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Research Article

Rheumatoid Arthritis: Prescription Trends at Tertiary Care Hospitals

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ABSTRACT

Rheumatoid arthritis is one of the most prevalent auto-immune diseases impacting the world's population, causing joint inflammation, synovium growth, and articular cartilage degradation. Inflammatory cells (B-cells, T-cells and macrophages) secrete lysosomal enzymes, which damage cartilage and erode bones, while the PG produced in the process causes vasodilation and pain. RA is a chronic, progressive, and disabling disease with hair loss and damage. Many small joints of the hands and feet are generally affected; Deformities are created as the disease progresses.

Objectives: The purpose of this study was to examine the pattern of usage of antirheumatic medicines in a tertiary care hospital in Mohali, India.

Methods: The research included 85 individuals who were receiving antirheumatic medication. The demographic information of the patient, co-morbid conditions, medicines prescribed, and Adverse Drug Reactions (ADRs) were utilised to examine the pattern of drug usage.

Results: Only one patient was administered sulphasalazine, while nine others were prescribed hydroxychloroquine alone. Methotrexate and hydroxychloroquine were the most often prescribed DMARDs combination, accounting for 23% of all prescriptions. Methotrexate, sulphasalazine, and hydroxychloroquine were the most often given three DMARDs, i.e., six times.

Conclusion: The most often given drugs were DMARDs, vitamin-D3 and calcium supplements, and analgesics, according to the drug prescription pattern. From NLEM 2015, 75.40% of medications were prescribed.

Keywords: Prescription pattern; Rheumatoid arthritis; Autoimmune illness; Health

INTRODUCTION

Rheumatoid Arthritis (RA) is a chronic autoimmune illness primarily affecting the synovium, resulting in discomfort and functional impairments. It is the most common type of inflammatory arthritis and a major cause of morbidity and mortality [1]. From the standpoint of primary care, early detection of this disease and its extra-articular manifestations can speed up the course of treatment and improve health outcomes while still preserving joint performance [2]. The pathogenesis of RA comprises persistent synovial membrane inflammation, which can injure articular cartilage and juxta articular bone. This disorder is recognized as a systemic ailment because of the aetiology that also affects internal organs, including the heart, lungs, kidneys, blood vessels, and brain [3,4]. The condition affects 0.75 percent of the adult Indian population, and the incidence rises between the ages of 25 and 55 before peaking until the age of 75 when it starts to decline [5]. In the current therapy of rheumatoid arthritis, the advantages of initial Disease-Modifying Anti-Rheumatic Drugs (DMARDs) are emphasized [6]. These drugs are distinguished by their capacity to lessen or eliminate signs and symptoms, ameliorate impairment, and enhance quality.

Writing prescriptions is a crucial duty a doctor performs when managing a patient. A prescription is a set of written directions for drugs that are provided to a patient [7]. Additionally, it gives insight into the fundamentals of the healthcare delivery system. Analyzing the recent trend in prescription patterns through examination and monitoring of prescriptions and medication consumption studies might assist uncover issues and give feedback to prescribers. Drug utilization patterns can be defined to give prescribers useful input on how to change their prescribing practices [8].

METHODOLOGY

After receiving clearance from the institutional ethics committee, the prospective study was conducted at the medicine OPD at

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Grecian Super Specialty Hospital in Mohali, Punjab, for six months. All patients and legal guardians provided written informed consent. The trial included every patient with rheumatoid arthritis (RA) who had been diagnosed. Rheumatoid factor and Anti-ccp (Anticyclic Citrullinated Peptide Antibody) was the lab parameters used to diagnosis patients based on clinical evaluation. The medications provided for RA was examined using drug use WHO indicators, including medication formulations and medications from the 2015 National Essential Drug List. The following information was noted for each prescription: (1) demographic profile, (2) details of disease including lab data, (3) comorbid conditions (4) treatment prescribed and adverse drug reaction (if any) (5). Data was recorded in a structured questionnaire that contained above 5 information in each prescription. The entire completed questionnaire was pooled together. The data collected was entered and analyzed using statistical software Graph Pad Prism (version 9).

