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Original Article

Drug Utilization Review on Rheumatoid Arthritis Patients

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ABSTRACT

The objective of the study was to evaluate the drug utilization review on rheumatoid arthritis in a multispecialty hospital. A prospective study was carried out at Vivekanandha Medical Care Hospital, Tiruchengode. The study was conducted for 6 months. 73 prescriptions of rheumatoid arthritis were analyzed. It was done in the patients who were diagnosed with rheumatoid arthritis. The patient details and prescriptions were analyzed, and it was attached to the data analysis form. Microsoft excel 2019 was used to analyze the data. In this Non-Steroidal Anti-Inflammatory Drugs (21.28%) were widely prescribed along with Disease Modified Anti-Rheumatic Drugs (14.28%) and with Steroids Methylprednisolone (12.04%). The major co-morbidity of rheumatoid arthritis was Diabetes Mellitus and Cardiovascular disease. The age of the population was between 21-80 years. The prevalence was higher in female than males. The prescribing trends in the pharmacological management of Rheumatoid Arthritis and its associated co-morbidities were analyzed. This study provides additional knowledge to the healthcare providers on the importance of rational use of drugs in the treatment of Rheumatoid Arthritis and helps to get a better understanding of reason trends in management. Overall helps in reduced duration of hospitality and reduced risk of infection associated with Rheumatoid Arthritis.

Keywords: Rheumatoid Arthritis, DMARDs, Prospective Study

INTRODUCTION

Rheumatoid Arthritis: Rheumatoid arthritis is defined as a systemic inflammatory disease that is characterized by persistent synovitis and production of autoantibodies against various factors, which includes rheumatoid factor and cyclic citrullinated peptide. Rheumatoid arthritis mostly affects the synovial lining of joints, although it targets the lungs, heart, blood vessels, and including other organ systems[1]. Rheumatoid arthritis results in substantial disability, loss of productivity, and increased mortality. In early disease function, irreversible damage of joint and inflammatory changes was seen[2].

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Classification

Table 1: Drug Classification of Rheumatoid Arthritis

Classification	Drug Name
1.**Disease Modified Anti-Rheumatic Drugs:** **A.Non-biological drugs** **B. Biological agents**	I. Immunosuppressants Methotrexate Azathioprine Cyclosporine II. Sulfasalazine III. Chloroquine or Hydroxychloroquine IV. Leflunomide I. TNF inhibitors Etanercept Infliximab Adalimumab II.IL-I antagonist: Anakinra
2. Adjuvant drugs	I. Corticosteroids Prednisolone[3].

Drug Utilization Review in Rheumatoid Arthritis: The analysis of prescribing patterns in RA is an important tool for the assessment of rational and irrational prescribing and WHOs drug use indicators.This drug pattern is analyzed by drugs prescribed per prescription, formulation, dose, brand names, defined daily dose. The most commonly prescribed drugs are disease-modifying anti-rheumatic drugs. Analgesics, vitaminD3, and calcium supplements. Antacids, ondansetron, amitriptyline, and clozapine are also prescribed.Primarily drug use pattern of RA was found to be DMARDs. Further study of drug patterns was an important part in monitoring evaluating and making sufficient modifications to achieve rational use and cost-effectiveness[4]. Nowadays Disease Modified Anti Rheumatic Drugs become a mainstay in the treatment of rheumatoid arthritis[5].

Rheumatoid joint pain is one of the numerous ongoing incendiary sicknesses that prevail in females. The current examination seen that solitary 35 % of drugs were endorsed by their conventional name and the excess 65% were inabrand name. The generics apportioned from the clinic drug store were more (49%)because patients who have endorsed drugs with the brand names were apportioned the conventional medications by the drug specialist.This form of medication replacement by network just as medical clinic drug specialist[6].

Co-Morbid Conditions: Co-morbidities results in increased healthcare cost, functional disability, poorer quality of life, treatment interferences, and excess mortality and depression leads to disability. The increased prevalence of co-morbid states increases the economic burden on patients, family, and society. Most of the co-morbid states are recognized and untreated[7].

