Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/jptcp.v31i7.6982

STUDY OF PRESCRIPTION PATTERN ANALYSIS OF DRUGS USED IN THE TREATMENT OF RHEUMATOID ARTHRITIS IN A TERTIARY CARE HOSPITAL: AN OBSERVATIONAL STUDY

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ABSTRACT

Objective: This study was conducted to analyse the prescription pattern of Rheumatoid arthritis in a tertiary care hospital in India.

Methodology: The study was conducted in 180 patients of Rheumatoid arthritis who were given various forms of therapy and fulfilled the inclusion and exclusion criteria. Data was collected in case report format and the prescription pattern was analysed using patient's demographic details, presence of comorbidities, usage of complementary and alternative medicine, details of drugs prescribed with dosage and combination therapies

Results: The results of this study showed that DMARDs were the most commonly prescribed drugs out of which Methotrexate was the preferred drug. Monotherapy was given in 34.5% of patients while DMARD dual combination was given in 61% of patients which contributed to the majority of the prescription. A triple DMARD therapy was given in only 4.5% of patients. Methotrexate was the most commonly prescribed DMARD either in monotherapy or in combination and constituted 87.6% of prescriptions

Combination therapy of Methotrexate and Hydroxychloroquine covered the maximum number of prescriptions (68%). Sulfasalazine and Leflunomide were given in 29% and 3% of patients respectively. The prescriptions also included NSAIDs, Calcium and Vitamin D3 supplements as most common additional drugs followed by PPIs. Corticosteroids like Prednisolone were given in 12.5% of patients and were mostly preferred in long standing and refractory cases.

Conclusion:

Methotrexate is the most prescribed DMARD, often used in combination to enhance efficacy. DMARD combination of Methotrexate and HCQ was the most commonly used regimen compared to monotherapy and triple-drug therapy.

Keywords: Rheumatoid arthritis, Prescription analysis, DMARD

INTRODUCTION:

Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by inflammation of the joints, leading to pain, stiffness, and potentially joint damage if not managed effectively.

It affects millions globally, approximately 0.5-1% of the global population, impacting quality of life and posing significant healthcare challenges, with significant morbidity and economic burden. In India, 0.75% of adults have RA, which is a rather high prevalence.[1] RA predominantly affects women more than men, with peak onset typically between the ages of 30 and 50. The prevalence varies geographically, influenced by genetic, environmental and socio-economic factors. In tertiary care hospitals, patients often present with more severe disease manifestations, requiring aggressive treatment approaches to achieve disease control and prevent long-term joint damage. Erosive arthritis with resulting deformities add to the disability and poor quality of life of these patients, with a high mortality related to accelerated atherosclerosis associated with this prolonged inflammatory state, [2] Treatment strategies have evolved significantly over the years, driven by advances in understanding the pathophysiology of RA and the development of new therapeutic agents. The goals of RA treatment include achieving clinical remission or low disease activity, preserving joint function, and improving quality of life. Current guidelines from the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) emphasize early diagnosis and treatment initiation with Disease-Modifying Anti Rheumatic Drugs (DMARDs). Methotrexate remains the cornerstone of therapy due to its efficacy and safety profile as a first-line DMARD. Conventional DMARDs (csDMARDs) like methotrexate (MTX), sulfasalazine (SSZ), hydroxychloroquine (HCQ), leflunomide (Lef) are the common drugs currently being used in the management of RA worldwide, particularly in developing countries like India, where the majority of the population cannot afford biologic agents. Although many patients respond well to initial treatment with conventional synthetic disease-modifying antirheumatic drugs, a substantial number of patients experience an inadequate response or intolerance to these treatments.[3] The choice of therapy takes into consideration many factors including disease severity, comorbidities, patient preferences, and cost-effectiveness. Treat-to-target strategy recommends that such patients are treated with advanced therapies, including biologic DMARDs (bDMARDs) and targeted synthetic DMARDs (tsDMARDs). [4] Biologic agents, such as TNF-α inhibitors (e.g., adalimumab, etanercept), interleukin-6 inhibitors (e.g., tocilizumab), and newer targeted therapies (e.g., JAK inhibitors like tofacitinib), have expanded treatment options and improved outcomes, particularly for patients who do not respond adequately to conventional therapies or have moderate to severe disease or in refractory cases. EULAR guidelines suggest that pertinent risk factors are considered for oral Janus kinase inhibitors (JAKi). [5] If triple therapy fails, then, bDMARDs are prescribed. Glucocorticoids may be given as adjuvant bridge therapy, until the action of the initial DMARD has started.[6] The primary objectives of the therapy are to raise the quality of life (QoL) and lessen disability.[7] However, effective management requires a multidisciplinary approach, often cantered in tertiary care settings where specialized expertise and access to advanced treatment options are available.