RESULTS AND DISCUSSION

A total of 85 individuals were included in the trial, with 30 (35.29%) being male and 55 (64.70%) being female. Male to female ratio is 2:1. The average age for RA was 52.4 years. Females had a mean age of 52.22 years, while men had a mean age of 52.73 years. Many people assume that women are more prone to arthritis because of hormonal differences. As women approach menopause, their estrogen levels decrease. Estrogen assists in inflammatory defense, which may have a part in the increased risk of arthritis, whereas testosterone is a masculine hormone that aids in muscle building. This usually leads to stronger legs. Stronger muscles give more support to joints, lowering the likelihood of developing arthritis (Table 1 and Figure 1).

Table 1: Demographic profile

Parameters		Profile	Mean age ± SEM
Gender	Female	57 (67.05%)	52.22 ± 1.821
	Male	28 (32.94%)	52.73 ± 2.605
Age	18-35	8 (9.41%)	30.63 ± 1.523****
	36-55	39 (45.88%)	45.23 ± 0.9557****
	>55	38 (44.70%)	64.86 ± 1.398****
Positive RA factor	N/A	66 (77.64%)	N/A
Raised Anti-CCP	N/A	51 (60.00%)	N/A
Morbidities	TYPE 2 Diabetes Mellitus	1 (1.17%)	N/A
	Hypertension	6 (7.05%)	N/A
	Hypothyroidism	1(1.17%)	N/A
	Anemia	2 (2.35%)	N/A
	Others	6 (7.05%)	N/A

Note: All values are expressed as Mean ± SEM by one-way ANNOVA Method Significant at P<0.05*, 0.01** and 0.001***.

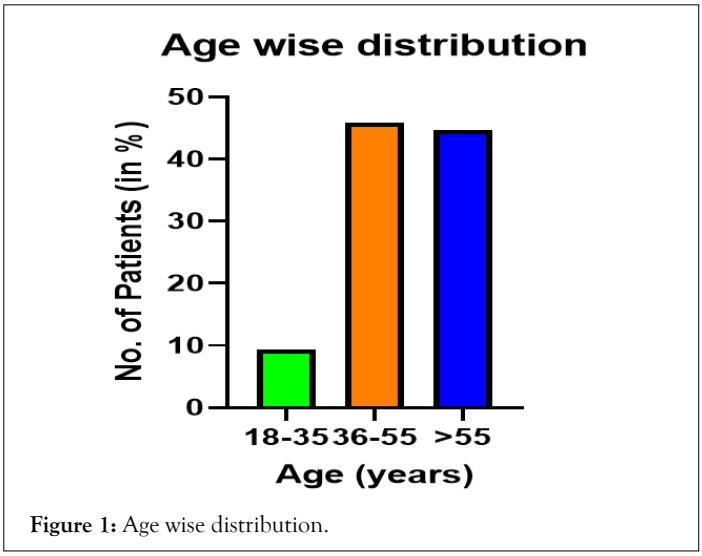

Figure 1: Age wise distribution.

The prevalence rate is highest in adults aged 36-55 years, at 39 (45.88%), followed by people aged more than 55 years, at 38 (44.70%), and lowest in younger adults aged 18-35 years, at 8 (9.41%). A research done in a tertiary hospital in Mumbai, India, found similar results, with a mean age of 41.43 13.57 years.

During the research period, 553 medications were prescribed. Disease-modifying anti-rheumatic drugs were administered 153 times (27.66%), corticosteroids 37 times (6.69%), analgesics 116 times (20.97%), vitamin D3 and calcium supplements 94 times (16.99%), antacids 66 times (11.93%), and others 87 times (15.73%).

