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Drug utilization patterns and dosing appropriateness of antirheumatic drugs in outpatients with rheumatoid arthritis at Harapan dan Doa General Hospital, Bengkulu City, Indonesia

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Abstract: Rheumatoid arthritis (RA) is an autoimmune disease that requires long-term treatment and careful management. Inappropriate therapy may increase morbidity and mortality; therefore, appropriate drug selection and prescribing are essential to improving healthcare quality, particularly in hospital settings. This study aimed to determine the prescribing patterns of medications for patients with rheumatoid arthritis at Harapan dan Doa General Hospital in Bengkulu City. A descriptive, quantitative design was employed, utilizing a total sampling technique. The results showed that, based on drug combination patterns, most patients received triple-drug therapy (46.66%), followed by dual therapy (31.61%) and monotherapy (21.64%). The most common monotherapy was etoricoxib (8.33%), while the most frequent two-drug combination was methotrexate and methylprednisolone (11.66%). The predominant three-drug combination consisted of methotrexate, methylprednisolone, and meloxicam (15%). Based on therapeutic class, the prescribed drugs included nonsteroidal anti-inflammatory drugs (NSAIDs) (80%), corticosteroids (71.66%), disease-modifying antirheumatic drugs (DMARDs) (61.66%), and analgesics (10%). Although all prescribed drugs followed the recommended dosing guidelines, NSAIDs and corticosteroids were used more frequently than methotrexate. This pattern may reflect variations in clinical practice or differences in patient characteristics.

Keywords: Disease-modifying antirheumatic drugs, drug utilization, nonsteroidal anti-inflammatory drugs, prescribing patterns, rheumatoid arthritis

Introduction

Rheumatoid arthritis (RA) is a chronic systemic inflammatory autoimmune disease that affects multiple tissues, particularly the joints. It is caused by the proliferation of non-suppurative synovitis, which progresses and leads to the destruction of articular cartilage and underlying bone, resulting in joint inflammation [1]. The long-term consequences of RA include joint damage and disability. Approximately 60% of RA patients experience disability that prevents them from working within 10 years of symptom onset. Moreover, mortality rates among RA patients show a significant increase, with an average reduction in life expectancy of 7 years for men and 3 years for women compared to the general population. Appropriate treatment can reduce or eliminate pain and inflammation, slow or halt joint destruction, and prevent systemic complications, thereby improving patients' ability to carry out daily activities and work [2].

Globally, the prevalence of RA is estimated to be 0.3–1% of the adult population, with higher rates observed in women and older adults [3]. In Indonesia, the prevalence of joint-related complaints is reported at 23.6% [4]. However, the prevalence of specific RA is lower and varies by region [5]. In Indonesia, the prevalence of RA-related pain is 23.6%, equivalent to 55 million individuals. The incidence rate of RA-related pain is considered high, affecting 1–2% of the total population. This disease is more common among

elderly individuals, particularly those aged 50 years and above [6]. Nationally, the highest prevalence of joint diseases is reported in Aceh Province (13.26%), followed by Bengkulu (12.11%), Bali (10.46%), and Papua (10.43%) [4].

Given the increasing prevalence of rheumatoid arthritis, the use of appropriate and rational medications is crucial to ensure effective disease management and to prevent complications associated with long-term therapy. The selection of an appropriate therapeutic regimen represents a key component of rational prescribing practice. According to the World Health Organization (WHO), rational drug use involves prescribing medications that are appropriate to clinical needs, in the correct dose, for an adequate duration, and at the lowest possible cost to patients and the community. Therefore, physicians must prescribe carefully to minimize adverse drug reactions and potential drug interactions. Prescription errors are still frequently encountered, particularly in drug selection, route of administration, dosage, and dosage form. The incidence of inappropriate prescribing, including incorrect drug selection for specific patient conditions, remains relatively high [7].

Several studies have examined prescribing patterns in RA therapy, focusing on drug appropriateness and dosage accuracy to ensure optimal therapeutic outcomes. A previous study at Semarang City Hospital evaluated prescribing practices in RA patients. The results showed that the most frequently prescribed immunosuppressants were conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), with methotrexate (MTX) prescribed to 94 patients. The most common therapeutic dose was 7.5 mg per week, administered orally to 61 patients. The combination of MTX and sulfasalazine was the most frequent immunosuppressive regimen (23%), followed by MTX monotherapy (20%). MTX is the preferred first-line therapy for RA, either as monotherapy or in combination [8].