METHODOLOGY

Prospective Observational Study was done in the private hospital and institutional ethical committee was approved by Vivekanandha Medical Care Hospital, and the study duration was December 2019-June 2019 for 6 months period of time.80 patients were recruited for the study, among the total population 73 patients were selected according to inclusion criteria. Our study included both female and male patients and Patients prescribed with DMAR drugs and Patient with Co-morbidities. Severely ill patients, and Pregnancy patients were excluded in our study. Patient details are collected from the patient history and treatment chart.Case was collected towards the patients who were diagnosed with rheumatoid arthritis and the prescriptions pattern was analyzed and the patients was segregated according to their different disease conditions and their prescriptions were checked. Here Microsoft Excel Software is used for Percentage Calculation.

RESULTS

Gender Wise Distribution: From the 73 prescription records, 36% of patients were male and 64% were female. The demographic characteristics of the patients included in the current study, as shown in Table 2.

Table 2: Gender Wise Distribution

Gender	Number of patients	Percentage (%)
Male	26	36
Female	47	64

Age Group Categorization of Cases

Among 73 patients enrolled in the study, Patients in the age between 51-60 years (40%) were most predominantly diagnosed with rheumatoid arthritis followed by 33% (24 patients) of 41-50years and 12% (9 patients) of 61-70 years and 11% (8 patients) of 31-40 years and 3% (2 patients) of 21-30 years and 1% (1 patient) of 71-80years of age respectively, as shown in table 3.

Table 3: Age group categorization of cases (n= 73)

Age range	Number of patients(n)	Percentage (%)
21-30	2	3
31-40	8	11
41-50	24	33
51-60	29	40
61-70	9	12
71-80	1	1

Categorization of Cases with Social History: Among 26 patient, 60% (15 patients) were smoker and 40% (10 patients) were alcoholic, as shown in table 4.

Table 4: Categorization of cases with social history (n = 26)

Social history	Number of Patients	Percentage (%)
Smoker	15	60
Alcoholic	10	40

Categorization of Cases with Co-Morbid Conditions: From 73 prescription records 28% (20 Patients) were diagnosed with Rheumatoid Arthritis alone, 18% (13 Patients) were diagnosed with Rheumatoid Arthritis and Diabetes Mellitus, 18% (13 Patients) were diagnosed with Rheumatoid arthritis and Cardio Vascular Disease, 16% (12 Patient) were diagnosed with Rheumatoid Arthritis and Hypertension, 13% (10 Patients) were diagnosed with Rheumatoid Arthritis and Hypertension, Diabetes Mellitus, 7% (5 Patient) were diagnosed with Rheumatoid Arthritis and Thyroid, as shown in table 5.

Table 5: Categorization of Cases with Co-morbid Conditions (n = 73)

Disease condition	Number of patients	Percentage (%)
Rheumatoid Arthritis	20	28
Rheumatoid Arthritis + Diabetes Mellitus	13	18
Rheumatoid Arthritis + Hypertension	12	16
Rheumatoid Arthritis + Diabetes mellitus + Hypertension	10	13
Rheumatoid Arthritis + Cardio vascular disease	13	18
Rheumatoid arthritis + Thyroid	5	7

Overall Drugs Prescribed for Rheumatoid Arthritis: Drugs prescribed for Rheumatoid Arthritis are Non-Steroidal Anti-Inflammatory Drugs 46.48% – Diclofenac 4.1%, Aceclofenac 5.47%, Indomethacin 1.36%, Etoricoxib 12.32%, Tramadol 2.73%, Ketorolac 2.73%, Combination of Tramadol+ Paracetamol 2.73%, Aceclofenac and Paracetamol 5.47%, Diclofenac and paracetamol 1.36%. Disease Modified Anti Rheumatic Drugs 21.85% - Methotrexate 16.4%, Hydroxychloroquine 2.73%, Leflunomide 1.36%, Sulfasalazine 1.36%. Folic Acid 21.91%. Steroids 27.36% - Prednisolone 17.8%, Dexamethazone – 2.73%, Deflazacort – 2.73%, Adalimumab – 4.1%. Proton Pump Inhibitor 20.49% - Rabeprazole – 5.47%, Pantoprazole – 8.21%, Pantoprazole + Domperidone 1.36%, Ranitidine 1.36%, Rabeprazole + Domperidone 2.73%, Omeprazole 1.36%, as shown in table 6.