Folic acid was administered 45 (51.72%), multivitamins 17 (19.54%), nerve tonics or Vitamin B12, B1, B6 9 (10.34%), Collagen peptide, Hyaluronic acid, and Choldroitin sulphate (Cartibind) 3 (3.44%), Domperidone 7 (8.04%), and Ondansetron 6 (6.89%) to combat DMARD adverse effects (Table 2).

Table 2: Pattern of drugs used in rheumatoid arthritis.

Drug groups	Name of drugs	Number (%)
DMARDs 153 (27.66%)	Methotrexate	44 (28.75%)
	Hydroxychloroquine	61 (39.86%)
	Sulphasalazine	36 (23.52%)
	Leflunomide	12 (7.84%)
Corticosteroids 37 (6.69%)	Methyl prednisolone	37 (6.69%)
Analgesics 116 (20.97%)	NSAIDs-Cyclooxygenase-1 or COX-1 inhibitors (Paracetamol, Diclofenac, Indomethacin, Piroxicam)	49 (42.24%)
Analgesics 116 (20.97%)	NSAIDs-Cyclooxygenase-2 or COX21 inhibitors (Etoricoxib, Celecoxib)	35 (30.17%)
	Opioid analgesics (Tramadol)	9 (7.75%)
	Serratiopeptidase, Trypsin-Bromelain-Rutoside (For swelling)	23 (19.82%)

Vitamin D3 and Calcium 94 (16.99%)	Calcium+Vitamin D3	40 (42.55%)
	Vitamin D3	54 (57.44%)
Antacids 66 (11.93%)	Proton pump inhibitors or PPI (Pantoprazole, Rabeprazole)	66 (11.93%)
Others 87 (15.73%)	Folic acid	45 (51.72%)
	Multivitamins	17 (19.54%)
	Nerve tonics or Vitamin B12, B1, B6	9 (10.34%)
	Collagen peptide, Hyaluronic acid and Chondroitin sulphate (Cartibind)	3 (3.44%)
	Domperidone	7 (8.04%)
	Ondansetron	6 (6.89%)

According to the current study, the most usually administered DMARD was hydroxychloroquine (61 (39.86%) in the 85-study group, followed by methotrexate (44 (28.75%)). A similar pattern was reported in research in which methotrexate and hydroxychloroquine were prescribed the most, 51.90% and 48.10%, respectively.

Corticosteroids are also used to treat rheumatoid arthritis's acute pain and inflammation. They have better anti-inflammatory effects than Nonsteroidal Anti-Inflammatory Drugs (NSAIDs), but they have a more unfavourable adverse effect profile. Corticosteroids impact gene expression by binding to glucocorticoid receptors. They particularly promote anti-inflammatory gene expression while reducing pro-inflammatory gene expression. This helps to lessen acute symptoms by reducing the inflammatory effects of circulating monocytes and eosinophils. Methylprednisolone 37 (6.69%) was the most prevalent corticosteroid in the current investigation. According to the recommendations, chronic use of GCs up to 15 mg/day reduces disease activity, and we are adding low-dose GCs (7.5 mg/day) to DMARDs in early RA resulted in a considerable decrease in radiographic progression. Pain reduction is the main objective of intra-articular GCs in RA.

Nonsteroidal anti-inflammatory medicines are the meds that are most frequently utilized for symptomatic management (NSAIDs). In addition to DMARDs, 73 patients received Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) when required. Indomethacin, Paracetamol, and Diclofenac were the NSAIDs most frequently recommended. When compared to COX-1 inhibitors, the utilisation of COX-2 inhibitors like celecoxib and etoricoxib was lower, at 35 (30.17%).

In our study, calcium and vitamin D3 supplements were given to 40 (42.55%) patients while vitamin D3 was given to 54 (57.44%) patients. According to a 2012 study, Vitamin D deficiency is incredibly frequent in people with RA and has been linked to how severe the disease is. Insufficient vitamin D has been related to musculoskeletal discomfort. Vitamin D supplements may be given to RA patients in order to treat their discomfort and avoid osteoporosis.