Prescription patterns in rheumatoid arthritis (RA) reflect evolving treatment strategies aimed at controlling disease activity and improving patient outcomes. Despite these therapeutic advances, challenges persist, medication adherence remains a significant issue due to complex regimens and potential side effects. Access to biologics, which are often costly, poses barriers, limiting their availability to patients who could benefit. Safety concerns, including risks of infections and long-term complications from immunosuppressive therapies, necessitate rigorous monitoring and management Moreover, personalized medicine approaches, including biomarker-driven strategies, are emerging to optimize treatment selection and minimize adverse effects.

In tertiary care hospitals, where complex cases are often referred, the prescription patterns reflect the current standards of care, challenges in management, and emerging trends in RA therapy.

Understanding the prescription patterns in these settings provides insights into the treatment trends, adherence to clinical guidelines, effectiveness of therapies, and areas needing improvement.

Such studies analyse the current trends of prescribing pattern which can detect irrational use and provide feedback to clinicians, thereby increasing awareness in order to improve the prescribing behaviour[2]. The research on this topic focuses on analysing prescription patterns in rheumatoid

arthritis (RA), providing insights into current treatment trends and their implications for patient management.

MATERIALS AND METHODS:

The study was observational and prospective research carried out at The Oxford medical college hospital, Bangalore a tertiary care hospital. Study participants included 180 patients with Rheumatoid arthritis, fulfilling the 2010 ACR/EULAR Classification Criteria of RA, presenting to the Orthopedic/Rheumatology OPD. A written informed consent was obtained from each participant and only those who agreed to provide the Informed consent were included in the study.. The case record forms included demographic data, relevant medical history, past and family history including complementary alternative medicine (CAM) therapy, and co-morbidities. The prescription pattern was analysed using the following indicators: Percentage (%) of drugs prescribed, average number of drugs received by the patient, percentage of drugs given parenterally/orally, combination drugs , drugs prescribed by brand names or generic names etc.
Inclusion criteria

1. Both male and female patients suffering from RA fulfilling the 2010 ACR/EULAR Classification Criteria of RA
2. Patients who have provided written informed consent and those willing for participation in the study.
3. Age above 20 years

Exclusion criteria

1. Patients having a history of mental illness and liver, kidney, or gastrointestinal disorders
2. Patients requiring hospitalization
3. Patients unwilling for the study participation.
4. Pregnant and lactating females
5. Paediatric population
6. Other causes of arthritis including osteoarthritis, ankylosing spondylitis, bacterial arthritis, fibromyalgia, vasculitis etc

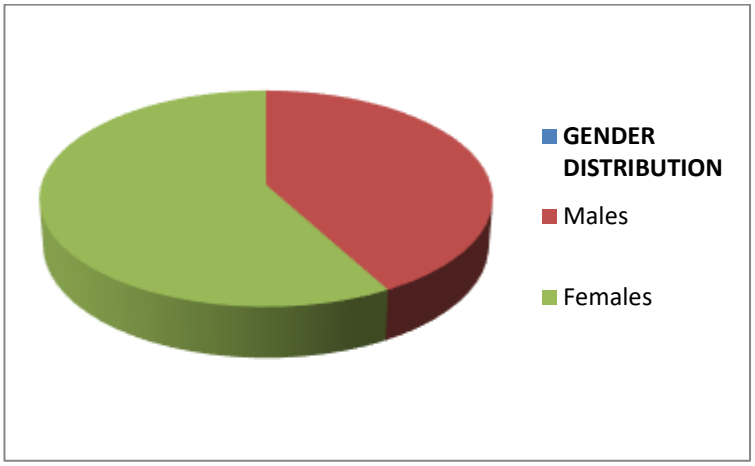
Results:

The study included a total of 180 patients who were diagnosed with rheumatoid arthritis and fulfilled the 2010 ACR/EULAR Classification Criteria of RA
Among the total number of study participants, 104 (58%) were females and 76 (42%) were males
The most common age group affected with RA belonged to 40–60 years, The mean age in the study was around 49.3 years. Table 1 shows the demographic characteristics of the participants. Family history was positive in 23% of patients. With regard to the presence of comorbidities, it was observed that 15% of the individuals had type 2 Diabetes mellitus, 11.3% had Hypertension, 14% had coexisting Osteoarthritis, 9.2% had some form of coronary artery disease, 6.5% had Chronic renal disease and 7.2% had Gastroesophageal reflux disease. 36.5% of the individuals had received some form of alternate therapy.

Table 1: Demographic characteristics of patients

DEMOGRAPHIC CHARACTERISTICS	PERCENTAGE OF STUDY POPULATION
Gender distribution	
Males	42%
Females	58%
Age	
<40	16
40-60	63%
>60	21
MEAN AGE	49.3 years

Family history	23%
On alternate therapy	36.5%



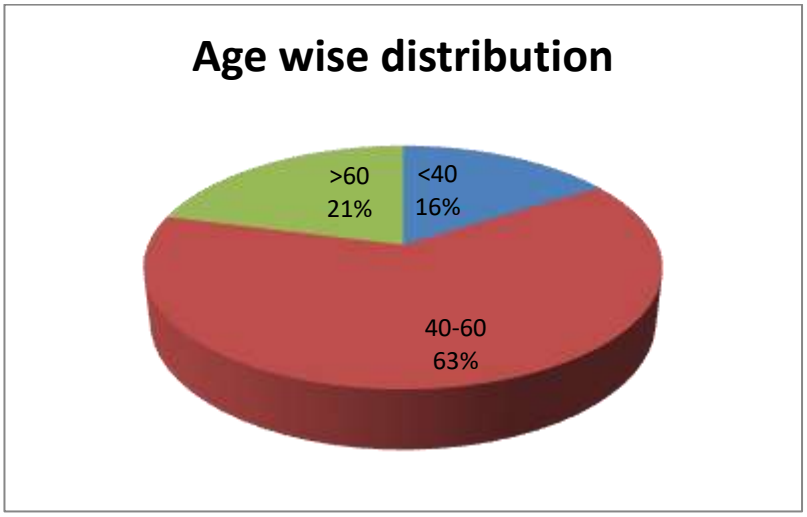


Table 2: Presence of comorbidities

COMORBIDITIES	% POPULATION
Type II diabetes mellitus	15
Hypertension	11.3
Peptic ulcer disease	7.2
Osteoarthritis	14
Coronary artery disease	9.2
Chronic renal disease	6.5