Overall Drugs Prescribed for Rheumatoid Arthritis with Diabetes Mellitus

Among 13 prescriptions records the drugs prescribed for Rheumatoid Arthritis with Diabetes mellitus were Metformin 6.84%, Glibenclamide+ Metformin 5.47%, Glimepiride + Metformin 5.47%, Insulin 2.73%, Metformin + Vildagliptin 2.73%, Glimepiride 1.36%, Methyl prednisolone 9.58%, Methotrexate 4.1%, Hydroxychloroquine 6.84%, Adalimumab 2.73%, Levofloxacin 1.36%, tramadol 4.1%, Etoricoxib 2.73%, Aceclofenac + Paracetamol 4.1%, Paracetamol+ Tramadol 1.36%,, Paracetamol 4.1%, Aceclofenac 2.73%, Diclofenac 1.36%, Rabeprazole 1.36%, Pantoprazole 5.47%, Ranitidine 2.73%, Iron and Folic acid 1.36%, Folic acid 8.21% respectively, as shown in table 7.

Table 6: Overall Drugs Prescribed for Rheumatoid Arthritis

Sl. No	Drugs	Number of Drugs	Percentage (%)
1.	Diclofenac	3	4.1
2.	Aceclofenac	4	5.47
3.	Indomethacin	1	1.36
4.	Etoricoxib	9	12.32
5.	Tramadol	2	2.73
6.	Ketorolac	2	2.73
7.	Tramadol + Paracetamol	2	2.73
8.	Aceclofenac + Paracetamol	4	5.47
9.	Diclofenac + Paracetamol	1	1.36
10.	Methotrexate	12	16.4
11.	Hydroxychloroquine	2	2.73
12.	Leflunomide	1	1.36
13.	Sulfasalazine	1	1.36
14.	Folic Acid	16	21.91
15.	Prednisolone	13	17.8
16.	Dexamethasone	2	2.73
17.	Deflazacort	2	2.73
18.	Adalimumab	3	4.1
19.	Ranitidine	1	1.36
20.	Pantoprazole	6	8.21
21.	Rabeprazole + Domperidone	2	2.73
22.	Rabeprazole	4	5.47
23.	Paracetamol+ Domperidone	1	136
24.	Omeprazole	1	1.36

Overall Drugs Prescribed for Rheumatoid Arthritis with Hypertension: Out of 10 prescriptions records the drugs prescribed for Rheumatoid Arthritis with Hypertension were Folic acid 9.58%, Telmisartan 8.21%, Methotrexate 6.84%, Methylprednisolone 5.47%, Hydroxychloroquine 5.47%, Diclofenac 5.47%, Adalimumab 4.1%, Paracetamol 4.1%, Pantoprazole 4.1%, Tramadol l2.73%, Telmisartan + Hydrochlorthiazide 2.73%, Etoricoxib 2.73%, Ranitidine 2.73%, Alprazolam 1.36%, Ferric ammonium sulphate 1.36%, Mext-kit 1.36%, Bisoprolol 1.36%, Ibuprofen 1.36%, Zolpidem 1.36%, Dexamethazone 1.36%, Telmisartan + Amlodipine 1.36%, Nebivolol 1.36%, Paracetamol + Tramadol 1.36%, as shown in table 8.

Table 7: Overall Drugs Prescribed for Rheumatoid Arthritis with Diabetes Mellitus

Sl. No	Drugs	Number of Drugs	Percentage (%)
1.	Methylprednisolone	7	9.58
2.	Folic acid	6	8.21
3.	Metformin	5	6.84
4.	Hydroxychloroquine	5	6.84
5.	Glibenclamide+ Metformin	4	5.47
6.	Glimepride+ Metformin	4	5.47
7.	Pantoprazole	4	5.47
8.	Aceclofenac + Paracetamol	3	4.1
9.	Paracetamol	3	4.1
10.	Tramadol	3	4.1
11.	Methotrexate	3	4.1
12.	Insulin	2	2.73
13.	Ranitidine	2	2.73
14.	Adalimumab	2	2.73
15.	Aceclofenac	2	2.73
16.	Etoricoxib	2	2.73
17.	Metformin+ Vildagliptin	2	2.73
18.	Glimepiride	1	1.36
19.	Paracetamol+ Tramadol	1	1.36
20.	Levofloxacin	1	1.36
21.	Iron + Folic acid	1	1.36
22.	Diclofenac	1	1.36
23.	Rabeprazole	1	1.36

