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A STUDY ON PRESCRIPTION PATTERN AND IMPACT OF PATIENT COUNSELLING IN RHEUMATOID ARTHRITIS

Sara fatima[*1], Mazharuddin Ali Khan[2], Akbar basha[3], Sadiya Mustafavi[4], Sariya Nooreen[5], Seema Tabassum[6]

[1]Assisstant professor, Department of pharmacy practice, Deccan school of pharmacy, Hyderabad, Telangana, India. [2]Professor, Department of Orthopaedics, Deccan college of medical sciences, Hyderabad, Telangana, India. [3]PG, Department of Orthopaedics, Deccan college of medical sciences, Hyderabad, Telangana, India.
[4,5,6]Doctor of Pharmacy student, Department of pharmacy practice, Deccan school of pharmacy, Osmania university, Hyderabad, Telangana, India.

ABSTRACT

Rheumatoid arthritis (RA) is a chronic autoimmune disorder that primarily affects joints of hands, wrist and feet leading to deformities. This disease has an effect on approximately 1% of the adult population, the prevalence of RA in India is approximately 0.75%. Better treatment strategies and patient counselling helps to improve the quality of life (QOL) in Rheumatoid Arthritis. To study the Prescription pattern and Impact of Clinical Pharmacist mediated patient counselling on health-related quality of life (HRQOL) in rheumatoid arthritis. A prospective observational study was conducted in both the Outpatient and Inpatient departments of Orthopaedics at OHRC, Hyderabad for 6 months. A total of 82 RA diagnosed patients were included in the study. The lab parameters such as CRP, RA factor, ASO titer, ESR, CBP and X-ray were measured. The DAS -28, MMAS-8 and WHO causality assessment scale were used to check the disease severity, medication adherence and ADRs respectively. The statistical method used was student paired 't' test to analyze the significant difference between baseline and follow up and the level of significance with p values less than 0.05 were considered to be statistically significant. Total of 82 prescriptions were analyzed: females 55(67%), males 27(33%). RA factor was positive in 35 (42.6%) patients; ESR was raised in 69 (84.1%) patients. The main prescribed drugs were DMARDs 65(79.2%), NSAIDS 82 (100%), Corticosteroids 27 (33%). Through MMAS-8 scale 18 (21.9%) patients at first visit and 38(46.3%) patients after consequent visit were in the high adherence category.This study concludes the positive influence on various domain of quality of life in RA patients by providing the patient counselling and educating the patients through the patient information leaflet.

Key words: Disease modifying anti-rheumatic drugs, DAS -28, MMAS-8, WHO causality assessment.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic auto immune disorder that primarily affects joints of hands, wrist and feet leading to deformities. It is characterized by symmetrical polyarticular inflammation of the synovium, the small joints of the hands (MCP and PIP), wrists and feet. This inflammation results in pain and stiffness and can lead to progressive joint damage resulting in deformities and loss of function [1].

The etiology of RA is unknown and involves genetic predisposition supported by the high incidence of RA in monozygotic twins and certain families (30% concordance). The highest risk for occurrence of RA is reported in twins who have HLA-DRB1 allele. The class II MHC complex allele HLA-D4 and related alleles are identified to be most important genetic risk factors for RA. In a specific region on chromosome 3 the Polymorphisms

Corresponding Author :- **Sara fatima** Email:- sarafatima703@gmail.com

in TNF and IL-10 genes is also associated with rheumatoid arthritis [2]. RA may result due to infectious agents which include Mycoplasma, Epstein bar virus, Cytomegalo virus, Parvo virus, Rubella virus [3]. Possible environmental trigger related with the rheumatoid arthritis is cigarette smoking [4]**.** Anxiety and depression are most commonly seen in rheumatoid arthritis patients. The severity of the depression depends upon the progression of disease and individual perceptions. Along with this lack of social support, loss of valued activities and poor socioeconomic status can develop the depression and anxiety. Rheumatoid arthritis can influence socioeconomic status by diminishing the income due to disability [5].

The factors associated with immune activation and disease progression involve the adaptive and innate immune pathways, along with cytokines, growth factors, and intracellular signaling molecules. The cells of the immune system, including macrophages, mast cells, and natural killer cells, also are important in the pathophysiology of synovial inflammation in RA. Macrophage maturation is mediated by granulocyte colony stimulating factor and granulocyte-macrophage colony stimulating factor. Macrophages are activated by toll-like receptors and nucleotide-binding oligomerization domain like receptors which secretes TNF-α, IL-1, IL-6, IL-12, IL-15, IL-18, IL-23, and are involved in the release of matrix degradation enzymes, phagocytosis, antigen presentation, and reactive oxygen intermediates. Neutrophils, present in the synovial fluid, synthesize inflammatory prostaglandins, proteases, and reactive oxygen intermediates. Mast cells release cytokines, chemokines, proteases, and vasoactive amines [6].