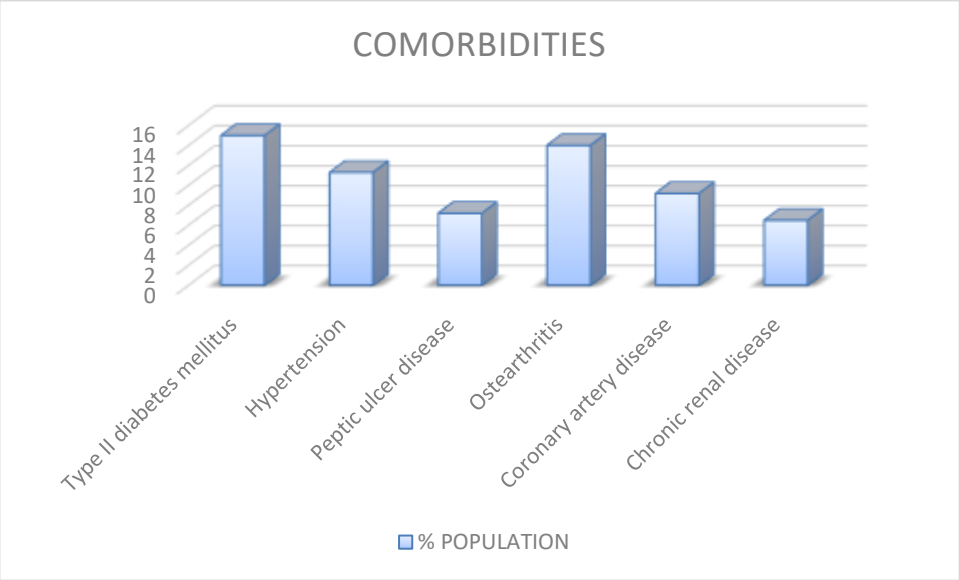


Table 3: Details of prescriptions

Average no of drugs prescribed per prescription	4.5%
Percentage of drugs prescribed by generic name	37%
Percentage of drugs prescribed by trade name	63%
Percentage of prescriptions containing injectable	0

Table 4: Details of drugs prescribed

GROUP OF DRUG	NAME OF DRUG	%PRESCRIBED
DMARDs	Methotrexate Hydroxychloroquine Sulfasalazine Leflunomide	87.6 68 29 3
NSAIDs	Etoricoxib Aceclofenac and Paracetamol Diclofenac Indomethacin Etodolac	54.5 23.8 6.7 3.8 2
OPIOID ANALGESICS	Tramadol	17.4
CORTICOSTEROIDS	Prednisolone	12.5
PROTON PUMP INHIBITORS	Pantoprazole Rabeprazole	17.8 13.9
ANTIDEPRESSANTS	Amitriptyline Fluoxetine Duloxetine Quetiapine	3.2%
NEUROPATHIC DRUGS	Pregabalin Gabapentin	8.6%
GLUCOSAMINE AND DIACERINE		7.3
CALCIUM		63
VITAMIN D3		76

Table 5: Combination drugs prescribed

DRUG COMBINATION	% PRESCRIBED
Methotrexate + Hydroxychloroquine +	68
Methotrexate + Sulfasalazine	29
Methotrexate + Hydroxychloroquine + Etoricoxib	45.5
Methotrexate + Hydroxychloroquine + Indomethacin	3.8

Methotrexate + Hydroxychloroquine + Prednisolone	12.5
Methotrexate + Hydroxychloroquine + Diclofenac sodium	5.4
Methotrexate + Hydroxychloroquine + Aceclofenac/Paracetamol	23.8
Methotrexate + Hydroxychloroquine +Etodolac	2
Methotrexate + Sulfasalazine + Etoricoxib	9
Methotrexate + Sulfasalazine + Diclofenac sodium	1.3