Overall Drugs Prescribed for Rheumatoid Arthritis with Hypertension and Diabetes Mellitus: Among 13 prescription records the drugs prescribed for Rheumatoid arthritis with Hypertension were Folicacid 9.58%, Telmisartan 8.21%, Methylprednisolone 6.84%, Methotrexate 5.47%, Hydroxychloroquine 5.47%, Amlodipine 4.1%, Diclofenac 4.1%, Metformin 4.1%, Nebivolol 4.1%, Metformin+Glimipride 2.73%, Etoricoxib 2.73%, Metformin+vildagliptin 2.73%, Metformin+Glimepride+Voglibose 2.73%, Rabeprazole 2.73%, Pantoprazole 2.73%, Paracetamol+Aceclofenac 2.73%, Paracetamol+Tremadol 2.73%, Paracetamol 2.73%, Dexamethazone 1.36%, Celecoxib 1.36%, Telmisartan+Hydroxychloroquine 1.36%, Atenolol 1.36%, Ranitidine 1.36%, Bisoprolol 1.36%,

Acetaminophen 1.36%, Domperidone+Rabeprazole 1.36%, as shown in table 9.

Table 8: Overall Drugs Prescribed for Rheumatoid Arthritis with Hypertension

Sl. No	Drug	No of Drugs	Percentage (%)
1.	Folic acid	7	9.58
2.	Telmisartan	6	8.21
3.	Methotrexate	5	6.84
4.	Methylprednisolone	4	5.47
5.	Hydroxychloroquine	4	5.47
6.	Diclofenac	4	5.47
7.	Adalimumab	3	4.1
8.	Paracetamol	3	4.1
9.	Pantoprazole	3	4.1
10.	Tramadol	2	2.73
11.	Telmisartan+Hydrochlorthiazide	2	2.73
12.	Etoricoxib	2	2.73
13.	Ranitidine	2	2.73
14.	Alprazolam	1	1.36
15.	Ferric ammonium sulphate	1	1.36
16.	Mext-kit	1	1.36
17.	Bisprolol	1	1.36
18	Ibuprofen	1	1.36
19.	Zolpidam	1	1.36
20.	Rosuvastatin	1	1.36
21.	Aceclofenac	1	1.36
22.	Amolodipine	1	1.36
23.	Dexamethazone	1	1.36
24.	Telmisartan+Amlodipine	1	1.36
25.	Nebivolol	1	1.36
26.	Paracetamol+Tramadol	1	1.36

Table 9: Overall Drugs Prescribed for Rheumatoid Arthritis with Hypertension and Diabetes Mellitus

Sl. No	Drugs	Number of Drugs	Percentage (%)
1.	Folic acid	4	5.47
2.	Telmisartan	6	8.21
3.	Methylprednisolone	5	6.84
4.	Methotrexate	4	5.47
5.	Hydroxychloroquine	4	5.47
6.	Amlodipine	3	4.1
7.	Diclofenac	3	4.1
8.	Metformin	3	4.1
9.	Nebivolol	3	4.1
10.	Metformin+ Glimepiride	2	2.73
11.	Etoricoxib	2	2.73
12.	Metformin+ vildagliptin	2	2.73
13.	Metformin+ Glimepiride+ Voglibose	2	2.73
14.	Rabeprazole	2	2.73
15.	Pantoprazole	2	2.73
16.	Paracetamol+ Aceclofenac	2	2.73
17.	Paracetamol + Tramadol	2	2.73
18.	Paracetamol	2	2.73
19.	Dexamethasone	1	1.36
20.	Celecoxib	1	1.36
21.	Telmisartan+ Hydroxychloroquine	1	1.36
22.	Atenolol	1	1.36
23.	Ranitidine	1	1.36
24.	Bisoprolol	1	1.36
25.	Acetaminophen	1	1.36
26.	Domperidone+ Rabeprazole	1	1.36

Overall Drugs Prescribed for Rheumatoid Arthritis with Thyroid: From 5 prescription records, drugs prescribed were thyroxine sodium 6.84%, methotrexate 5.47%, folic acid 5.47%, prednisolone 1.36%, tramadol 2.73%, paracetamol 1.36%, diclofenac 1.36% respectively, as shown in table 10.