Similarly, a study by Nata et al. (2023) at Ulin Regional Hospital in Banjarmasin examined prescribing patterns in patients with rheumatoid arthritis (RA) [2]. The results indicated that physicians primarily initiated pharmacological therapy with DMARDs, with conventional synthetic DMARDs (csDMARDs) being the most frequently prescribed as first-line treatment. Methotrexate (MTX) is recommended as the primary csDMARD, either as monotherapy or in combination, for patients who are intolerant of or have contraindications to MTX; leflunomide or sulfasalazine may be used as alternatives, either alone or in combination with corticosteroids and/or NSAIDs. If therapeutic goals are not achieved within 3–6 months with the initial csDMARD, a second csDMARD may be added as combination therapy. Building on this evidence, the present study aims to investigate the prescribing patterns of anti-inflammatory therapy in RA patients according to disease severity. The findings are expected to provide a reference for selecting appropriate RA therapy, minimizing adverse effects, and achieving optimal therapeutic outcomes.

Methods

A descriptive research design was employed to provide an objective overview of drug utilization patterns among patients with rheumatoid arthritis (RA) at Harapan and Doa General Hospital, Bengkulu. Ethical approval was obtained from the Health Research Ethics Committee, Faculty of Dentistry, University of Jember (No. 2904/UN25.8/KEPK/DL/2024). Data were collected retrospectively from archived outpatient prescription records. The study population consisted of RA outpatients who had received prescribed medications, and samples were selected based on predefined inclusion and exclusion criteria.

Inclusion criteria: (1) patients diagnosed with RA at Harapan and Doa General Hospital, Bengkulu City; (2) patients receiving prescriptions either as monotherapy or combination therapy; and (3) patients with complete medical records, including personal information, examination date, diagnosis, and prescribed therapy. Exclusion criteria: (1) incomplete or illegible prescriptions; and (2) RA patients who were pregnant.

The study was conducted between September 2023 and February 2024, involving 60 patients who met the inclusion criteria. This study involved a single variable—the prescribing pattern of drug use in RA patients—which included therapeutic classes, types, and combinations. The collected data were analyzed descriptively using patient prescription data from RA outpatients who received pharmacological therapy at the hospital. Patient data included demographic characteristics (age and sex) and medication details (drug type, therapeutic class, dosage, and frequency of use). Data were processed using Microsoft Excel, and the results were presented in distribution tables and interpreted descriptively.

Table 1. Characteristics of rheumatoid arthritis patients at Bengkulu City Hospital

Patient Characteristics	Frequency	Percentage (%)
Gender		
Male	10	16.67
Female	50	83.33
Age (years)		
18–25	2	3.3
26–35	3	5
36–45	15	25
46–55	16	26.67
56–65	14	23.33
>65	10	16.67
Comorbidities		
Without comorbidity	35	58
Hypertension	12	20
Diabetes Mellitus	6	10
Dyspepsia	1	1.6
Dyslipidemia	5	3.3
GERD	1	1.6
Total	60	100

Results

Characteristics of rheumatoid arthritis patients

This study analysed data from 60 patients diagnosed with rheumatoid arthritis who received treatment at the outpatient unit of Harapan dan Doa General Hospital, Bengkulu City, in 2023. Patient characteristics were categorized by gender, age, and comorbidities, as presented in Table 1.

The demographic profile of RA patients showed a strong female predominance, with 50 female patients (83.33%) compared to 10 male patients (16.67%). The age distribution revealed that the majority of patients were in the middle-aged to elderly groups. The largest proportion was in the 46–55-year age range (n=16, 26.67%), followed closely by the 56–65-year group (n=14, 23.33%) and the 36–45-year group (n=15, 25%). Patients aged 46 years and above collectively represented 76.67% of the total sample. In contrast, younger patients were less represented, with only 3 patients (5%) in the 26–35-year group and 2 patients (3.3%) in the 18–25-year group. Ten patients (16.67%) were over 65 years of age.

Regarding comorbidities, more than half of the patients (n=35, 58.33%) had no concurrent medical conditions. Among those with comorbidities, hypertension was the most common, affecting 12 patients (20%), followed by diabetes mellitus in 6 patients (10%). Other less common comorbidities included dyslipidemia (n=5, 8.33%), dyspepsia (n=1, 1.67%), and gastroesophageal reflux disease (GERD) (n=1, 1.67%). The presence of cardiovascular risk factors such as hypertension and diabetes mellitus in approximately one-third of patients highlights the importance of comprehensive management approaches in RA care.