In the adjuvant treatment, calcium was frequently used since RA induces bone loss. Nearly all patients receiving methotrexate, or 45 (51.72%), were taken folinic/folic acid, a folate antagonist that lessens the negative effects of the drug. By greatly reducing the possibility of gastrointestinal side effects and hepatic impairment, folic or folinic acid reduces the risk that patients may stop taking methotrexate. Folic acid delivery the day following methotrexate inhibits the interaction by reducing the competition between folate and methotrexate for absorption, which reduces the therapeutic effectiveness of methotrexate when used concurrently.

Six adjuvant medications were given to 65 individuals in our research, or 76.47 percent of them (approx.). Similar findings were made in another study, which also indicated that folic acid, proton inhibitors (PPIs), and calcium supplements were often recommended together with DMARDs. In our study, 47.05% of patients received calcium supplements, whereas 77.64% of patients used PPIs. This was in line with other research that discovered gastro protective drugs and calcium supplements in a sizable percentage of prescriptions. These medications are most often used to prevent Adverse Drug Reactions (ADRs) such epigastric pain and osteoporosis linked to RA or caused by glucocorticoids.

A supplement called Cartibind comprises chondroitin sulphate, hyaluronic acid, and collagen peptide. It lessens joint swelling and effusion and stops the joint space from getting smaller. At both the chondral and synovial levels, chondroitin sulphate inhibits inflammation. A collection of enzymes produced from pineapple are used to create Bromelain-Rutoside. It could have painkilling and anti-inflammatory effects. Some patients also received prescriptions for nerve tonics. The B complex vitamins are present. It is helpful in the treatment of arthritis because it promotes the general health of the bones, joints, and cartilage (Figure 2 and Table 3).

Table 3: Details of types of therapy.

Therapy	Total no. of patients (%)
Monotherapy	12 (14.11%)
Combination therapy	65 (76.47%)
Surgeries (due to arthritic changes)	5 (5.88%)
No Therapy	3 (3.52%)
Total	85 (100%)

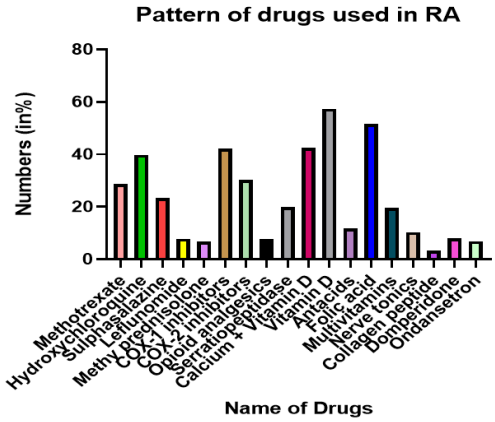

Figure 2: Pattern of drugs used in RA.

Per prescription, 3.67 medicines were prescribed. 404 medications (75.37 percent) were given from the 2015 National List of Essential Medicines (Table 4).

Table 4: Analysis of WHO parameters.

Parameters	Number (%)
Drugs prescribed per prescription	6.5
Drugs prescribed from National List of Essential Medicines (NLEM-2015)	417 (75.40%)

Per prescription, 6.50 medications were prescribed. Brand names were prescribed for 553 medicines, or 100%. 417 (75.40%) medications from the 2015 national list of essential medications were administered. In each of these investigations, more medications are often administered than what the WHO recommends. It has been recommended that the optimum number of drugs that can be provided per prescription be two and that any extra medications need to be justified due to the higher likelihood of drug interactions. Due to the overall increase in prescriptions, patients may not be able to pay or take the recommended drugs. Therapy non-compliance might exacerbate the illness and extend the course of the treatment (Table 5).

Table 5: Analysis of DMARDs used.