It begins with fatigue, Anorexia, Generalized weakness, and vagus musculoskeletal symptoms until the existence of synovitis. In some of the patient's symptoms like fever, splenomegaly, and lymph adenopathy is also seen. Characteristic changes of the hands and feet include ulnar deviation, swan neck deformity, boutonniere deformity [7].

Rheumatoid arthritis (RA) is based on the duration of symptoms. The disease may be diagnosed as early as within 3 months of clinical onset to two years when the disease is established this time duration has relevance to the concept of therapeutic window.

Four of the seven criteria must be present and that first four (1-4) must be present for at least six weeks

EULAR: European league against rheumatism

ACR: American college of rheumatology

There are two categories of drugs for the management of rheumatoid arthritis: DMARDS (disease modifying anti rheumatoid drugs) which includes non-biologics and biologics. Adjuvant drugs which includes NSAIDS and Glucocorticoids [8].

The Morisky Medication Adherence Scale (MMAS-8) is one of the most widely used adherence screening tool to assess patient adherence. It is composed of 4 Yes/No questions about past medication use patterns and is thus quick and simple to use during drug history interviews. It is a simple tool used to help identify barriers to medication adherence[9].

The DAS28 is a measure of disease activity in rheumatoid arthritis (RA). DAS stands for 'disease activity score' and the number 28 refers to the 28 joints that are examined in this assessment [10]. The level of disease activity can be interpreted as low (DAS 2.4), moderate (DAS 2.4 - 3.7), or high (DAS 3.7). A DAS 1.6 corresponds with being in remission according to the American Rheumatism Association (ARA) criteria. A change of 1.2 (2 times the measurement error) in the DAS is considered a significant change, because changes that large are unlikely the result of random measurement error (P 0.05).

PPMS is the method to facilitate the rational use of drugs in a population. Irrational use of medicines is a major problem worldwide. WHO estimates that more than half of all medicines are prescribed, dispensed or sold inappropriately, and that half of all patients fail to take them correctly. The overuse, underuse or misuse of medicines results in wastage of scarce resources and widespread health hazards [11].

Disease-modifying antirheumatic drugs (DMARDs) have been used to treat inflammatory arthritis and slow down joint destruction. However, previous guidelines have recommended non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids without DMARDs for the initial management of RA until evidence of joint damage appeared [12].

Patient counselling is the means of providing medication information orally or in written form to the patients or their representatives on directions of use, advice on side effects, precautions, storage, diet and life style modifications [13].

Rheumatoid arthritis may cause physical and emotional symptoms from reduced movement and long-lasting pain to depression. Physical exercise is strongly recommended for rheumatoid arthritis patients at least for short term to improve pain, and muscular strength 14].

The extreme physical inactivity of RA patients becomes a vicious circle in terms of health and disease progression. Thus, it has become apparent that encouraging physical activity is an important and essential part of the overall treatment of RA [15].

Resistance exercise in RA is safe and effective. Indeed, aerobic exercises improves cardiovascular fitness and patient quality of life, while reducing RA-associated disability and pain [16]. The counselling regarding diet includes reducing the amount and type of fat you eat as its use in cooking influences blood cholesterol levels and influence the level of joint pain and inflammation. Vegan Diet that includes fruits and vegetables, Mediterranean Diet that includes oleic acid, omega-3 fatty acids, unrefined carbohydrates, and phytochemicals, Elemental

Diet glucose, vitamins, trace elements, and essential amino acids [17]. Excess weight is harmful to joint health and may increase pain, stiffness and swelling in the joints. If you are obese or overweight, try and lose the excess weight by combining healthy eating with regular exercise.
Omega 3 fatty acids present in fish is effective in reducing the clinical symptoms of rheumatoid arthritis [18].

METHODOLOGY

The Prospective Observational study was done on 82 patients with rheumatoid arthritis selected on the basis of inclusion and exclusion criteria at Owaisi Hospital and Research Centre for the duration of six months. The study was initiated after the approval by ethics committee (IRB).

Inclusion criteria was i). the patients of either gender diagnosed with rheumatoid arthritis ii) age above 12 years iii) patients who signed the written informed consent to participate in the study iv) out patients and in patients. Exclusion criteria was i) Pregnant women ii) patients having other auto immune diseases iii) AIDS iv) age above 85 years v) patients who are reluctant to participate in the study.

