The Professional Medical Journal
www.theprofesional.com

https://doi.org/10.29309/TPMJ/2021.28.07.6137

ORIGINAL PROF-0-6137

A study on prescribing patterns in patients with rheumatoid arthritis.

Sajid Naseem[1], Ambreen Zahoor[2], Zaidan Idrees Choudhary[3], Tania Sultana[4]

1. MBBS, FRCP
Assistant Professor Rheumatology
Fazai Medical College Islamabad/
2. MBBS, FCPS
Assistant Professor Medicine
HBS Medical and Dental College
Islamabad.
3. MBBS, FCPS (Psychiatry)
Assistant Professor Psychiatry
HBS Medical and Dental College
Islamabad.
4. MBBS, FCPS (Medicine),
FCPS (Rheumatology)
Senior Registrar Rheumatology
HBS Medical and Dental College
Islamabad.

Correspondence Address:
Dr. Sajid Naseem
House no 419, Chinar Street,
Park Road, Green Avenue, Islamabad.
sajidnaseem1975@gmail.com

Article received on:
08/10/2020
Accepted for publication:
17/12/2020

ABSTRACT… Objective: The aim of this study was to assess the prescribing patterns and frequency of use of various drug classes in patients with rheumatoid arthritis in a teaching hospital in Islamabad, Pakistan. **Study Design:** Descriptive Cross Sectional study. **Setting:** Medical Outpatient Department of HBS General Hospital, Islamabad. **Period:** August 2018 to March 2019. **Material & Methods:** Patients of rheumatoid arthritis were included in the study using non-probability consecutive sampling technique. Socio-demographic details and medication history was collected on pre-designed proforma. Data was analyzed using SPSS version 22. **Results:** A total of 112 patients were included in the study.108 patients (96.4%) were using disease modifying anti-rheumatic drugs. The most prescribed medication in the patients was methotrexate (n=82, 73%). One disease modifying anti-rheumatic drugs with a steroid was the preferred combination (n=32, 28%). Non-steroidal anti-inflammatory drugs (21%) and steroids (20%) were the other major drug classes among the total medications prescribed. Only one patient included in the study was using biologics. **Conclusion:** Conventional disease modifying anti-rheumatic drugs in combination with steroids and non-steroidal anti-inflammatory drugs are the preferred therapy in patients of Rheumatoid arthritis in local settings. Methotrexate is the most commonly used disease modifying anti-rheumatic drugs. The use of biological agents remains low as compared to the developed world owing to their high cost.

Key words: Disease Modifying Anti Rheumatic Drugs, Prescribing Trends, Rheumatoid Arthritis.

Article Citation: Naseem S, Zahoor A, Choudhary ZI, Sultana T. A study on prescribing patterns in patients with rheumatoid arthritis. Professional Med J 2021; 28(7):1044-1048. https://doi.org/10.29309/TPMJ/2021.28.07.6137

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic inflammatory disease that primarily affects the joints and leads to erosion of bone and cartilage. The global prevalence of RA in adult population is approximately 1%.[1] Studies conducted on RA patients in Pakistan show point prevalence up to 12.6% with most patients being females, uneducated and unemployed.[2]

Over the last two decades there have been rapid developments related to the treatment of RA. The latest guidelines by American College of Rheumatology (ACR) and European League against Rheumatism (EULAR) recommend that patients of RA should be treated with traditional disease-modifying antirheumatic drugs (DMARDs), either alone or in combination.[3] Studies show that early intensive treatment with DAMRDs helps patients achieve low disease activity or clinical remission.[4] Owing to its relatively low cost and good efficacy, methotrexate is the most commonly prescribed DMARD in the world.[5] Patients who show inadequate response to DMARDs, either due to inefficacy or intolerability, may benefit from the use of biologic therapies (referred to as biologics), including tumor necrosis factor (TNF) inhibitors, interleukin (IL)-6 inhibitors, rituximab and abatacept. These agents have shown to decrease morbidity and disability and improve quality of life in patients with poor response to traditional DMARDs.[6] Tumour necrosis factor inhibitors (TNFi) were the first biologics developed and remain the most popular.[7] Apart from the traditional and biological DAMRDs, other classes of drugs continue to be prescribed in the management of RA. The use of non-steroidal anti-inflammatory drugs (NSAIDs)

remains the cornerstone of pain alleviation in patients of RA.[8] Guidelines also suggest the use of steroids in combinations with DMARDs and biologics in patients who show poor response after months of treatment, underlying the benefits of steroid therapy.[9] On the other hand, there is also a high awareness of glucocorticoid associated adverse effects (osteoporosis, diabetes, weight gain) especially when used at high doses for prolonged periods.

