

Evaluation of Drug Prescription Pattern in Patients of Rheumatoid Arthritis

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Abstract

Background: The most prevalent autoimmune arthritis, Rheumatoid Arthritis (RA), affects approximately 1% of adult Indians. It is an inflammatory condition that causes swelling and discomfort in both bilateral joints. Joints are destroyed by swelling, which also causes long-lasting abnormalities such as ankylosis. The current study aimed to determine the prescription pattern for the treatment of RA patients visiting our tertiary care hospital.

Methods: A pre-designed and validated proforma was used for the collection of demographic profile as well as the other details of the cases in the study. All the cases were subjected to investigations that included ESR, C Reactive Protein, Serological rest for RA, Anti-CCP, LFT, and RFT. The patients were subjected to X-ray investigations based on the joints involved. The drug details which were noted were the names of the prescribed drugs, the dose of the drugs, the route of administration and duration of therapy, and drug adverse reactions if any reported during the subsequent follow-up.

Results: In this study, 93.75% of cases were diagnosed with seropositive RA and anti-cyclic citrullinated peptide (ACCP) was positive in all these cases. Rheumatoid factor was found to be positive in 92.5% of cases and abnormally increased ESR was found in 85% of the cases. Based on the prescription pattern of drugs Disease-modifying antirheumatic drugs (DMARDs) were the most commonly prescribed drugs followed by NSAIDs and corticosteroids. Out of the NSAIDs, the commonly prescribed drug was Naproxen followed by aceclofenac. In DMARDs methotrexate was commonly prescribed followed by hydroxychloroquine and combinations.

Conclusion: In the current study, which involved n=80 patients with rheumatoid arthritis and in the majority of RA patients the drug users were DMARDs. Methotrexate with hydroxychloroquine was the most often utilized medication combination. NSAIDs, corticosteroids, and opioid analgesics act as both analgesics and anti-inflammatory drugs. Early identification of the patients was followed by an aggressive, goal-oriented approach was the pattern utilized in the treatment.

Keywords: Rheumatoid Arthritis (RA), Prescription Pattern, Disease-Modifying Antirheumatic Drugs.

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Introduction

Rheumatoid arthritis (RA) is a symmetrical polyarthritis-associated chronic inflammatory condition with uncertain cause. It is the most prevalent kind of inflammatory arthritis and frequently causes physical impairment and joint damage. Fatigue, subcutaneous nodules, lung involvement, pericarditis, peripheral neuropathy, vasculitis, and hematologic abnormalities are some of the extraarticular symptoms of this systemic illness. [1, 2] The prevalence of rheumatoid arthritis is 0.5% to 1% worldwide, and it is 0.75% in India. It affects females more frequently than males (female to male ratio is 3:1). It can start at any age, with the greatest beginning occurring in women's fourth or fifth decades and men's sixth to eighth decades. [3-5] Low socioeconomic class individuals are more likely to develop RA-related issues. [6] It is hypothesized that both environmental and genetic variables have a role in the genesis of RA. [7] Smoking has been recognized as the most modifiable environmental risk factor. [8] With several variations and the finding of susceptibility MHC genes, such as the HLA-DRB1 allele, RA is linked to being a hereditary condition in 65% of patients. The presence of the common epitope is strongly associated with autoantibodies like rheumatoid factor (RA) and anti-citrullinated peptide antibodies (ACCP). [9]

By further weakening the immune system, disruption of immunological tolerance as well as the psychological state may play a significant impact. Any patient with joint pain and swelling for more than six weeks should be evaluated for RA. Commonly polyarticular (affecting more than four joints) and symmetrical, joint pain can also initially be oligoarticular (affecting two to three joints) or even monoarticular (affecting one joint). The distal interphalangeal joints are often unaffected.