The patients who satisfied the inclusion criteria were selected. The clinical examination was done and demographic details like age, gender, diet history, family history and baseline characteristics like pain intensity, number of swollen & tender joints, CRP, ESR, RA factor, ASO titer, CBP were taken. Concomitant comorbidities were also addressed and specific treatment was given based on patients' condition.
Patients were explained in detail about the medications prescribed, its nature of action, the course of treatment, frequency of medications and its side effects. Once the patients agreed to the treatment, informed valid written consent was taken. All the patients were initially treated with NSAIDS, followed by DMARDS; and corticosteroids were prescribed in severe cases. Based on disease severity and duration of disease combination of these drugs were also prescribed.

Patient assessment was done using 'disease activity score 28' (DAS28) scale given by American College of Rheumatology (ACR). This scale shows extent of disease activity in RA patients and the questionnaires regarding the physical activity in the scale were used to assess the quality of life (QOL). Medication Adherence was checked by using MORISKY 8 item medication adherence (MMAS 8) scale on first visit and consequent follow up. The Adverse drug reactions were checked by WHO causality assessment scale.

At the first visit through direct patient interview the questions present in the scale were asked to the patients. It was filled properly and suitable scores were given according to the MMAS 8 scale. After collecting the data from the patients, counselling was provided regarding disease, drug, exercise, lifestyle modifications, advantages and disadvantages of medication adherence and non-adherence respectively through the patient information leaflet to improve the patient's knowledge towards the disease and their medication taking behaviour.

At the second visit once again, the patients were asked questions present in the scale. It was filled properly and suitable scores was given. Then the results of first (baseline) and second visit (subsequent follow up) were compared and outcomes were measured.

RESULTS

A total of 82 patients have been reported with rheumatoid arthritis. Out of which the male population was found to be 27 (33%) and female population was about 55 (63%). Hence, it is concluded that females are more prone to this disease when compared to males (see Figure 1).

About 3(3.6%) patients were in the age group of adolescence, 59 (71.9%) patients were under the age group adults and 20 (24.3%) patients were in the elderly age group (see Figure 2).

The risk factor associated with RA observed in our study were smokers 12 (15%), obesity 13 (16%), infection 11(13%), gender 55(67%) and family history of **RA** 19(23%). (see figure 3).

The patients were categorized into different stages of **RA** as follows: Very early **RA** 17(20.7%), 1 year early established **RA** 35(42.6%), Late established **RA** 16(19.5%), Established stable **RA** 14(17%).

The co - morbities found in patients were hypertension 15 (18.2%), Diabetes mellitus 9 (10.9%), Hypothyroidism 17 (20.7%), Osteoporosis 13 (15.9%), Gout 7 (8.5%), and Hypocalcemia 23 (28.0%) patients (see figure 4).

The most common drugs prescribed were disease modifying anti-rheumatic drugs (DMARD'S) to 65 (79.2%) patients, non-steroidal anti-inflammatory drugs (NSAIDS) to 82 (100%) patients, corticosteroids (CS) to 27 (33%) patients, calcium supplements to 53 (65.8%) patients and antacids to77 (93%) patients (see figure 5).
18 patients at first visit and 38 patients after consequent visit were in the High adherence category, 29 patients at first visit and 32 patients after consequent visit were in the Medium adherence category, 35 patients at first visit and 12 patients after consequent visit were in the Low adherence category (see figure 6).

ADR'S reported system wise were as follows:10 adrs reported were GIT related, 4 adrs were reported for liver dysfunction, 5 adrs were reported for ENT, 23 adrs were reported for CNS, 10 adrs were reported for skin and 1 ADR was reported for blurred vision. (see figure 7).
The order proceeds as follows:

CNS > GIT > SKIN > ENT > LIVER DYSFUNCTION > OPHTHALMOLOGY

Table 1. Classification of RA based on stages

DURATION	STAGES
0-3 months	very early RA
3 Months	1 year early established
1 – 2 years	Late established RA
More than 2 years	Established stable RA

Table 2. EULAR/ACR Criteria

S.No	CRITERIA	YES/NO
1	Morning stiffness (at least one hour).	
2	Arthritis (soft-tissue swelling or fluid) in three or more joint areas simultaneously (observed by the physician)	
3	Arthritis involving the proximal interphalangeal, metacarpophalangeal, or wrist joints.	
4	Symmetrical arthritis	
5	Rheumatoid nodules (subcutaneous, over bony prominence or extensor surfaces)	
6	Presence of rheumatoid factor	
7	Radiographic changes of RA in hand and/or wrist joints (e.g., erosions, periarticular osteopenia)	