DMARDs prescribed	Number
Single DMARD	
Hydroxychloroquine	9
Methotrexate	2
Sulphasalazine	1
Two DMARDs	
Methotrexate+Hydroxychloroquine	23
Hydroxychloroquine+Sulphasalazine	16
Methotrexate+Sulphasalazine	7
Sulphasalazine+Leflunomide	1
Hydroxychloroquine+Leflunomide	2
Three DMARDs	
Methotrexate+Hydroxychloroquine+Sulphasalazine	6
Methotrexate+Hydroxychloroquine+Leflunomide	1
Hydroxychloroquine+Sulphasalazine+Leflunomide	4

Most patients at the research facility were given one or more standard DMARDs (non-biologics). The majority of patients (76.47%) in the study population were administered two or more DMARDs. Only 7.18% of patients were given three DMARDs, whereas 12 (14.11%) were given single DMARDs. There were 9 patients on Hydroxychloroquine alone, 2 on Methotrexate alone, and only 1 patient was on Sulphasalazine. However, no patient has been prescribed Leflunomide alone. Methotrexate and hydroxychloroquine were the most commonly prescribed DMARDs combination, accounting for 23. Methotrexate, Sulphasalazine, and Hydroxychloroquine were the most often given three DMARDs, i.e., six times (Table 6).

Table 6: Action taken by physician.

Action taken	Number
Additional treatment given	7
Drug stopped	0
Drug altered	0

In the study, ADRs were discovered in 7 prescriptions out of 85 prescriptions, including nausea and vomiting in 6 (7.05%) patients, poor taste and acidity in 2 (2.35%), and 3 (3.52%) patients, respectively. ADRs were treated by providing further therapy, and the medicine was not stopped, the dose was not changed, and the functional test was monitored. Methotrexate depletes cells of folate (vitamin B type), which is required for cell survival. They disrupt healthy cells that divide quickly, such as the mucus membrane in the mouth and the lining of the GI tract. These regions are particularly sensitive to methotrexate, which may explain why some patients experience nausea and vomiting.

All ADRs were submitted to the physicians, who performed the required management actions, including administering Ondansetron 4 mg for nausea and vomiting and PPIs alone or PPI+Domperidone for acidity (Table 7).

Table 7: Details of drugs causing ADR and its management.

Drugs	ADR	Management
Hydroxychloroquine or Methotrexate	Nausea and vomiting	Ondansetron and Domperidone
	Bad taste	-
	Acidity	Pantoprazole

CONCLUSION

DMARDs were found to be the most often used drugs in RA patients. The numerous prescription treatment plans include the use of DMARDs, analgesics, corticosteroids, vitamin-D3 and calcium supplements, antacids, multivitamins etc. The current study shows that the most commonly prescribed DMARDs was Hydroxychloroquine i.e., 61 (39.86%) in 85 study population followed by Methotrexate 44 (28.75%). The most frequently prescribed DMARDs combination was Methotrexate and Hydroxychloroquine i.e., 23. The most prescribed 3 DMARDs combination was Methotrexate, Sulphasalazine and Hydroxychloroquine i.e., 6 times. Out of 85 prescriptions ADRs were identified in 7 prescriptions in which nausea and vomiting was in 6 (7.05%) patients, bad taste, acidity was observed in 2 (2.35%) and 3 (3.52%) patients respectively.

The prudent use of medicines highlights the necessity of providing patients with therapies that are appropriate for their clinical needs. The investigation of prescription patterns is an important aspect of medical auditing in order to acquire appropriate and cost-effective medical treatment. It assists in monitoring, analyzing, and making necessary changes to prescription procedures.

- Due to irrational prescription practices and rising medication resistance, the medical and social impact of Rheumatoid arthritis is tremendous.
- Proper diagnosis and established criteria are necessary for the optimal selection of DMARDs therapy.

• Specific hospital recommendations should be created to allow for the sensible selection of DMARDs in arthritis.

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