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# ASSOCIATION OF MEDICATION NON-ADHERENCE WITH FLARE FREQUENCY IN RHEUMATOID ARTHRITIS PATIENTS ON CONVENTIONAL DMARDS: A CROSS-SECTIONAL STUDY

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**ABSTRACT** **Background:** Rheumatoid arthritis (RA) requires strict adherence to disease-modifying antirheumatic drugs (DMARDs) for long-term disease control. Non-adherence contributes to increased disease activity, frequent flares, and disability. **Objective:** To evaluate the association between medication non-adherence and flare frequency in RA patients receiving conventional DMARDs. **Methods:** A cross-sectional study of 85 RA patients on DMARDs was conducted over 1 year. Adherence was defined as taking ≥80% of prescribed doses; non-adherence as <80%. Disease flare was defined by clinical worsening and/or DAS28 increase >1.2. Statistical analysis included chi-square test and odds ratio (OR). **Results:** 30.7% were non-adherent. Methotrexate was the most prescribed DMARD (54.7%), followed by combination therapy (29.7%). Disease flare occurred in 45.8% of patients. Non-adherent patients had a significantly higher flare frequency (p=0.0003), with 3.3-fold increased risk compared to adherent patients. **Conclusion:** Non-adherence strongly correlates with flare occurrence in RA patients on conventional DMARDs. Interventions to improve adherence are crucial for reducing flares and long-term morbidity.

**KEYWORDS :** Rheumatoid arthritis; DMARDs; Medication adherence; Disease flare

## INTRODUCTION

Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease characterized by persistent synovitis and progressive joint destruction, leading to disability and impaired quality of life if not adequately controlled[1] . Early initiation and sustained use of conventional synthetic DMARDs—such as methotrexate, sulfasalazine, hydroxychloroquine, and leflunomide—are key to achieving low disease activity or remission[2,3].

Despite proven efficacy, adherence to DMARD therapy is suboptimal, with global rates ranging from 22–80% depending on methodology[4,5]. Non-adherence results in increased disease activity, frequent flares, radiographic progression, and greater healthcare burden[6,7,8]. Factors such as regimen complexity, side effects, socioeconomic barriers, and poor health literacy contribute to suboptimal adherence[9,10].

Given this, understanding the link between medication non-adherence and RA flares is critical. This study investigates the association in a cross-sectional cohort of Indian RA patients receiving conventional DMARDs.

## MATERIALS AND METHODS

**Study Design & Setting:** Hospital-based cross-sectional study conducted in the Department of Medicine, Assam Medical College and Hospital, Dibrugarh, over one year (Nov 2023–Oct 2024). Ethical clearance was obtained.

**Inclusion Criteria:** Patients ≥18 years, fulfilling 2010 ACR/EULAR RA criteria, on conventional DMARDs ≥6 months.
**Exclusion Criteria:** Patients on biologic DMARDs, overlap syndromes, or refusal to consent.

**Data Collection:** Demographic details, disease duration, DMARD use, flare status, and adherence were recorded.

- Flare: DAS28 increase >1.2 or clinical worsening.
- Non-adherence: ≥20% missed doses in past month, assessed by self-report and prescription refill review.

**Analysis:** SPSS used for descriptive statistics. Chi-square test applied.odds ratios (ORs) with 95% confidence intervals (CI) calculated.

## RESULT:

**Table 1. Baseline Characteristics and DMARD use (n=85)**

| Variable | Category | n (%) |
|---|---|---|
| Gender | Male | 23 (27.1) |
| | Female | 62 (72.9) |
| Disease duration | <1 yr | 9 (10.6) |
| | 1–5 yrs | 36 (42.3) |
| | 6–10 yrs | 28 (33.0) |
| | >10 yrs | 12 (14.1) |
| Mean disease duration | Years | 5.6 ± 3.6 |
| DMARDs used | Methotrexate | 46 (54.8) |
| | Hydroxychloroquine | 7 (8.3) |
| | Leflunomide | 4 (4.8) |
| | Sulfasalazine | 1 (1.2) |
| | Combination | 25 (29.7) |

- Majority were female patients (72.9%), consistent with RA's known female predominance.
- Most had disease duration 1–5 years (42.3%), with mean duration 5.6 ± 3.6 years, highlighting chronicity.
- Methotrexate (54.8%) was the most prescribed DMARD, followed by combination therapy (29.7%); other single DMARDs were used less frequently.

**Table 2. Flare Occurrence and Frequency**

| Flare Status | n (%) | Flare Episodes in 6 months | n (%) |
|---|---|---|---|
| Flare | 39 (45.8) | 1 episode | 18 (46.1) |
| | | 2 episodes | 11 (28.2) |
| | | ≥3 episodes | 10 (25.6) |
| No Flare | 46 (54.2) | - | - |

- 45.8% of patients experienced at least one disease flare within 6 months.
- Among those with flares, 46.1% had one flare, 28.2% had two, and 25.6% had three or more.
- 54.2% of patients remained flare-free.

**Table 3. Association Between Adherence and Flare**

| Adherence | Flare (n=39) | No Flare (n=46) | Total | p-value | OR (95% CI) |
|---|---|---|---|---|---|

| | | | | | |
|---|---|---|---|---|---|
| Adherent | 19 | 40 | 59 | | |
| Non-adherent | 20 | 6 | 26 | 0.0003 | 3.3 (1.4–7.5) |

- Among non-adherent patients (30.7%), 20/26 (76.9%) experienced flares.
- In contrast, only 19/59 (32.2%) of adherent patients had flares.
- Non-adherence was significantly associated with flares (p = 0.0003), with a 3.3-fold higher risk compared to adherent patients.

## DISCUSSION

This study found that nearly one-third of RA patients were non-adherent to conventional DMARDs, comparable to international data reporting non-adherence between 25–40%[11,12]

The predominance of females (73%) aligns with known RA epidemiology (female-to-male ratio 2–3:1)[13]. Methotrexate remains the cornerstone of RA treatment[14], with significant use of combination therapy in resistant cases. Mean disease duration of 5.6 years highlights chronicity.

Almost half (45.8%) experienced disease flares, consistent with flare rates reported in European and Asian cohorts (30–50%) (15,16). Importantly, one-fourth of flare patients had ≥3 flares within 6 months, emphasizing the clinical burden.

Non-adherence showed a strong association with flares, conferring a 3.3-fold increased risk. This effect size is higher than in Korean (2.1-fold) and Japanese cohorts (48% flare risk reduction with adherence)[17,18]. Our findings reinforce evidence from Egyptian studies where adherence interventions lowered flare frequency[19]. Collectively, this underlines that adherence directly determines disease stability.

**Clinical Implications:** Poor adherence exacerbates RA activity and disability, adding to healthcare costs. Regular patient counseling, simplified regimens, and digital adherence monitoring may mitigate risks.

**Limitations:** Cross-sectional design precludes causal inference. Adherence measured by self-report and refill history may overestimate compliance. Single-center data limits generalizability.

## CONCLUSION

Medication non-adherence significantly increases flare risk in RA patients on conventional DMARDs. With non-adherent patients being 3.3 times more likely to experience flares, adherence interventions should be integrated into RA management strategies.

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