Fig 1. Patient distribution based on gender

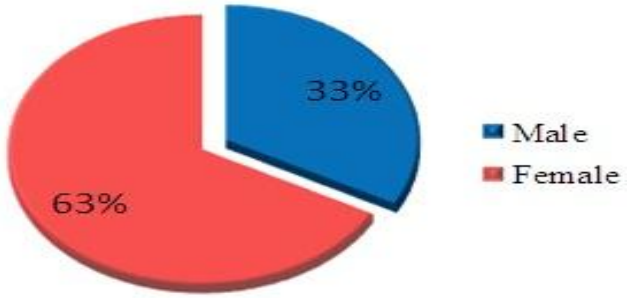


Fig 2. Prevalence of RA across various age groups

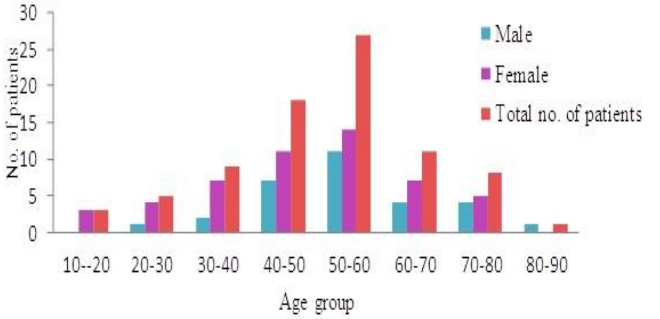


Fig 3. Pie chart depicting risk factors associated with R

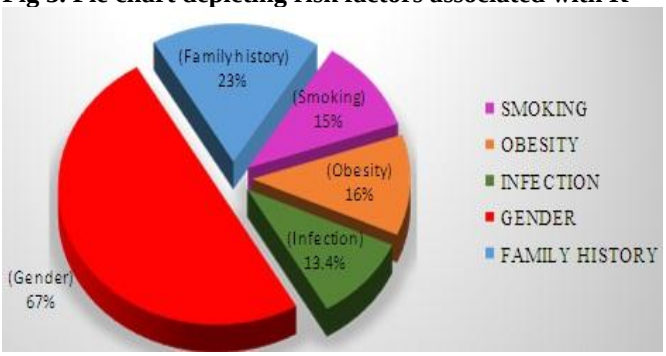


Fig 4. Patient distribution based on different stages of RA

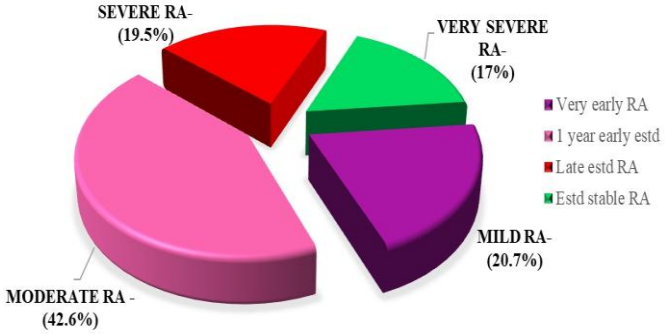


Fig 5. Patient distribution based on co-morbidities

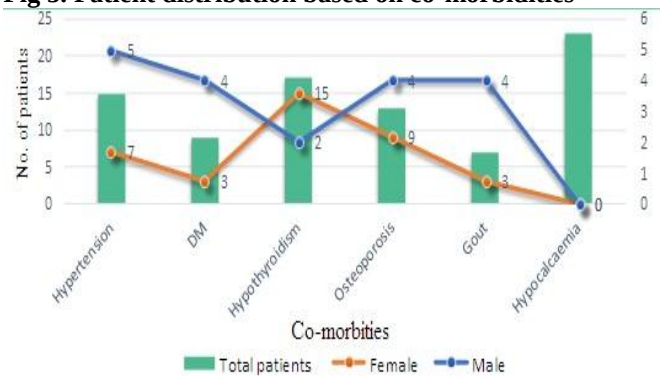


Fig 6. Frequency of various drugs prescribed

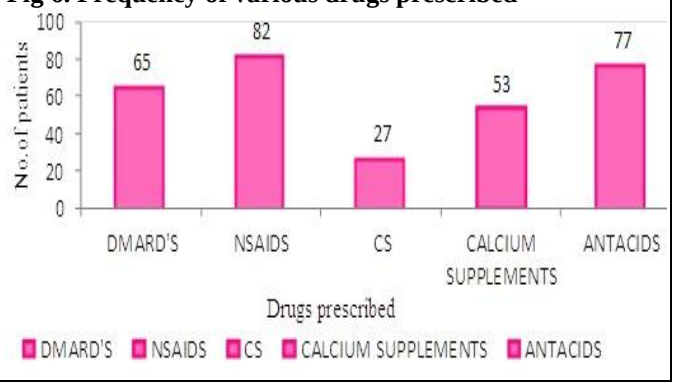


Fig 7. Patients Medication Adherence improvement as calculated using MORISKY scale of Adherence