There is a paucity of data related to the treatment being received by RA patients in Pakistan. The aim of the current study was to look at the prescribing trends in the management of RA in local settings. This information can be used to ascertain whether these treatments are in line with internationally accepted evidence-based guidelines. The highlighted areas requiring improvements can be used to educate local physicians to optimize treatment for RA patients in the community.

MATERIAL & METHODS

This descriptive cross-sectional study was conducted at the medical outpatient department of HBS General Hospital, Islamabad from August 2018 to March 2019. The ethical approval was obtained from the institution's research ethics review board (EC REF. No. 21/P/18) before the initiation of the study. The participants were informed about the design and aims of the study and written consent was taken from all patients willing to participate.

The sample size was calculated from previous literature on the subject.[10] Using non-probability consecutive sampling technique, 112 patients of rheumatoid arthritis were included in the study according to the following criteria:

Inclusion Criteria

Diagnosed patients with RA of either sex.
Age greater than or equal to 18 years.
On treatment for at least 6 months.

Exclusion Criteria

Patients with acute or chronic medical conditions requiring hospitalization.
Patients with neurobehavioral disorders.

The demographic profiles of patients along with history of associated medical or surgical illness were documented. From prescription records, number of drugs prescribed, generic/brand names, drug dose, dosage form, and frequency were recorded. Descriptive analysis was conducted using SPSS version 22. Continuous variables were presented as mean values ± standard deviation (SD), and categorical variables were presented as percentages.

RESULTS

112 patients with a diagnosis of RA were enrolled in the study. Among the study participants, 80 (71.4%) were females and 32 (28.9%) were males. Average duration of disease was 4.6 years with a range of 2 to 13 years. The demographic details and disease-related information have been represented in Table-I.

	Males	Females	Overall
Gender n (%)	32 (28.5)	80 (71.4)	112 (100)
Mean age (years)	43.28	42.25	42.3
Avg duration of RA (years)	3.4	4.9	4.6
Co-morbidity n (%)	7 (21.8)	37 (46.2)	44 (39.2)

Table-I. Demographics and disease information of the study participants.

DMARDs were the most commonly prescribed medications among the RA patients included in the study- 55% of the total medications prescribed belonged to the group. NSAIDs and steroids were the other commonly prescribed classes. Only one patient among the study sample was using biologics (Figure-I).

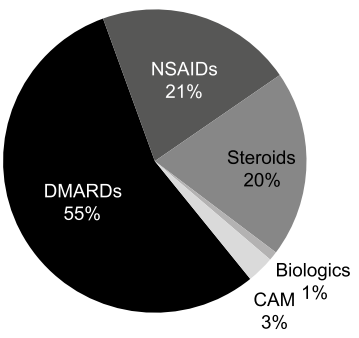


Figure-I. Percentages of different drug classes prescribed in the study patients

(DMARDs: Disease-modifying anti-rheumatic drugs, NSAIDs: Non-steroidal anti-inflammatory drugs, CAM: Complementary and alternative medicines).

108 patients (96.4%) included in the study were using DMARDs. Methotrexate was the most common drug prescribed from this group. 62 patients (55%) were on NSAIDS with diclofenac being the most prescribed medication (Table-II).

Total DMARDs	128
Methotrexate	82 (64.1)
Sulfasalazine	33 (25.7)
Leflunamide	13 (10.1)
Total NSAIDs	62
Dilofenac	32(48.2)
Naproxen	9(14.5)
Aceclofenac	5(10.3)
Celecoxib	5 (8.6)
Flurbiprofen	5 (8.6)
Meloxicam	4 (6.1)
Lornoxicam	2 (3.2)

Table-II. Prescription analysis of the study participants. N (%)

16 of the patients included in the study were on monotherapy; 12 of them on DMARD while 4 were on steroids only. The remaining 96 patients were on different combinations of drug classes. The most common combination used was DMARD with a steroid n=32 (28%). The details of combinations of drug classes prescribed are given in Figure-2.

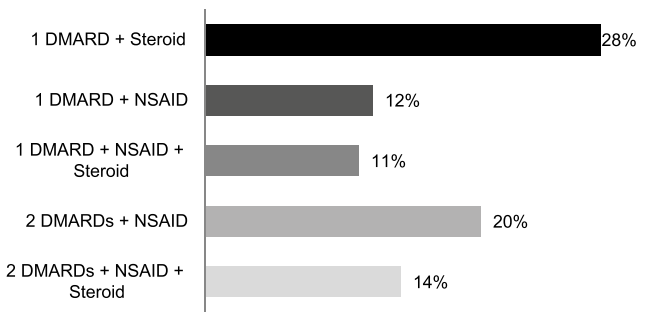


Figure-2. Percentage of various combinations prescribed in the study patients.