Prescribing patterns of rheumatoid arthritis drugs based on the number of drugs

The prescribing patterns were analyzed according to the number of medications used in each treatment regimen. As shown in Table 2, combination therapy was more common than monotherapy. Three-drug combinations were prescribed to 28 patients (46.66%), representing the most prevalent treatment approach. Two-drug combinations were used in 19 patients (31.61%), while monotherapy was prescribed to 13 patients (21.64%).

Table 2. Treatment profiles for rheumatoid arthritis therapy

Treatment Profile	Frequency	Percentage (%)
Monotherapy		
DMARD – Methotrexate	1	1.66
DMARD – Sulfasalazine	1	1.66
Corticosteroid – Methylprednisolone	1	1.66
NSAID – Etoricoxib	5	8.33
NSAID – Meloxicam	2	3.33
NSAID – Diclofenac sodium	3	5
Two-drug combinations		
Methotrexate + Methylprednisolone	7	11.66
Sulfasalazine + Methylprednisolone	1	1.66
Sulfasalazine + Diclofenac sodium	1	1.66
Methotrexate + Etoricoxib	1	1.66
Methylprednisolone + Diclofenac sodium	3	5
Methylprednisolone + Etoricoxib	1	1.66
Methylprednisolone + Meloxicam	2	3.33
Meloxicam + Paracetamol	1	1.66
Diclofenac potassium + Paracetamol	1	1.66
Etoricoxib + Ibuprofen	1	1.66
Three-drug combinations		
Methotrexate + Methylprednisolone + Meloxicam	9	15
Methotrexate + Methylprednisolone + Diclofenac sodium	5	8.33
Methotrexate + Etoricoxib + Methylprednisolone	8	13.33
Sulfasalazine + Etoricoxib + Methylprednisolone	3	5
Methylprednisolone + Etoricoxib + Ibuprofen	3	5
Total	60	100

Prescriptions by therapeutic class in rheumatoid arthritis patients

The medications prescribed for RA patients were categorized into four main therapeutic classes: disease-modifying antirheumatic drugs (DMARDs), corticosteroids, nonsteroidal anti-inflammatory drugs (NSAIDs), and analgesics. Table 3 presents the distribution of prescriptions by therapeutic class and individual drug.

Appropriateness of rheumatoid arthritis drug dosing

The appropriateness of prescribed dosages was evaluated by comparing the prescribed doses with standard therapeutic recommendations from Pharmacotherapy: A Pathophysiologic Approach (10th edition) [9] and guidelines from the Indonesian Rheumatology Association (2014) [10]. Table 4 summarizes the evaluation of dosing appropriateness.

While all doses were within recommended ranges, it is important to note that dosing appropriateness alone does not reflect the overall quality of prescribing. Factors such as the timing of DMARD initiation, appropriateness of drug selection for disease severity, and adherence to treatment sequencing guidelines are equally important considerations that were not evaluated in this analysis.

Discussion

This study examined drug utilization patterns in 60 rheumatoid arthritis (RA) patients at Harapan and Doa General Hospital, Bengkulu City. The findings revealed that combination therapy was the predominant

Table 3. Prescriptions of rheumatoid arthritis drugs by therapeutic class

Therapeutic Class	Drug Name	Frequency	Percentage (%)
DMARD	Methotrexate	31	51.66
	Sulfasalazine	6	10
Corticosteroid	Methylprednisolone	43	71.66
NSAID	Diclofenac sodium	12	20
	Meloxicam	13	21.66
	Etoricoxib	22	36.66
	Diclofenac potassium	1	1.66
Analgesic	Paracetamol	2	3.33
	Ibuprofen	4	6.66

Table 4. Appropriateness of prescribed doses for rheumatoid arthritis drugs

Drug	Recommended Dose	Prescribed Dose(s) in This Study	Accuracy (%)
Methotrexate	Oral: 7.5 mg/week or 2.5 mg every 12h, 3×/week; SC/IM: 10–15 mg (max 15 mg)	Oral 2.5 mg 3×/week	100
Sulfasalazine	Oral: 0.5–1 g/day	Oral 500 mg 1×/day	100
Methylprednisolone	Oral daily: low dose <7.5 mg, moderate dose 7.5–30 mg	Oral 4 mg 1×/day, 8 mg 2×/day, 16 mg 1×/day	100
Diclofenac sodium	Oral daily: 100–200 mg or 50–75 mg 2×/day	Oral 50 mg 1–2×/day	100
Diclofenac potassium	Oral daily: 100–200 mg or 50–75 mg 2×/day	Oral 50 mg 2×/day	100
Meloxicam	Oral: 7.5–15 mg/day	Oral 15 mg 1×/day	100
Etoricoxib	Oral: 90–120 mg/day	Oral 90 mg 1×/day	100