Table 10: Overall Drugs Prescribed for Rheumatoid Arthritis with Thyroid

Sl. No	Drugs	Number of Drugs	Percentage (%)
1.	Thyroxine Sodium	5	6.84
2.	Methotrexate	4	5.47
3.	Folic Acid	4	5.47
4.	Methyl prednisolone	1	1.36
5.	Tramadol	2	2.73
6.	Paracetamol	1	1.36
7.	Diclofenac	1	1.36

Overall Drugs Prescribed for Rheumatoid Arthritis with Cardio Vascular Disease

Among 13 prescription records the drugs prescribed for cardiovascular disease were methotrexate 10.95%, folic acid 10.95%, methyl prednisolone 9.58%, pantoprazole 9.58%, atorvastatin 8.21%, clopidogrel 5.47%, nebivolol 5.47%, rabeprazole 4.1%, ecospirin 2.73%, aspirin 2.73%, diclofenac 2.73%, tramadol 2.73%, rosuvastatin 2.73%, aceclofenac + paracetamol 2.73%, amitriptyline 1.36%, minilactone 1.36%, amlodipine 1.36%, furosemide 1.36%, Paracetamol1.36%, Tramadol + Acetaminophen 1.36%, Domperidone + Rabeprazole 1.36%, as shown in table 11.

Classes of Drugs Prescribed

Among 73 prescriptions 15 classes of drugs were prescribed NSAIDs (21.28%), DMARDs (14.28%), Anti- ulcerative (12.28%), Folic acid supplements (12.04%), Steroids (12.04%), Anti- hypertensive (8.96%), Anti- diabetics (7.56%), Opioid analgesics (3.081%), Lipid lowering agents (2.52%), Anti-platelets (2.24%), Anti- thyroids (1.4%), Diuretics (0.84%), Antibiotics (0.56%), Anti- depressants (0.28%), Sedatives (0.28%), as shown in table 12.

Table 11: Overall Drugs Prescribed for Rheumatoid Arthritis With Cardio Vascular Disease

Sl. No	Name of The Drug	Number of Drug	Percentage (%)
1.	Methotrexate	8	10.95
2.	Folic acid	4	5.47
3.	Methyl prednisolone	7	9.58
4.	Pantoprazole	7	9.58
5.	Atorvastatin	6	8.21
6.	Clopidogrel	4	5.47
7.	Nebivolol	4	5.47
8.	Rabeprazole	3	4.1
9.	Ecospirin	2	2.73
10.	Aspirin	2	2.73
11.	Diclofenac	2	2.73
12.	Tramadol	2	2.73
13.	Rosuvastatin	2	2.73
14.	Aceclofenac + paracetamol	2	2.73
15.	Amitriptyline	1	1.36
16.	Minilactone	1	1.36
17.	Amlodipine	1	1.36
18.	Furosemide	1	1.36
19.	Paracetamol	1	1.36
20.	Tramadol+Acetaminophen	1	1.36
21.	Domperidone+Rabeprazole	1	1.36

Table 12: Classes of Drugs Prescribed

Sl. No	Class of Drugs	Number of Drugs	Percentage (%)
1.	NSAIDs	76	21.28
2.	DMARDs	51	14.28
3.	Anti- ulcerative	46	12.28
4.	Folic acid supplements	43	12.04
5.	Steroids	43	12.04
6.	Anti – hypertensive	32	8.96
7.	Anti - diabetics	27	7.56
8.	Opioid analgesics	11	3.081
9.	Lipid lowering agents	9	2.52
10.	Anti- platelets	8	2.24
11.	Anti- thyroids	5	1.4
12.	Diuretics	3	0.84
13.	Antibiotics	2	0.56
14.	Anti-depressants	1	0.28
15.	Sedatives	1	0.28

Drug Interactions

Among 73 prescriptions, 4 major interactions, 6 moderate and 1 minor interaction were found, as shown in table 14.