Though not specifically associated with RA, morning stiffness lasts for more than an hour and gets better over the day. RA is characterized by the presence of symmetrical joint swelling. In contrast to a self-limited process, patients with synovitis and symptoms for more than 6 weeks are more likely to have a progressive condition. [10, 11] Each of the disease subgroups that make up the clinical condition known as RA is an inflammatory cascade that, if left untreated, generally results in joint and organ destruction. The diagnosis is based on a pattern of physical exam findings and symptoms, with or without the presence of radiographic or serologic abnormalities. [12] It has a considerable detrimental effect on everyday functioning, including the capacity to carry out the job and domestic duties, and health-related quality of life, which increases morbidity and mortality. [13-15] Glucocorticoids, non-steroidal anti-inflammatory drugs (NSAIDs), and disease-modifying antirheumatic drugs (DMARDs), which are broadly categorized as synthetic (encompassing the traditional DMARDs and newer therapies such as JAK-2 inhibitors) and biological drugs, are among the treatments currently used for managing RA (e.g., anti-TNF). [16] Medication usage studies (DUS) help provide denominators for rates of reported adverse drug responses and in monitoring the use of pharmaceuticals from therapeutic areas where specific issues might be predicted. [17] Drug usage research may produce hypotheses that serve as a guide for rational prescribing and the creation of a list of necessary medications that will help reduce irrational drug use.

Material and Methods

This cross-sectional study was done in the Department of Orthopedics, Kakatiya Medical College, and MGM Hospital Warangal. Institutional Ethical committee

permission was obtained for the study. Consent was obtained from all the patients included in the study. The included patients were the cases showing signs and symptoms of rheumatoid arthritis which was confirmed by investigations.

Inclusion criteria

1. Aged 20 years and above
2. Males and Females
3. OPD visitors of MGM Warangal
4. Diagnosis of RA confirmed with investigations
5. Prescribed medications

Exclusion criteria

1. Patients with doubtful RA
2. Pregnant females
3. Old RA cases with remissions/relapse

A pre-designed and validated proforma was used for the collection of demographic profile as well as the other details of the cases in the study. The data also included chief complaints, signs and symptoms, duration of symptoms, and comorbid conditions if any. All the cases were subjected to investigations that included ESR, C Reactive Protein, Serological test for RA, Anti-CCP, LFT, and RFT. The patients were subjected to X-ray

investigations based on the joints involved. The drug details which were noted were the names of the prescribed drugs, the dose of the drugs, the route of administration and duration of therapy, and drug adverse reactions if any reported during the subsequent follow-up.

Statistical Analysis: The acquired data were statistically examined using descriptive statistics. For numerical variables, the results are displayed as counts and percentages and are stated as the mean. The results are presented in tables and graphs when appropriate. To do statistical analysis, SPSS version 22.0 on windows format and Microsoft Excel were used.

Results

In the present study out of the total n=80 cases included the majority of the cases were between the age groups of 41 – 50 years followed by the age group 31 – 40 years both age groups accounting for 71.25 % of the cases included in the study details of distribution based on the age is given in table 1. Similarly, the sex-wise distribution of the cases in the study found n=16(20%) males and n=64(80%) females. The male-to-female ratio was 1:4.

Table 1: Age-wise distribution of cases in the study

Age in years	Frequency	Percentage (%)
20 – 30	04	05.00
31 – 40	24	30.00
41 – 50	33	41.25
51 – 60	10	12.50
> 60	09	11.25
Total	80	100.00

N=41(51.25%) of cases of RA were with other co-morbid conditions along with rheumatoid arthritis given in table 2. Based on the number of joints involved in RA n=8(10%) cases were with monoarticular arthritis and n=24(30%) cases were oligoarticular arthritis and n=48(60%) cases were with polyarticular arthritis details depicted in Figure 1.

