



Drug Utilization Pattern and Cost Analysis in Rheumatoid Arthritis Patients – A Cross-Sectional Study in Tertiary Care Hospital, Mumbai

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Authors' contributions

This work was carried out in collaboration between all authors. Authors SRG, YCS and UJK designed the study, wrote the protocol, wrote the first draft of the manuscript and managed the analyses of the study. Authors SM and MYN managed the literature searches and helped in writing the first draft of the manuscript. All authors read and approved the final manuscript.

Research Article

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ABSTRACT

Aims: To study the current prescription pattern and to analyze the cost of the treatment Prescribed to RA patients referred to rheumatology OPD in KEM hospital.

Study Design: Cross-sectional study.

Place and Duration of Study: Department of Medicine and Department of Pharmacology, Seth GSMC & KEM Hospital, between July 2011 and December 2011.

Methodology: The study protocol was approved by the institutional ethics committee. Patients attending Rheumatology OPD for existing RA disease were recruited as per inclusion criteria. Written informed consent was sought. It was a cross-sectional study. Total 100 consecutive rheumatoid arthritis patients (fulfilling the American College of Rheumatology Criteria 1987) were recruited from 1st July to 1st September 2011.

Results: Majority of patients (67%) in the study population were on combination of two DMARDs. Most frequently prescribed two DMARDs combination was methotrexate and hydroxychloroquine (64%). Average total cost per prescription was found to be 763.39 ₹ (US\$ 14), while average hospital and out of pocket expense were 281.12 ₹ (US\$ 5) and

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482.88 ₹ (US\$ 9) respectively.

Conclusion: The drug use pattern in RA was found to be DMARDs based and majority of the cost was borne by the patient. The total cost increased was due to administration of drugs to treat the adverse drug reaction. Prospective studies in a larger number of patients are needed to assess the utility of prescription audit and cost analysis of drugs used in RA.

Keywords: Rheumatoid arthritis; observational study; prescribing patterns.

1. INTRODUCTION

Health economics is concerned with efficient allocation of resources in healthcare sector as majority of the expenses are carried out by the public budget. Due to general economic factors, there is disparity in the amount of resources used for healthcare across countries. Thus, economic analyses are always country specific, it depends on organization of health care, treatment patterns, and the relative and absolute cost of individual resources. Hence, it is impossible to conclude from the results of one study in a given country on the possible situation in another country [1].

The per capita total expenditure on health in India is US\$ 23, of which the per capita Government expenditure on health is US \$ 4. Total health expenditure is around 5% of GDP, with breakdown of public expenditure (0.9%); private expenditure (4.0%). The private expenditure can be further classified as out-of-pocket (OOP) expenditure (3.6%) and employees/community financing (0.4%). It is thus evident that public health investment has been comparatively low. The proportion of insurance in health-care financing in India is very low. Only around 10% of the population is covered through health financing schemes [2]. Moreover the role of Pharmacoeconomics in India is in infancy at present [3]. However it is necessary to do economic analysis of diseases as there is health gap situation in India between technological developments and affordable resources and this scenario is not likely to improve because of rising healthcare costs and India's growing population. In India common fatal diseases like Cancer, cardio-vascular diseases get more financial attention, a relatively non-fatal disease like Rheumatoid arthritis (RA) will get only poor attention.

Rheumatoid arthritis is chronic inflammatory disease with high prevalence. Approximately 1% of the adult population is affected by RA worldwide [4]. About 0.75% of adult Indian population is affected by the disease [5]. It negatively affects patient's quality of life, function, and life expectancy. Besides the consequences on the health status of individuals, RA has a substantial economic impact on patients, their family and society [6]. Drug treatment of RA has witnessed a major shift in the recent past. Disease modifying anti rheumatoid drugs (DMARDs) have now become mainstay of treatment [7]. They are more expensive and beyond the reach of majority of patients [8]. These developments have actually posed new challenges to those practicing rheumatology in a resource poor country like ours.

So, economic analysis on drugs prescribed in RA patients will be very helpful for the policy makers to maximize the effectiveness with minimal economic loss. But, studies on economic analysis of RA drugs are limited [9, 10, 11].

Moreover, these economic evaluations were conducted in western countries and the results could not be extrapolated to developing countries like India. Keeping these facts in

consideration the present study was planned to define the pattern of drug use for the RA, their availability in the hospital pharmacy and to analyze the cost of each prescription in the Rheumatology Out Patient Department (OPD) at Tertiary Care Hospital in Mumbai, India.

2. METHODOLOGY

2.1 Study Design

This was a cross-sectional study conducted between July 2011 and September 2011, in Rheumatology OPD of KEM Hospital and the Department of Pharmacology and Therapeutics of Seth G.S. Medical College, Mumbai.

