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A Cost Variation Analysis of Drugs Prescribed for The Treatment of Rheumatoid Arthritis

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ABSTRACT

Background: The rheumatologists have several drugs to choose from, either alone or in combination; each with different costs, monitoring protocols, and potential risks and benefits. Pharmacoeconomic analysis results help rheumatologists choose drugs for their patients.

Objective: Objective of this prospective observational study was to perform a cost-variation analysis of drugs prescribed for the treatment of rheumatoid arthritis (RA) in a Western-Indian tertiary care teaching hospital.

Materials and Methods: This prospective observational study was conducted in the rheumatology department of the study site. Study population included patients of both gender male and female, diagnosed with rheumatoid arthritis and on treatment. Prices of the drugs prescribed to the patients were obtained from different offline and online sources. The lowest and highest cost of brands in rupees (INR) for each drug, the cost ratio, percentage cost variation, and monthly cost for all the prescribed drugs were calculated.

Results: In our study, out of total 142 patients, 93 were females and 49 were males and the mean age was 49.11±15.89 years. Most patients were prescribed with Disease-modifying antirheumatic drugs (DMARDs). Frequently used non-steroidal anti-inflammatory drug (NSAID) was Diclofenac (n=48). A maximum cost ratio (15.6) was observed with prednisolone 5 mg TDS. The costliest and cheapest brand of prednisolone 5 mg TDS accounted for the maximum cost variability (1460%). Mean monthly cost varied among different drug classes.

Conclusion: Average cost of illness of patient with RA was estimated to be in the range of 2406/month to 2858/month in the year 2021.

INTRODUCTION

Rheumatoid arthritis (RA) an autoimmune condition is characterized by erosive and symmetric synovitis with extra-articular involvement in some cases. [1] Uncontrolled inflammatory reactions of the disease may lead to joint damage and functional disability. Depending on the level of inflammation, the symptoms of RA vary and include joint stiffness and pain, fever, anorexia, and fatigue. Joints inflammatory reactions commonly occur in a symmetric manner. Sometimes, RA may manifest as a systemic autoimmune condition affecting the nervous, respiratory, musculoskeletal, renal, cardiovascular, and hematological systems. [2]

The worldwide prevalence of RA is estimated to be around 1%, affecting women two or three times more than men. It is reported that in India, the prevalence of rheumatoid arthritis is 0.75%. This indicates that in India there are more than one crore patients affected with this devastating disease. [3]

Treatment for RA is aimed at relieving pain, reducing joint swelling, slowing or preventing joint damage and improving physical function and wellbeing. [4] Conven-

tional medicines used for RA include non-steroidal anti-inflammatory drugs (NSAIDs), Disease-modifying antirheumatic drugs (DMARDs), biological response modifiers and corticosteroids.[5] Non-pharmacological treatments include physical therapy, modified exercise programs and devices that ease physical stress on the joints (such as splints). People with RA are also encouraged to make lifestyle changes such as balancing activity with rest, eating a healthy diet and reducing emotional stress. [6]

The economic burden of RA relates to the cost of the treatment, which is significant for the individual and also for the health care and social care system. [7,8,9] The cost can be calculated by measurement of three costs, i.e., direct cost, indirect cost and intangible cost. Direct medical costs include expenditures for physician and health care worker visits, medications, diagnostic tests and procedures, and hospitalizations. Indirect costs result from loss of productivity and include sick leave, absence from duties, and early retirement from work. Intangible costs are defined as pain and suffering of a patient because of disease and include a reduction in physical function, increased psychological distress and reduced social function, which are usually excluded from pharmacoeconomic studies. [10]

A kind of pharmacoeconomic analysis called cost of therapy provides a true picture of the cost impact of a disease condition on both the patient and society.

In view of the above, this prospective observational study was performed which aimed to analyze a cost variation of drugs prescribed for the treatment of rheumatoid arthritis in a Western-Indian tertiary care teaching hospital.

MATERIALS AND METHODS

This hospital-based prospective observational study was conducted in the rheumatology department of a tertiary care teaching hospital in Western India. The study population included patients of both gender male and female, diagnosed with rheumatoid arthritis and on treatment. The study was conducted over one year, from June 2021 to May 2022. A total of 13 patients were excluded from the study due to loss to follow-up. The study population was composed of 142 patients.

Ethical clearance of the study protocol was obtained from the Institutional Review Board. The study site was visited, and appropriate study participants were approached. Study participants were briefed about the study. Those willing to participate in the study were included only. The written informed consent of such patients was taken. The case record sheets of those who gave written informed consent were reviewed. All the relevant data like sociodemographic details of patients, co-morbid conditions, duration of disease, drugs used (total number of drugs prescribed, a dose of the drug used, dosage form, route of administration, use of fixed-dose combinations, any adverse drug reactions) were collected from the case record sheets of the patients and recorded in pre-designed case record form. Confidentiality of collected information was maintained.

