleh AM, et al.: Rheumatoid arthritis: a brief overview of the treatment. Med. Prin. Pract. 2018; 27(6): 501-507. PubMed Abstract | Publisher Full Text
9. Kumar P, Banik S: Pharmacotherapy options in rheumatoid arthritis. Clin. Med. Insights: Arthritis Musculoskelet. Disord. 2013; 6: CMAMD.55558. Publisher Full Text
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