treatment approach, with three-drug combinations being most common (46.66%), followed by two-drug combinations (31.61%) and monotherapy (21.64%). The most frequently prescribed three-drug regimen consisted of methotrexate, methylprednisolone, and meloxicam (15%). By therapeutic class, NSAIDs were prescribed to 80% of patients, corticosteroids to 71.66%, DMARDs to 61.66%, and analgesics to 10%. Although all prescribed medications adhered to recommended dosage ranges, the prescribing pattern showed higher utilization of NSAIDs and corticosteroids compared to DMARDs, particularly methotrexate, which is considered the cornerstone of RA therapy according to current guidelines.

The demographic profile showed a strong female predominance (83.33%) compared with male patients (16.67%). This finding is consistent with Nata et al. (2023), who reported RA prevalence of 78.8% among females versus 21.2% among males [2]. The sex disparity in RA prevalence is attributed to multiple factors, including variations in immune function, genetic factors, and hormonal influences. Estrogen stimulates TNF-α production, a cytokine central to RA pathogenesis. With age, hormonal imbalance, particularly the decline of estrogen during and after menopause, increases the risk of RA among women [12]. The highest proportion of RA patients was within the 46–55-year age group (26.67%), which corresponds with the aging process that typically begins between 40 and 60 years and is marked by significant hormonal changes in women [11]. Similarly, Hernawati et al. (2024) reported that 46.7% of RA patients were within this age group [13]. In contrast, patients aged 18–25 years accounted for only 3.3%, reflecting the lower incidence of autoimmune conditions in younger adults [14].

Regarding comorbidities, 58.3% of patients had no concurrent conditions, while hypertension (20%) and diabetes mellitus (10%) were the most frequently observed. The presence of hypertension in RA patients can be attributed to several factors: RA itself is a recognized risk factor for cardiovascular disease due to chronic systemic inflammation, and

long-term corticosteroid therapy may contribute to elevated blood pressure [15]. Gastrointestinal disorders, including dyspepsia (1.6%) and GERD (1.6%), were less common but are clinically significant as they are often associated with chronic NSAID use. NSAIDs can cause a spectrum of gastrointestinal adverse effects ranging from mild symptoms such as nausea and dyspepsia to serious complications including bleeding and perforation [16].

The prescribing patterns observed in this study reveal important insights into RA management practices at the study site. As shown in Table 2, monotherapy was employed in 21.64% of cases, with etoricoxib being the most commonly prescribed single agent (8.33%). This preference for selective NSAIDs such as etoricoxib reflects their efficacy in managing musculoskeletal pain and inflammation. However, it is important to note that selective COX-2 inhibitors require careful monitoring due to potential cardiovascular risks, particularly in patients with pre-existing cardiovascular conditions or risk factors [17]. The relatively frequent use of NSAID monotherapy raises concerns about adherence to current treatment guidelines, which emphasize early initiation of disease-modifying therapy rather than relying solely on symptomatic treatment.

The most common two-drug combination was methotrexate and methylprednisolone (11.66%), which represents an appropriate therapeutic approach combining a DMARD with corticosteroid for disease control. However, the observation that some patients received combinations of NSAIDs with corticosteroids without DMARDs (e.g., methylprednisolone + diclofenac sodium, 5%; methylprednisolone + etoricoxib, 1.66%) suggests that disease-modifying therapy may not have been prioritized in all cases. Current guidelines from the American College of Rheumatology emphasize that DMARDs, particularly methotrexate, should be initiated early in the disease course to prevent joint damage and disability [18].

Three-drug combinations were the most prevalent treatment pattern (46.66%), with methotrexate, methylprednisolone, and meloxicam being the most frequently prescribed regimen (15%). This combination represents a comprehensive approach that includes a DMARD for disease modification, a corticosteroid for inflammation control, and an NSAID for symptom relief. The second most common three-drug combination was methotrexate, methylprednisolone, and etoricoxib (13.33%). While these combination therapies may provide effective symptom control, it is concerning that some three-drug regimens consisted of multiple NSAIDs without DMARDs (e.g., methylprednisolone + etoricoxib + ibuprofen, 5%). The concurrent use of multiple NSAIDs increases the risk of adverse effects without providing additional therapeutic benefits and is generally not recommended.