DMARDs: Disease-modifying antirheumatic drugs, NSAIDs: Nonsteroidal anti-inflammatory drugs.

DISCUSSION

Studies looking into the prescribing trends of drugs are essential to improve the clinical outcomes in patients. The current study aimed to review the use of non-biological and biological DMARDs in the treatment of patients with rheumatoid arthritis in local settings. To the best of our knowledge this is the first study of its kind in Pakistan.

The results of the study showed a significant predominance of females among RA patients as compared to men (71% vs 28%). In general chronic inflammatory conditions are more common in females and previous studies have also shown this skew in patients of RA. A study conducted by Alam et al. at a tertiary care hospital in Karachi reported a gender ratio of 4:1 in favour of females among the 633 patients of RA included in the study.[11] Another study conducted by Dahiya et al. in a tertiary care hospital in Delhi reported that more that 77% of the RA patients were females[12], results which agree with ours. A high number of patients reported co-morbidities (39%). This result has also been previously observed in other similar studies.[13,14]

The most commonly prescribed DMARD in our study patients was methotrexate (n=82, 73%). However there was a wide range of combinations in which methotrexate was being used. In 12 patients it was prescribed as monotherapy while the other patients were receiving it in different combinations with other DAMRDs, NSAIDs or steroids. Similar stats were revealed by a study carried out in UK by Satish et al and in India by Gawdeet al.[15,10] Considering that methotrexate is the recommended first line treatment for RA, most of these prescriptions were in accordance with international guidelines.

Out of the total 112 patients, 96 (85.7%) were on combination therapy. The combination of DMARD with a steroid was the most common one used (n=32, 28%). Previous studies on this aspect have yielded differing results. Sukhpreet

et al. from India found that the combination of two DMARDs was the most commonly prescribed while Nikolaisen et al. from Norway reported only 2% of the study patients on combination therapy.[16,17] The variability in combinations may be due to the differing disease characteristics of the patients such as intensity of symptoms at time of consultation. They may also be a part of a broader trend of poly-pharmacy common in Pakistan and other developing countries.

Biological agents (Rituximab, Etanercept, Adalimumab) are available in Pakistan but only one patient from the current study sample was using them. Prescribing trend studies from India have also revealed either no or minimal use of biological drugs. In the study conducted by Dharani et al., only 6% of RA patients received biological DMARDs.[18] If we compare our finding with the western countries there is a marked difference in the practice. For example, the study conducted by Yusuf Yazici et al. in USA shows marked increased in use of biological agents from 3% in 1999 to 26% in 2006.[19] The primary reason for this low use of biologics in our settings is the high cost of the medicines resulting in physician's reluctance to prescribe them.

The current study also revealed some areas of concern regarding the prescribing practices. Despite the warning about the use of NSAIDs in patients with IHD and hypertension about half of these patients were on these medications. In total, 55.3% (n=62) of the patients were receiving NSAIDs with diclofenac sodium being the most common even though it is associated with the worst side effects. There is an urgent need to re-educate the physicians about the potential health risk of NSAIDs especially diclofenac and reduce their use. Similarly, 53.5% (n=60) of the patients were using steroids but a majority of them did not receive prophylaxis against osteoporosis.

One of the limitations of the current study was that the data was collected from a single tertiary care hospital and the results may not be representative of other parts of the country. Future studies may look to incorporate data from different centres of the country.

CONCLUSION

DMARDs are the most commonly prescribed medications in the management of RA in local settings. The combination of a single DMARD with a steroid was the preferred therapy in most cases. Biologics use is almost non-existent owing to their relatively high cost.

REFERENCES

1. Smolen JS, Aletaha D, McInnes IB. **Rheumatoid arthritis.** 2016 Oct 22; 388(10055):1984]. Lancet. 2016; 388(10055):2023–2038. doi:10.1016/S0140-6736(16)30173-8.

2. Naqvi AA, Hassali MA, Aftab MT. **Epidemiology of rheumatoid arthritis, clinical aspects and socio-economic determinants in Pakistani patients: A systematic review and meta-analysis.** J Pak Med Assoc. 2019; 69(3):389–398.

3. Singh JA, Furst DE, Bharat A, et al. **2012 update of the 2008 American College of Rheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis.** Arthritis Care Res (Hoboken). 2012; 64(5):625–639. doi:10.1002/acr.21641.

4. Verstappen SM, Albada-Kuipers GA, Bijlsma JW, et al, **For the utrecht rheumatoid arthritis cohort study group (SRU). A good response to early DMARD treatment of patients with rheumatoid arthritis in the first year predicts remission during follow up.** Ann Rheum Dis. 2005. 64:38-43.