2.2 Ethics Committee Approval

The Institutional Ethics Committee permission was taken prior to initiation of the study. Written Informed Consent was taken from all the participating patients. Confidentiality was maintained by coding each patient's case record forms with a unique identification number.

2.3 Hospital Background

It is a tertiary care hospital which receives referrals from other private clinics, hospitals and general physicians. Most of the patients attending this center belong to lower socioeconomic group. Rheumatoid arthritis patients attending the OPD are examined either by professors, lecturers, registrars and house surgeons which are part of the unit and any one of these can give hand-written prescriptions on OPD case paper to the patient. There is no facility to maintain patient's health records electronically. Patients receive the drugs prescribed to them either from hospital pharmacy, free of cost, if available or else they need to purchase it from a private pharmacy shops.

2.4 Sample Size

The general load of RA patients in our OPD is on average 5 - 7 new patients per OPD. Every month there is on an average 20 new patients, so at least 240 patients per year. Out of which we included only 100 patients. Since the study involves drug utilization and cost analysis only, we expected that the sample size of 100 will give adequate information in the rheumatoid arthritis patients and will form the baseline for future studies in India.

2.5 Patient Enrollment

Patients were enrolled via convenience sampling. Patients were recruited as per inclusion criteria.

Inclusion criteria:

- Male or female patients with age more than or equal to 18 years, who are attending Rheumatology OPD in KEM Hospital for existing RA disease (fulfilling the ACR criteria 1987).
- Disease duration more than 1 year and patients receiving stable therapy for at least 3 months.
- Willing to give informed consent.

Exclusion Criteria:

- Patients with acute or chronic medical conditions requiring hospitalization.

Physicians were asked neither to change their routine-practice behavior nor to selectively invite patients for participation.

2.6 Patient Data Collection Form

Demographic profiles of patients along with history of associated medical or surgical illness, documented in OPD case paper were recorded on the Case record Form. The detailed information on the prescription records given at the time of enrolment was recorded from OPD case papers. From prescription record, number of drugs prescribed for the period of 1 month, use of generic/brand names, drug dose, dosage form, and frequency was recorded. Cost analysis was done per prescription. For cost analysis we only considered total drug treatment cost. All drug unit costs were calculated in Indian rupee from the Current Index of Medical Specialties (CIMS). For each drug the cost was calculated as either cost per µg, mg, g, or ml, as appropriate. We further divided the total drug cost into two parts, first, the total cost of drugs which were freely available in hospital pharmacy and second, the total cost of drugs which are purchased from private pharmacy shops. The data abstraction was done by an independent person, who was not involved in prescription writing.

2.7 Statistical Analysis

Statistical analysis was done by using descriptive statistics. Data were collected in a predesigned Microsoft® Excel 2007. Continuous variables were presented as mean values ± standard deviation (SD), and categorical variables were presented as percentages.

3. RESULTS

3.1 Demographic Data

Out of 112 patients approached for the study, total 100 patients agreed to give informed consent for study participation. Among the 100 patients, 87 were females and 13 were males. Their average age was 41.43 ± 13.57 years. The mean age of onset was found to be 40.57 ± 13.69 years. Total 19 patients had history of associated co-morbid conditions. The detail information on demographic data and baseline disease activities are given in Table 1.

3.2 Prescription Analysis

In our study, the average number of drugs per prescription was found to be 6.17. The present study found out that only 35% drugs were prescribed by their generic name and the remaining 65% were in brand name. Drugs which are dispensed from the hospital pharmacy were only 49% (Table 2).

Table 1. Demographic characteristics and disease activity

Demographic data	Results
Age in years (mean \pm SD)	41.43 \pm 13.57
Gender	87 % Female
Age of onset (years)(mean \pm SD)	40.57 \pm 13.69
VAS (mean \pm SD)	4.287 \pm 2.5
HAQ DI (mean \pm SD)	0.9546 \pm 0.62258
DAS 28 (mean \pm SD)	4.598 \pm 1.5194
ESR (mm/h) (mean \pm SD)	33.3 \pm 16.47
Literacy status [number (%)]	
a) Illiterate	21
b) Primary education	42
c) Secondary education	32
d) Graduate	3
e) Post graduate	2
Co-morbid conditions [number of RA patients]	
a) Hypertension	6
b) Diabetes mellitus (DM)	4
c) Hypercholesterolemia	5
d) Hypertension & DM	1
f) Hypothyroidism	1
g) Anemia	1
h) Idiopathic thrombocytopenic purpurae	1

(HAQ DI - Health Assessment Questionnaire Disability Index,

DAS 28 -Disease Activity Score in 28 Joints,

ESR - Erythrocyte Sedimentation Rate,

DMARD - Disease Modifying Anti Rheumatic Drugs.