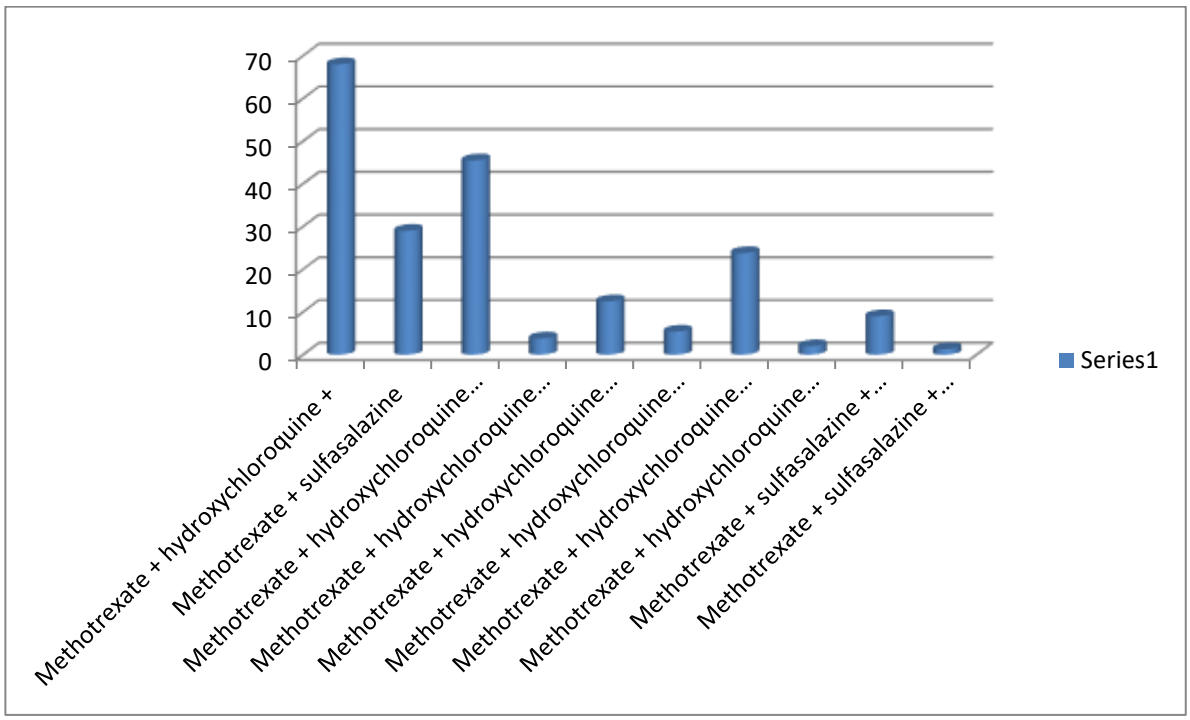


Table 3 and 4 shows the details of pharmacological therapy received by these subjects during the study period. Table 5 shows the list of combination DMARDs therapy prescribed.

According to the data collected, Majority of the patients received some form of DMARD. out of which Methotrexate was the most commonly prescribed drug at a dose of 7.5mg once a week. Monotherapy was given in 34.5% of patients while DMARD dual combination was given in 61% of patients which contributed to the majority of the prescription. A triple DMARD therapy was given in only 4.5% of patients. Methotrexate was the most commonly prescribed DMARD either in monotherapy or in combination and constituted 87.6% of prescriptions.

Combination therapy included Methotrexate and Hydroxychloroquine, prescribed in 68% of patients in combination group. Hydroxychloroquine was given at a dose of 200mg-400mg depending on the body weight of the patient.

Combination of Methotrexate and Sulfasalazine was given in of 29% patients. and 3% of patients received Leflunomide**. T**he most commonly used drug combination was Methotrexate and HCQ.

NSAIDs were the most common second group of drugs prescribed after DMARDs. Among NSAIDs, Etoricoxib was most commonly prescribed analgesic in 54.5% of patients followed by Aceclofenac and Paracetamol in 23.8%% of patients, Indomethacin in 9.2%, Diclofenac in 6.7%, Etodolac in 5.8%. Opioid analgesic Tramadol was prescribed in 17.4% of the patients

This was followed by Vitamin D3 which was given to 76% of the patients, calcium supplements to 63% of the patients.

Based on the data, it was discovered that a combined treatment of DMARDs, NSAIDs, calcium, and Vitamin D3 was the most often given therapy in RA, accounting for 72.6% of the cases, followed by combined treatment of DMARD, calcium, and Vitamin D3 in 27.4% of the patients. PPIs were given in 31.7% Of patients out of which Pantoprazole and Rabeprazole and were used in 17.8% and 13.9% of patients. Corticosteroids were given in 12.5% of patients out of which

Prednisolone was the most commonly prescribed drug. It was prescribed at a dosage of 5-20mg per day.
Neuropathic drugs like GABA analogues such as gabapentin and pregabalin was also used in 8.6% number of patients. Other adjuvant drugs used drugs like antidepressants such as Amitriptyline, Fluoxetine, Duloxetine was used in 3.2% of patients. Only 1 patient was on a combination of Fluoxetine and Quetiapine.
7.3% of patients were on combination of Glucosamine and Diacerine for coexisting osteoarthritis.