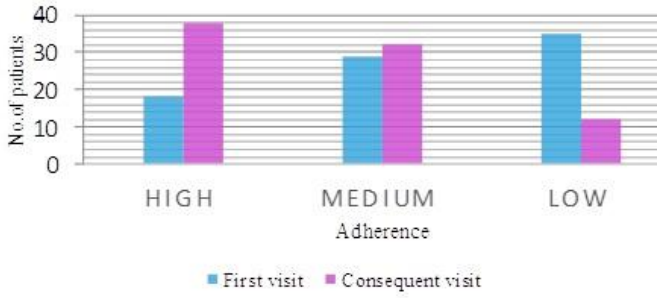
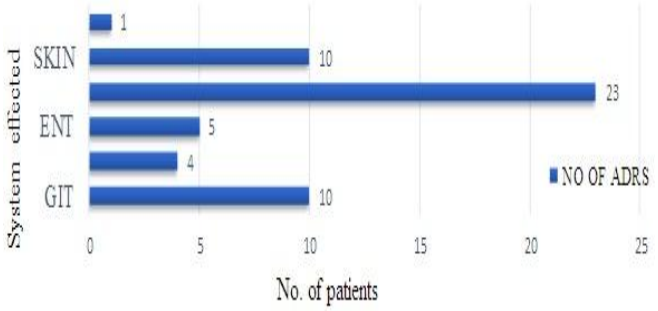


Fig 8. Graph showing systems affected by ADR



DISCUSSION

A total of 82 patients have been reported with rheumatoid arthritis. Out of which the male population was found to be 27 (33%) and female population was about 55 (63%). About 3(3.6%) patients were in the age group of adolescence, 59 (71.9%) patients were under the age group adults and 20 (24.3%) patients were in the elderly age group. The most common risk factor associated with RA, observed in our study was female gender which constitutes about 55(67%). The co - morbities in patients was found to be hypertension 15 (18.2%), Diabetes mellitus 9 (10.9%), Hypothyroidism 17 (20.7%), Osteoporosis 13 (15.9%), and Gout 7 (8.5%). It was observed that 17(20.7%) patients developed Very early RA, 35(42.6%) patients developed 1 year early established RA, 16(19.5%) patients developed Late established RA, 14(17%) patients developed Established stable RA categorized based on Turek's classification of rheumatoid arthritis. The most common drug therapy prescribed was disease modifying anti-rheumatic drugs (DMARD'S) which were prescribed to 65 (79.2%) patients, non-steroidal anti-inflammatory drugs were prescribed to (NSAIDS) 82 (100%), corticosteroids were prescribed to 27 (33%) and calcium supplements were prescribed to 53 (65.8%). It was observed that a total of 45 (69.2%) patients were prescribed with hydroxychloroquine (HCQ) and 13 (20%) patients were prescribed with sulfasalazine followed by the least prescribed drug leflunomide which constitutes 7 (10.7%) patients. The monotherapy [only (HCQ)] was prescribed to 17 (26%) patients and NSAIDS was prescribed to 82 (100%) patients. This indicates that all the patients were initially prescribed with NSAIDS at their first visit. Among 82 patients Monotherapy i.e.1 DMARD + NSAID were given to 21 (43.7%) patients and Dual therapy i.e. 2 DMARDS + 1 NSAIDS were given 14(29%) patients. 18 patients at first visit and 38 patients after consequent visit were in high adherence category; and 35 patients at first visit and 12 patients after consequent visit were in low adherence category. Highest ADRS were reported due to HCQS i.e. 25.6% and the least were reported due to Deflazacort i.e. 3.6%; and the system more affected was found to be CNS.

CONCLUSION

Rheumatoid arthritis is a long-standing disease and continues to deteriorate despite intensified treatment with disease modifying anti-rheumatoid drugs (DMARDS), hence patient counselling regarding diet, exercise, lifestyle modification, and medication adherence reduces the extent of disease severity. Clinical Pharmacist plays an important role in the management of rheumatoid arthritis by providing the pharmaceutical care.

Our study concludes the positive influence on various domain of quality of life by providing the patient counselling and educating the patients through the patient information leaflet. Clinical Pharmacist based patient education and counselling may have greater impact on the quality of life in rheumatoid arthritis patients.

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