Table 2: Comorbid conditions of the cases included in the study

Co-morbid Conditions	Frequency	Number of patients
Hypertension	10	12.50
Diabetes	12	15.00
Thyroid disorders	4	05.00

Anemia	15	18.75
No co-morbidities	39	48.75

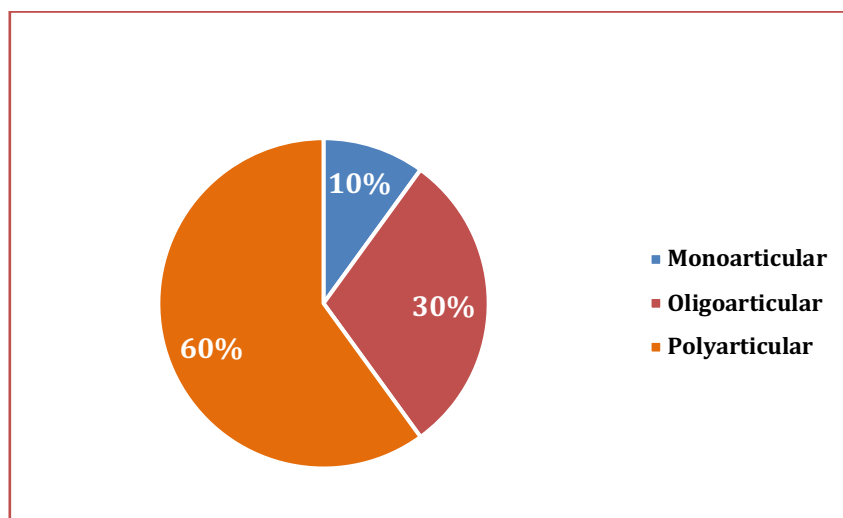


Figure 1: Distribution of cases based on the number of joints involved in the study

The most commonly involved joint with RA was the knee in 33.75% of cases followed by the foot in 27.50% of cases. Hand RA was found in 21.25% of cases wrist RA and elbow RA was reported in 6.25% and 5.0% respectively. Hip RA was reported in 3.75% of cases and shoulder RA and sacroiliac joint RA was in 1.25% of cases each. The most common symptom

was joint tenderness reported in 95% of cases followed by joint pain in 90% of cases. Morning tenderness was reported in 83.75% of cases. Painful joint movements were experienced in 30% of cases and joint swelling was noted in 27.5% of cases and joint deformity in 15% of cases details depicted in figure 2.

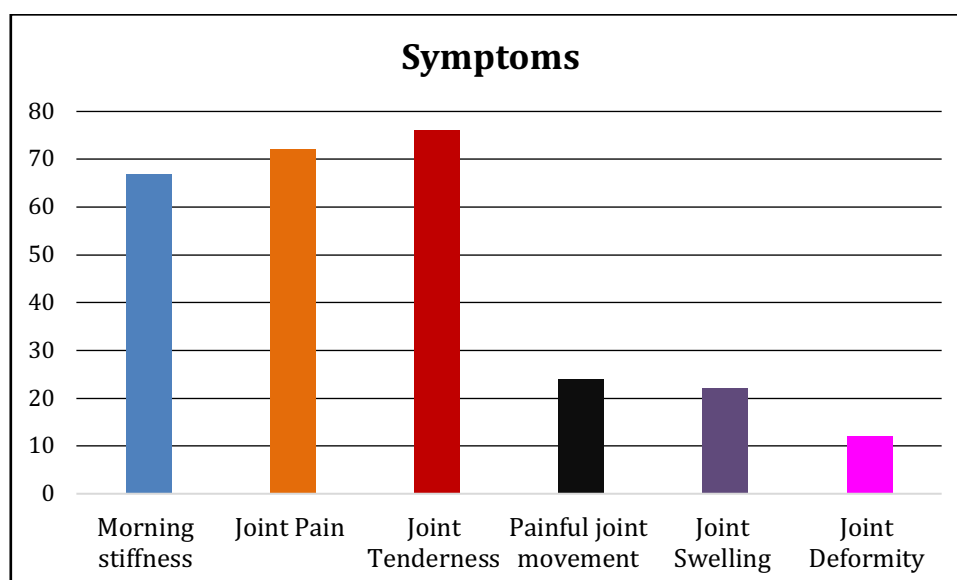


Figure 2: Distribution of symptoms reported in the cases of the study

In this study, 93.75% of cases were diagnosed with seropositive RA and anti-cyclic citrullinated peptide (ACCP) was positive in all these cases. Rheumatoid factor was found to

be positive in 92.5% of cases and abnormally increased ESR was found in 85% of the cases other details of the parameters are depicted in table 3.