Discussion:
Prescription analysis studies can address many different aspects of medicines use and reveals several trends. One of the primary purposes for undertaking prescription analysis studies is to ensure rational use of medicines and to optimize pharmacotherapy with an emphasis on maximizing benefits while reducing harm
Prescription pattern analysis in tertiary care hospitals provides valuable insights into the evolving landscape of RA management. While adherence to guidelines and utilization of effective therapies are evident, challenges such as medication adherence, access to biologics, and optimizing long-term safety remain critical.
Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by inflammatory arthritis and extra-articular involvement. It is a chronic inflammatory disorder caused in many cases by the interaction between genes and environmental factors, including tobacco, that primarily involves synovial joints.[8] Joint inflammation over time leads to the destruction of the joint with loss of cartilage and bone erosions. RA, if untreated, is a progressive disease with morbidity and increased mortality.[9]
RA patients suffers from different degrees of pain, and for many people with RA, effective pain management is high on their priority list.[1] Factors influencing prescription decisions include disease severity, patient preferences, comorbidities (e.g., cardiovascular risks) and accessibility to therapies due to cost or insurance coverage limitations.
There are various challenges in RA Management like Medication Adherence where Complex treatment regimens and side effects can impact patient adherence, leading to suboptimal disease control, Access to Biologics where Cost and insurance coverage limitations may restrict access to newer, more expensive biologic therapies. There are also Safety Concerns like Monitoring for infectious complications and malignancies associated with long-term immunosuppression.
Recent studies underscore a shift towards early, aggressive treatment with disease-modifying anti-rheumatic drugs (DMARDs), particularly methotrexate, as the cornerstone of therapy. This approach aims to achieve rapid disease control and prevent joint damage. Combination therapies involving conventional DMARDs and biologic DMARDs (bDMARDs) have become increasingly common, offering enhanced efficacy for patients with moderate to severe disease who do not respond adequately to monotherapy.
This study demonstrated that the 58 % of patients affected were females and the most common age distribution was seen in 40-60 years group. It was observed that 15% of the individuals had type 2 Diabetes mellitus, 11.3% had Hypertension, 14% had coexisting osteoarthritis, 9.2% had some form of coronary artery disease, 6.5% had chronic renal disease and 7.2% had gastroesophageal reflux disease. 36.5% of the individuals had received some form of alternate therapy.
The prescription analysis of this study showed that DMARDs were the most commonly prescribed drugs out of which Methotrexate was the preferred drug. The most commonly used drug combination was methotrexate and HCQ which was similar to the results obtained in a study conducted by Dutta et all **[10]**. Combination therapy of Methotrexate and Hydroxychloroquine covered the maximum number of prescriptions in 68% of individuals similar to a study conducted by Gauri Mittal et all.**[2]**
Sulfasalazine and leflunomide were given in 29% and 3% of patients while nobody in this group received biological drugs. The prescriptions also included NSAIDs, Calcium and Vitamin D3

supplements as the most common add on drugs followed by PPIs. Corticosteroids like Prednisolone were given in 12.5% of patients and were mostly preferred in long standing and refractory cases.
Jebastine et all[11] showed that calcium and vitamin-D supplements were prescribed in 32.6% while this study included 72.6% of prescriptions. Dahiya et all **[12]** showed that average number of drugs per prescription were 8.06, Shakti B et all **[10]** study showed 3.67 while this study showed 4.58 drugs per prescription.
Future directions in RA management focus on personalized medicine approaches, leveraging genetic and biomarker insights to tailor treatment strategies. The increasing availability and affordability of biosimilars offer potential cost-effective alternatives to biologics, enhancing treatment accessibility. Ongoing research explores novel therapeutic targets, such as B-cell and T-cell modulators, aiming to expand treatment options and improve outcomes for RA patients.
Future research and clinical innovations aim to address these challenges, offering hope for improved outcomes and quality of life for patients with rheumatoid arthritis.