Table 14: Drug Interactions

Severity of Drug- Drug Interactions	Total Number	Percentage (%)
Major interaction	4	36.36
Moderate interaction	6	54.54
Minor interaction	1	9.09
TOTAL	**11**	**100**

DISCUSSION

In this Prospective ObservationalStudy, 73 prescriptions are collected from the orthopedic department for 6 months were analyzed to evaluate the prescription pattern of Rheumatoid Arthritis. Out of 73 cases, the male was 36% (26), the female was 64% (47). These results were similar to that of Mirza A Beg et al (2017) predominance of a female patientwith 64.38% and 35.6% of male patients with a total of 73 prescriptions studied[8].

In our study, most patients were aged between 61-70 years (40%). Similar study conducted by Rishab. P et al (2020) found that in the age group between 50 to 69 years[9]. In our study(60%) of smokers having Rheumatoid Arthritis. These results are similar to MedhaBarbhaiya et al (2013) shows that cigarette smoking is one of the environmental risk factors for Rheumatoid Arthritis. It is associated with the increased severity of the disease[10].

Our study shows that most of the Rheumatoid Arthritis patients having co-morbidities like Hypertension (16%), Diabetes Mellitus (18%). Similar results were observed by S. Chandrashekara et al (2017) Rheumatoid Arthritis with Hypertension (20.7%), Rheumatoid Arthritis with Diabetes Mellitus (14.4%)[11].

The most commonly used drug for Rheumatoid Arthritis is Methotrexate (16.4%). A similar study conducted by Akhil Dahiya et al (2016) found that mostly prescribed DMARDs was methotrexate in 150 prescriptions[12].

Out of 73 prescriptions, (12.04%) of folic acid supplementation was prescribed along with methotrexate. These results were similar to that S. L. Whittle et al (2004) study shows that folic acid supplementations be commonly prescribed to all patients receiving methotrexate for the treatment of Rheumatoid Arthritis[13].

In our study, Opioids analgesics (3.081%) were prescribed. These results differ from the Manuel E. Machado-Duque et al (2020) study shows that a high proportion of opioids (71.1%) use for pain management in patients with Rheumatoid Arthritis[14].

We found that Rheumatoid Arthritis patients with Hyperthyroidism were (6.84%). In similar Hussein Mahagna et al (2018) show that Rheumatoid Arthritis with Hyperthyroidism (1.81%) was studied[15].

In this study, (12.04%) of steroids were used in 73 cases. These results were different from those observed in a study by Liron Caplan et al (2007) was 35.5% of steroids were studied[16]. In our study, a total of 73 cases were studied. In this (12.28%) of anti-ulcerative drugs were given. A Similar study by Shakti B. Dutta et al (2017) et al shows that 12.33% were anti-ulcerative.

In this study (14.28%) of DMARDs were prescribed to Rheumatoid Arthritis patients. The results of Shakti B. Dutta et al (2017) also noticed that (35.18%) of DMARDs were prescribed to Rheumatoid Arthritis patients[4].

In our study 2.52% of lipid-lowering drugs were prescribed to Rheumatoid Arthritis patients. Bharath Manu Akkara Veetil et al (2013) study shows that 27% of lipid-lowering therapy was given to Rheumatoid Arthritis patients[17].

CONCLUSION

The prescribing trends in the pharmacological management of Rheumatoid Arthritis and its associated co-morbidities were analyzed. During the study, it was observed that females were more prone to Rheumatoid Arthritis than male patients. The most affected age group was found to be 41-60 years. Among 73 patients included in the study, the majority of the patients were prescribed with Non - Steroidal Anti - Inflammatory Drugs (NSAIDS-21.28%) followed by Drug Modified Anti Rheumatic Drugs (DMARDs) and Steroids for the treatment of Rheumatoid Arthritis. It was observed that Methotrexate was the most commonly prescribed drug among the DMARDs. Prednisolone was most commonly prescribed among steroids. The most common co-morbid condition was found to be Diabetes Mellitus and Cardiovascular disease.

This study provides the knowledge to the healthcare providers on the importance of rational use of drugs in the treatment of Rheumatoid Arthritis and helps to get a better understanding of reason trends in management. Overall helps in reduced duration of hospitality and reduced risk of infection associated with Rheumatoid Arthritis.

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