5. Hazlewood GS, Barnabe C, Tomlinson G, Marshall D, Devoe DJ, Bombardier C. **Methotrexate monotherapy and methotrexate combination therapy with traditional and biologic disease modifying anti-rheumatic drugs for rheumatoid arthritis: A network meta-analysis. Cochrane Database Syst Rev.** 2016; (8):CD010227. Published 2016 Aug 29. doi:10.1002/14651858.CD010227.pub2.

6. Fechtenbaum M, Nam JL, Emery P. **Biologics in rheumatoid arthritis: where are we going?.** Br J Hosp Med (Lond). 2014; 75(8):448–456. doi:10.12968/hmed.2014.75.8.448.

7. Machado MAÁ, Moura CS, Guerra SF, Curtis JR, Abrahamowicz M, Bernatsky S. **Effectiveness and safety of tofacitinib in rheumatoid arthritis: A cohort study.** Arthritis Res Ther. 2018; 20(1):60. Published 2018 Mar 23. doi:10.1186/s13075-018-1539-6.

8. Aletaha D, Smolen JS. **Diagnosis and management of rheumatoid arthritis: A Review. JAMA.** 2018; 320(13):1360–1372. doi:10.1001/jama.2018.13103.

9. Rau R. **Glucocorticoid treatment in rheumatoid arthritis.** Expert Opin Pharmacother. 2014; 15(11):1575–1583. doi:10.1517/14656566.2014.922955#.

10. Gawde RS, Shetty CY, Merchant S, Kulkarni JU, Nadakar YM. **Drug utilization pattern and cost analysis in rheumatoid arthritis patients: A cross sectional study in Tertiary Care Hospital, Mumbai.** British Journal of Pharmaceutical Research. 2013; 3(1):37-45.

11. Alam SM, Kidwai AA, Qureishi BM, Sami A, Qureishi HH, Mirza H. **Epidemiology of rheumatoid arthritis in a tertiary care unit, Karachi, Pakistan.** J Pak Med Assoc Feb2011; 61(2):123-6.

12. Dahiya A, Kalra BS, Saini A, Tekur U. **Prescription pattern in patients with rheumatoid arthritis in a teaching tertiary care hospital.** MAMC J Med Sci 2016; 2:33-7.

13. Gullick NJ, Scott DL. **Co-morbidities in established rheumatoid arthritis.** Best Pract Res Clin Rheumatol. 2011; 25(4):469–483. doi:10.1016/j.berh.2011.10.009.

14. Humphreys J, Hyrich K, Symmons D. **What is the impact of biologic therapies on common co-morbidities in patients with rheumatoid arthritis?** Arthritis Res Ther. 2016; 18(1):282. Published 2016 Dec 1. doi:10.1186/s13075-016-1176-x.

15. Satish MR, David AW, Adam Y, Patrick DWK, Ernest HC. **On behalf of the Early Rheumatoid Arthritis Network (ERAN), First-line DMARD choice in early rheumatoid arthritis—do prognostic factors play a role?,** Rheumatology, Volume 49, Issue 7, July 2010, Pages 1267–1271, https://doi.org/10.1093/rheumatology/kep389.

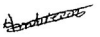
16. Sukhpreet, Agarwal V, Tiwari P. **Treatment and monitoring costs in rheumatoid arthritis: Preliminary results from an Indian setting.** Indian Journal of Pharmaceutical Sciences. 2007, 69 (2): 226-231.

17. Nikolaisen C, Kvien TK, Mikkelsen K, Kaufmann C, Rødevand E, Nossent JC. **Contemporary use of disease-modifying drugs in the management of patients with early rheumatoid arthritis in Norway.** Scand J Rheumatol. 2009; 38(4):240–245. doi:10.1080/03009740802609566.

18. Ranganath, D, Ganguly, D, Shankarappa, M, Nagaraj K, Chintha R. **Analysis of drug prescribing trends in treatment of rheumatoid arthritis at a tertiary care hospital, Karnataka, India.** International Journal of Basic & Clinical Pharmacology, 5(5), 1790-1797. doi:http://dx.doi.org/10.18203/2319-2003.ijbcp20163175.

19. Yazici Y, Shi N, John A. **Utilization of biologic agents in rheumatoid arthritis in the United States: Analysis of prescribing patterns in 16,752 newly diagnosed patients and patients new to biologic therapy.** Bull NYU HospJt Dis. 2008; 66(2):77–85.

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Sajid Naseem	Conception and design of study, Also design the data collection form and write up the article.	
2	Ambreen Zahoor	Conception and design of study, Also design the data collection form and write up the article.	
3	Zaidan Idrees Choudhary	Interpretation of data and statistical analysis.	
4	Tania Sultana	Interpretation of data and statistical analysis.