VAS- Visual Analogue Scale)

Table 2. Analysis of prescriptions of 100 patients as per different indicators

Prescribing indicators	Results
Average number of drugs per prescription (Mean \pm SD)	6.17 \pm 1.01
Percentage of drugs prescribed by generic name	35%
Percentage of drugs prescribed by Brand name	65%
Percentage of drugs actually dispensed from the hospital pharmacy	49.55%
DMARDs prescribed	
i) Single DMARD	
• Hydroxychloroquine	15
• Methotrexate	13
ii) Two DMARDs	
• Methotrexate + Hydroxychloroquine	64
• Sulfasalazine + Hydroxychloroquine	3
• Methotrexate + Sulfasalazine	1
iii) Three DMARDs	
• Methotrexate + Hydroxychloroquine+ Sulfasalazine	3
• Methotrexate + Hydroxychloroquine +Leflunomide	2

All patients at the study centre were prescribed one or more DMARDs. Majority of patients in the study population (67 %) were prescribed two DMARDs. Twenty eight percent of patients were given single DMARDs and only 5 % were given 3 DMARDs. Fifteen percent of patients were on Methotrexate alone and 13% were on Hydroxychloroquine alone. But no patient was prescribed Leflunomide and Sulfasalazine as a single agent. The most frequently prescribed DMARDs combination was Methotrexate and Hydroxychloroquine (64%). No patient was prescribed biological agents (Table 2).

In addition to DMARDs, 87 patients were prescribed non-steroidal anti-inflammatory drugs (NSAIDs) as and when required. Most commonly prescribed NSAIDs was Indomethacin (n = 77). A topical anti inflammatory gel was also prescribed in 26 patients, most common being Methyl salicylic acid. Most commonly prescribed Glucocorticoid was Prednisolone (n = 22). Along with anti-inflammatory agents, the most commonly prescribed anti-secretory agent was Ranitidine (n = 63). Calcium supplementation (n = 69), and Bisphosphonates (n = 7) were also prescribed in suspected cases of osteoporosis. Total 19 adverse drug reactions (ADRs) were reported by patients. Burning pain in chest and increased acidity were the most common ADRs. Other reported ADRs were facial puffiness, weight gain, water retention, nausea, vomiting, anorexia, constipation, menstrual irregularities, abdominal pain and angioedema. Among the drugs listed in the WHO's list of essential drugs for rheumatoid arthritis and scheduled in hospital formulary, Methotrexate, Indomethacin, Ranitidine were available in hospital pharmacy but, Omeprazole and Calcium lactate were not available. Though following essential drugs e.g. Hydroxychloroquine, Sulfasalazine, Prednisolone were frequently prescribed by rheumatologist, they were not scheduled in hospital formulary.

3.3 Cost Analysis

In our study, average total cost per prescription was 763.39 ₹ (US\$ 14). The average total cost of drugs which were freely available in hospital pharmacy was 280.51 ₹ (US\$ 5) and the average total cost of drugs which were to be purchased from private pharmacy shop was 482.88 ₹ (US\$ 9). Average cost of primary drugs to treat RA (DMARDs, Glucocorticoids, and NSAIDs) was 413 ₹ (US\$ 7.5) and average cost of Antisecretory agents, Calcium supplements and Bisphosphonates was 350 ₹ (US\$ 6.5).

4. DISCUSSION

The finding of the prescription pattern study conducted in a tertiary care hospital, Mumbai, gave us a snapshot of the demographic data, availability and cost of drugs prescribed in RA patients. Majority of the patients were females and the age of onset was middle age. Rheumatoid arthritis is one of the many chronic inflammatory diseases that predominate in females. The prevalence is about 2.5 times higher in females than males [12]. Our study showed a considerable female predominance of RA i.e. 87%. Recent study conducted by Mittal et al., in India has reported that more than 80% of the RA patients were females, in agreement with our study [13]. Another cost analysis study conducted in India has shown that female patients constituted 83.46 % of the sample population [7]. High prevalence of RA in females observed compared to developed countries is probably due to cultural and ethnic diversity, especially concerning occupation and living conditions. The finding of female predominance had mainly housewives and only few (8.69%) were working. This may not affect the source of family funding but may definitely impose socio economic burden on the family. Majority of the patients were literate. This was an encouraging finding, as it can make the patient understand the intricacies of therapy which includes rigorous monitoring and

follow – ups. Total 19 patients were associated with co-morbid conditions receiving treatment for the same, which in turn increased the cost of prescription. This finding is commonly seen in cases of RA [14].