Table 3: Distribution of patients according to laboratory parameters

Parameters	Frequency	Percentage
Seropositive RA	75	93.75
Seronegative RA	05	06.25
Abnormal C-Reactive Protein (CRP)	62	77.5
Abnormal Erythrocyte sedimentation rate (ESR)	68	85.0
Rheumatoid factor (RF) positive	74	92.5
Anti-cyclic citrullinated peptide (ACCP) positive	75	93.75
Raised Liver function test (LFT)	15	18.75
Raised renal function test (RFT)	2	2.5

Based on the prescription pattern of drugs Disease-modifying antirheumatic drugs (DMARDs) were the most commonly prescribed drugs followed by NSAIDs and corticosteroids. Out of the NSAIDs, the commonly prescribed drug was Naproxen followed by aceclofenac. In DMARDs methotrexate was commonly prescribed followed by hydroxychloroquine and a combination of both the details description of the prescription of drugs has been depicted in table 4.

The significant combination of drugs used was NSAIDs + DMARDs in 96.25% of cases of RA, followed by NSAIDs + DMARDs + corticosteroids in 35%. DMARDs are most commonly prescribed in 2 combinations than 3 combinations of drugs. Among the 2 combinations of DMARDs most preferred was Methotrexate + Hydroxychloroquine followed by hydroxychloroquine + sulfasalazine in patients depicted in table 5.

Table 4: Drug utilization pattern in the cases of study

Class of Drug	Name of Drug	Frequency of Prescriptions	Percentage (%)
NSAIDs	Paracetamol	21	7.0
	Diclofenac	15	5.06
	Etoricoxib	10	3.37
	Aceclofenac	23	7.77
	Naproxen	25	8.44
	Piroxicam	04	1.35
Total		75	25.33
DMARDs	Methotrexate	82	27.70
	Hydroxychloroquine	67	22.63
	Sulfasalazine	32	10.81
Total		181	61.15
Corticosteroid	Prednisolone	30	10.13
Total		30	10.13
Opioid analgesic	Tramadol	10	12.5
Total		10	12.5

Table 5: Drug combinations prescribed for the patients in the study

Combination Prescriptions	Frequency	Percentage
NSAIDs + DMARDs	77	96.25
Opioids + DMARDs	3	3.75
NSAIDs + DMARDs + Corticosteroids	28	35.0
Opioids + DMARDs + Corticosteroids	2	2.5
NSAIDs + DMARDs + Opioids	6	7.5
NSAIDs + DMARDs + Corticosteroids + Opioids	2	2.5

Rheumatoid Arthritis medications were logically prescribed in all the cases. However, only 70% of the patients were aware of the proper dosage and 3.5 medications per person on average were prescribed. The common side effect noted in the cases was increased LFT in 18.75%

of cases especially those on Methotrexate medication RFT was increased in 2.5% of cases prescribed with the Naproxen combination. All the ADRs were mild and self-limiting and did not require a change of medications given in table 6.