Conclusion:

Prescription pattern analysis in RA underscores the dynamic nature of treatment strategies in tertiary care settings. While adherence to guidelines and utilization of effective therapies are evident, challenges such as medication adherence, access barriers to biologics, and safety considerations persist. Future innovations in personalized medicine and emerging therapies hold promise for optimizing RA management, ultimately aiming to achieve better outcomes and quality of life for patients affected by this debilitating autoimmune disease.
Methotrexate is consistently the most prescribed DMARD, often used in combination with biologics to enhance efficacy. Biologics have seen increasing utilization as second-line or adjunct therapies, reflecting evolving treatment guidelines and clinical practice.
In conclusion, prescription patterns in RA are evolving towards more personalized and aggressive early intervention strategies using a combination of conventional and biologic DMARDs. Future research focusing on comparative effectiveness, long-term outcomes, and personalized medicine approaches will further refine these strategies, aiming to achieve better disease control and quality of life for patients with rheumatoid arthritis.

REFERENCES:

1. Siddiqui, A. Riyaz; Quazi, Shadma; Khan, Sharjeel; Shende, Tanaji R Drug Prescription Patterns and Quality of Life in Rheumatoid Arthritis Patients at a Tertiary Care Teaching Hospital in Central India: A Cross-Sectional Study*Journal of Datta Meghe Institute of Medical Sciences University* 18(3):p 422-426, Jul–Sep 2023.
2. Gauri Mittal, Manisha Bisht, Venkatesh S. Pai, Shailendra S. Handu. Evaluation of prescription practices in rheumatoid arthritis at the rheumatology clinic in a tertiary care teaching hospital in Uttarakhand: A cross-sectional study Journal of Family Medicine and Primary Care Volume 10 : Issue 2 : February 2021
3. Smolen JS, Landewé RBM, Bergstra SA, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2022 update. Ann Rheum Dis 2023;82:3-18..
4. Gerd R. Burmester, Filip Van den Bosch, John Tesser, Anna Shmagel, Yanxi Liu, Nasser Khan, Heidi S. Camp and Alan Kivitz. Upadacitinib in Rheumatoid Arthritis and Inadequate Response to Conventional Synthetic Disease-Modifying Antirheumatic Drugs: Efficacy and Safety Through 5 Years. The Journal of Rheumatology July 2024, 51 (7) 663-672;
5. Treatment Patterns and Effectiveness of Tofacitinib in Patients Initiating Therapy for Rheumatoid Arthritis: Results From the CorEvitas Rheumatoid Arthritis Registry.The Journal of Rheumatology May 2024, 51 (5) 452-461.

6. Singh JA, Saag KG, Bridges SL, Jr, Akl EA, Bannuru RR, Sullivan MC, et al. 2015 American college of rheumatology guideline for the treatment of rheumatoid arthritis. ;Arthritis Rheumatol. 2016 68:1–26
7. Jasani K, Jain P, Patel D, Pandya S, Rana D, Malhotra S. Evaluation of drug use pattern and quality of life in patients suffering from rheumatoid arthritis –A cross-sectional study at a tertiary care teaching hospital. Natl J Physiol Pharm Pharmacol 2019;10:1.
8. Klareskog L, Rönnelid J, Saevarsdottir S, Padyukov L, Alfredsson L. The importance of differences; On environment and its interactions with genes and immunity in the causation of rheumatoid arthritis. J Intern Med. 2020 May;287(5):514-533
9. Pincus T, O'Dell JR, Kremer JM. Combination therapy with multiple disease-modifying antirheumatic drugs in rheumatoid arthritis: a preventive strategy. Ann Intern Med. 1999 Nov 16;131(10):768-74
10. DuttaSB, BegMA, BawaS, KaurA, VishalS. Prescribing pattern in Rheumatoid Arthritis patients in a tertiary care teaching hospital.Int JBasic Clin Pharmacol 2017;6:1486-90.
11. JebastineMI,NasmiN,EliasN,NeethuVV,ArulB.Prescription pattern of drugs used in management of rheumatoid arthritis in a tertiary care hospital: A retrospective study. IndoAm.J.Pharm.Sci.2015;2(8):1198-205
12. DahiyaA, KalraBS, SainiA, TekurU. Prescription pattern in patients with rheumatoid arthritis in a tertiary care teaching hospital. MAMC J of Med Sci.2016;2:33