In our study, the average number of drugs per prescription was found to be 6, which is more than the WHO recommendations. It has been recommended that the limit of number of drugs prescribed per prescription should be two and that justification for prescribing more than two drugs would be required because of the increased risk of drug interactions [15]. The increase in the number of drugs per se also increases the cost of prescription and patients may not purchase or take the prescribed drugs. This non-adherence to the therapy can deteriorate the said condition, prolonging the treatment duration. The present study observed that only 35 % drugs were prescribed by their generic name and the remaining 65% were in brand name. The generics actually dispensed from the hospital pharmacy were more (49%), because patients who were prescribed drugs with the brand names were dispensed the generic drugs by the pharmacist. This version of drug substitution by community as well as hospital pharmacist is very commonly found in practice [16]. Thus patient's treatment depends on the knowledge and skills of the pharmacist which is unreliable and henceforth in the gamut of rational use of medicines pharmacist also is a stake holder who needs timely education.

The combination of methotrexate and hydroxychloroquine was preferred over other single agents and other combinations. A study conducted in North India by Sukhpreet et al., noted the similar findings [17]. However, another pharmaco-economic study done by Shini et al., has shown that majority of patients (69.66 %) were on single DMARD [7]. In our study, majority of the patients were on DMARDs combination probably because of study population had high disease activity reflected by high average DAS28 score.

Methotrexate was the only DMARD freely available in the hospital pharmacy and thus was frequently prescribed in our hospital, however it has modest efficacy, unfavourable toxicity profiles and require frequent monitoring [18]. In our study we observed that for managing ADRs caused by Methotrexate, drugs like ranitidine, omeprazole etc were given. Glucocorticoids and non steroidal anti inflammatory drugs are also widely used in RA. The treatment with Glucocorticoids can lead to osteoporosis thus calcium supplements were also prescribed, whereas NSAIDs are well known to produce gastric upset, thus a gastroprotective medicine was usually prescribed along with them, in turn increased the total cost of the treatment.

Prashker and Meenan considered the total cost of drug to be composed of 3 components i.e. the actual cost of drug, the cost of monitoring patients for side effects of the drugs and the cost of treating the side-effects when they occur [11]. They observed that the cost of monitoring and treating side effects contributed to over 60% of the total cost of all medications. The results of the present study demonstrated that cost of drugs like Antisecretory agents, Calcium supplements and Bisphosphonates which were given for the treatment or prevention of ADRs increased the total cost of RA therapy. Methotrexate was the cheapest drug in terms of acquisition; however, it is the most expensive drug in terms of treating the side effects. Hence, while prescribing medicines not only cost but also efficacy of the drug should be considered. This falls in the agreement of guidelines for rational use of medicines.

Among the drugs listed in the WHO's list of essential drugs for rheumatoid arthritis [19], Hydroxychloroquine, Sulfasalazine, Prednisolone, Calcium lactate were not available in

hospital pharmacy even though these drugs were prescribed frequently. Moreover, the brands prescribed from outside increased the cost of prescription dramatically. The average cost of drugs freely available in hospital pharmacy per prescription was much lesser as compared to average cost of drugs need to be purchased from private pharmacy shops. Hence, the average cost borne by patients was 2 times more as compared to cost borne by hospital pharmacy. These costs reflected the burden of disease in Rheumatoid Arthritis patients and in lack of insurance cover the patients has to bear these costs themselves.

4.1 Limitations

This study has several limitations. First, cross-sectional design, second, a limited number of patients were included in the study. The study focuses exclusively on direct cost for RA drugs treatment. Other direct costs of treatment, indirect costs and intangible costs remain disregarded.

Another limitation was that patients were enrolled via convenience sampling method. The patients were recruited as they appeared in the OPD to avoid any disruption of the standard clinical practice programme planned by the department. In addition, the researchers were involved in both, in recruiting as well as in the assessment. Consequently, even though the CRFs were coded and randomly distributed to independent evaluators, the evaluators were not independent of the study and the chances of bias creeping in cannot be overlooked.

5. CONCLUSION

The drug use pattern in RA was found to be DMARDs based. It was found that majority of the cost is borne by the patient as there are few drugs available at the hospital site. Majority of the drugs prescribed were by their brand names so generics should be made available which can reduce the cost of treatment.

Considering the polypharmacy, use of brand names and inappropriate selection of drugs which increased total cost of treatment, following measures are recommended -

- Revise hospital schedule formulary.
- Drugs on schedule should be made available throughout the year.
- Prescription auditing should be done on regular basis.
- Prospective, randomized, cohort studies should be planned in a larger sample size, so that policy-makers will get the better insight into present scenario and can provide ways to optimize the treatment of patients with RA.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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