Analysis of prescribing patterns by therapeutic class (Table 3) reveals that NSAIDs were the most frequently prescribed medications (80%), followed by corticosteroids (71.66%) and DMARDs (61.66%). This pattern is inconsistent with current evidence-based guidelines, which recommend DMARDs as the foundation of RA therapy. Methotrexate, prescribed to 51.66% of patients, remains the gold standard first-line DMARD due to its proven efficacy, favorable safety profile, and cost-effectiveness [8]. However, its prescription rate being lower than that of NSAIDs and corticosteroids suggests a potential gap between guideline recommendations and clinical practice. Sulfasalazine, an alternative DMARD for patients with contraindications to methotrexate, was prescribed to only 10% of patients. Methylprednisolone was the most frequently prescribed individual medication (71.66%), reflecting the widespread use of corticosteroids for managing inflammation and symptoms. While corticosteroids play an important role in RA management, particularly for achieving rapid symptom control, current guidelines recommend using them at the lowest effective dose and for the shortest duration possible due to their significant adverse effects with long-term use, including osteoporosis, metabolic disorders, and increased infection risk [18].

Among NSAIDs, etoricoxib was the most commonly prescribed (36.66%), followed by meloxicam (21.66%) and diclofenac sodium (20%). The preference for selective COX-2 inhibitors like etoricoxib and meloxicam may reflect efforts to reduce gastrointestinal adverse effects compared to non-selective NSAIDs. However, prescribers must balance this benefit against the potential cardiovascular risks associated with COX-2 inhibitors [16]. Analgesics, including paracetamol (3.33%) and ibuprofen (6.66%), were used less frequently, suggesting they were reserved for adjunctive pain management.

A critical finding of this study is that while all prescriptions adhered to recommended dosage ranges (Table 4), the overall prescribing pattern does not

fully align with the treatment paradigm advocated by international guidelines. Current RA management emphasizes a "treat-to-target" strategy, which involves early aggressive DMARD therapy, regular monitoring of disease activity, and treatment escalation or modification if treatment targets are not achieved within 3–6 months [18]. The observed pattern of higher NSAID and corticosteroid use relative to DMARDs suggests that symptom management may have taken precedence over disease modification in some cases. This approach may provide short-term relief but could potentially lead to suboptimal long-term outcomes, including progressive joint damage and disability.

Several factors may explain the observed prescribing patterns. First, patient-related factors such as contraindications to methotrexate, patient preferences, or concerns about DMARD adverse effects may have influenced treatment decisions. Second, disease severity and duration could play a role; patients with milder disease or those in the early stages might have been managed with NSAIDs and corticosteroids initially, with plans to escalate to DMARDs if needed. Third, access to regular laboratory monitoring required for DMARD therapy may be a practical consideration. Finally, variations in prescriber familiarity with current guidelines or differences in clinical judgment may contribute to the observed patterns.

This study has several limitations that should be acknowledged. The retrospective design and relatively small sample size from a single center limit the generalizability of the findings. Importantly, the study did not collect data on disease severity, disease duration, previous treatment history, or clinical outcomes, all of which are essential for comprehensively evaluating the appropriateness of prescribing patterns. Additionally, the reasons behind specific treatment choices were not documented, making it difficult to determine whether deviations from guidelines were justified by individual patient circumstances or represented gaps in adherence to evidence-based practice. Future prospective studies with larger sample sizes and more comprehensive clinical data are needed to better understand prescribing practices and their impact on patient outcomes in the management of RA in Indonesia.

Conclusion

The characteristics of rheumatoid arthritis (RA) patients were predominantly female (83.33%) and mainly within the 46–55-year age group (26.67%). Most patients had no comorbidities (58.33%), with hypertension (20%) and diabetes mellitus (10%) being the most common concurrent conditions. The most common prescribing pattern consisted of three-drug combinations (46.66%), with methotrexate, methylprednisolone, and meloxicam being the most frequently prescribed regimen (15%). By therapeutic class, NSAIDs were prescribed most frequently (80%), followed by corticosteroids (71.66%) and DMARDs (61.66%). Although all prescribed drugs adhered to recommended dosing guidelines, the prescribing pattern showed higher utilization of NSAIDs and corticosteroids compared to methotrexate, which is recommended as first-line therapy. This pattern suggests a potential gap between current guideline recommendations and clinical practice, with greater emphasis on symptom management rather than disease modification. These findings highlight the need for enhanced implementation of evidence-based RA treatment guidelines to optimize long-term patient outcomes.

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Declaration of interest

The authors declare that none of them has any conflict of interest with any private, public, or academic party related to the information contained in this manuscript.

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