Table 6: Distribution of patients according to adverse drug reactions

Adverse Drug Reaction	Frequency	Percentage (%)
Liver Function Test (LFT raised)	15	18.75
Renal Function Test (RFT raised)	2	2.5
Retinal toxicity	1	1.25
Allergic reactions	2	2.5
Loss of appetite	5	6.25

Discussion

With the advancement of our knowledge of the diverse pathogenic mechanisms underlying RA, including the intricate interplay of cytokines and cell-mediated autoimmunity, we have witnessed the emergence of biologics and small-molecule non-biologics that have completely changed the course of the disease for a wide range of patients by offering a variety of step-up therapies. [18, 19] Decreasing joint discomfort and swelling, avoiding deformity (like ulnar deviation), avoiding radiographic damage (like erosions), preserving the quality of life (personal and occupational), and managing extra-articular symptoms are all objectives of treatment. The cornerstone of RA treatment is DMARDs. Despite various additional anti-rheumatoid drugs entering the market over the past 20 years, there are still few effective treatments for rheumatoid arthritis. The sex-wise distribution of the cases in this study was n=16(20%) males and n=64(80%) females.

This observation is similar to that of N. Mittal et al., [20] who found 87% of cases in the study were females and similarly, Gawde SR et al., [21] in their study found 80% of females. On average in most of the studies on the subject the prevalence was found to be 2.5 times more common in females as compared to males. The high frequency of RA in females seen when compared to industrialized nations is likely a result of racial and cultural diversity, particularly in terms of profession and living circumstances. In the current study, the common comorbidities included Diabetes Mellitus, hypertension, and anemia. A similar study by I Jebastine et al., [22] found the common co-morbidities included hypertension, diabetes mellitus, and bronchial asthma. In the current study, most of the cases were of polyarticular arthritis in 60% of patients followed by oligoarticular arthritis in 30% of cases. The diagnosis of patients in the current study was determined to be 93.75% seropositive rheumatoid arthritis and

6.25% seronegative arthritis. All of the patients fulfill the new 2010 ACR/EULAR Definite Rheumatoid Arthritis Classification Criteria with a score of at least six. [10] In the current study, RA patients were treated as per the most recent recommendations, meaning that DMARDs were begun as soon as the diagnosis was made as opposed to the previous advice, which called for solely symptomatic therapy and a three-month break from DMARD usage. Early candidate identification during the "window of opportunity" combined with a targeted, aggressive strategy with DMARDs and the inclusion of biological agents led to gratifying functional recovery and even remission, which enhanced the quality of life for RA patients. In this study, a total number of 296 drugs were prescribed and their distribution is given in table 4. In this study, the NSAIDs were prescribed in 25.33% of all drugs and the most prescribed non-steroidal anti-inflammatory agent was Naproxen with 8.44% followed by aceclofenac in 7.77% and diclofenac in 5.06 % of all the drugs prescribed Gawde SR et al., have reported a higher prescription of NSAIDs in 33.5% of all cases. Tummeti VV et al., [23] 70% of patients in the study population were on a combination of two DMARDs, and methotrexate and HCQ were the most frequently prescribed and Boers et al., [24] have reported similar observations. In the current study, the typical prescription contains 3.5 different medications. The number of medications per prescription was greater than the optimum WHO norm, which is less than two (1.6–1.8). [25] A minimum of 3 and a maximum of 5 anti-rheumatoid medications were administered in our research. It has been suggested that the maximum number of medications that can be supplied on a single prescription be two and that a valid reason must be provided if more than two medications are ordered. [15] Patients may not be able to afford or take the recommended medications due to the growth in the

number of prescriptions as a whole. This therapeutic non-adherence might worsen the illness, extending the length of the treatment. [26] All the medications were given under their generic names. [27].

Conclusion

In the current study, which involved n=80 patients with rheumatoid arthritis and in the majority of RA patients the drug users were DMARDs. Methotrexate with hydroxychloroquine was the most often utilized medication combination. NSAIDs, corticosteroids, and opioid analgesics act as both analgesics and anti-inflammatory drugs. Early identification of the patients was followed by an aggressive, goal-oriented approach was the pattern utilized in the treatment. The most recent advancements in rheumatoid arthritis therapy techniques have significantly slowed the disease's course and improved patient outcomes.

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