Prices of the drugs prescribed to the patients were obtained from different sources, both offline and online. The offline sources accessed were the January – April 2022 edition of the "Drug Today", April – July 2021 edition of the "Current Index of Medical Specialties" (CIMS), and "Monthly Index of Medical Specialties" (MIMS) (December 2019 edition), while the online sources accessed were: "India Drug Index" and "Drug Brands" Drugs Update. The cost in rupees (INR) of each drug manufactured by different pharmaceutical companies in the same dose and dosage forms was noted. The costliest and cheapest brand for one particular drug in the same dose and dosage form was identified. The cost was calculated per 1 unit for all the drugs (1 unit = 10 tablets/10 capsules/1 injection). The cost ratio, i.e., the ratio of the price of the costliest to the cheapest brand of the same particular drug, was calculated. This determined the difference in the cost between the costliest brand to the cheapest one for each drug. The cost ratio reveals how many times the price of the costliest brand of the drug is higher than the cheapest brand for each drug. Percentage cost variation was calculated using the following formula.

$$\text{Cost variation } (\%) = \frac{(\text{Maximum cost} - \text{Minimum cost})}{\text{Minimum cost}} \text{x} 100$$

As rheumatoid arthritis is a chronic disorder and the medications have been prescribed for longer periods, the monthly cost was also calculated as per the treatment guidelines. The drugs manufactured and marketed by only one pharmaceutical company were not taken into consideration for cost variation analysis.

The collected data was entered into a GraphPad and appropriate statistical analysis was performed.

RESULTS

The demographic characteristics of the patients are shown in table 1. As per table 1, a total of 142 patients were consecutively enrolled in this study. 93 were females and 49 were males. The percentage of females was 65.49 and those of males was 34.51. This study shows a predominance of RA for females. The Male: Female ratio was found to be 1:1.89. Most of the patients (37.72%) belong to the age group of 41-50. The youngest patient was 30 years old, and the oldest was 72 years. The mean age was found to be 49.11±15.89 years. Occupational status showed that 49 (34.51%) of the patient population consists of housewives. This was preceded by professionals (n=53), patients who retired from their services (n=10), patients who worked for daily wages (n=3), and patients with business (n=27). The duration of the disease extends from over one year to 9 years.

Table 1: Demographic characteristics of the patients

Characteristics	Patients (n=142) (%)
Age groups (years)	
30-40	30 (21.13)
41-50	53 (37.32)
51-60	40 (28.17)
61-70	17 (11.97)
≥ 71	2 (1.41)
Gender	
Male	49 (34.51)
Female	93 (65.49)
Occupation	
Housewife	49 (34.51)
Business	27 (19.01)
Professionals	53 (37.32)
Retired	10 (7.04)
Daily Wages	3 (2.11)
Duration of disease (Years)	
One	3 (2.11)
Two	5 (3.52)
Three	20 (14.08)
Four	28 (19.72)
Five	32 (22.54)
Six	28 (19.72)
Seven	18 (12.68)
Eight	6 (4.23)
Nine	2 (1.41)

Table 2: Distribution of comorbidities among the study population

Comorbidities	Patients (%)
Diabetes	22 (15.49 %)
Hypertension	28 (19.72 %)
Thyroid disorder	9 (6.34 %)
Anemia	22 (15.49 %)
Dyslipidemia	8 (5.63 %)
Osteoarthritis	8 (5.63 %)
Chronic kidney disease	7 (4.93 %)

Out of a total of 142 patients, comorbidities were found in 84 patients. Hypertension was the most common comorbidity (28%) observed in these patients followed by diabetes and anemia (22%) (table 2).

A total of 415 drugs were recorded from the prescriptions of 142 patients. The maximum number of patients were prescribed DMARDs, which is the mainstay for the treatment of RA. Methotrexate was the most prescribed DMARD (n=112) followed by hydroxychloroquine (n=78). The frequently used NSAIDs were Diclofenac (n=48), and Indomethacin (n=35). Prednisolone was the most prescribed corticosteroid. Biological agents were prescribed to fewer patients (table 3).

A maximum cost ratio (15.6) was observed with prednisolone 5 mg TDS, while a minimum cost ratio (1.09) was found with adalimumab 40 mg injection. The costliest and cheapest brand of prednisolone 5 mg TDS accounted for the maximum cost variability (1460%), while that of adalimumab 40 mg injection accounted for the minimum cost variability (9.9%) (table 4 & 5).

Table 3: Drugs prescribed for rheumatoid arthritis

Drugs	Patients (%)
DMARDs (n=204)	
Methotrexate	112 (54.9%)
Hydroxychloroquine sulfate	78 (38.2%)
Sulfasalazine	7 (3.4%)
Leflunomide	5 (2.5%)
Azathioprine	2 (1%)
Corticosteroids (n=72)	
Prednisolone	29 (40.3%)
Methylprednisolone	12 (16.7%)
Deflazacort	28 (38.9%)
Hydrocortisone	3 (4.1%)
NSAIDs (n=120)	
Diclofenac	48 (40%)
Aceclofenac	6 (5%)
Etoricoxib	15 (12.5%)
Indomethacin	35 (29.2%)
Ibuprofen	6 (5%)
Naproxen	10 (8.3)
Biological agents (n=19)	
Adalimumab	5 (26.3%)
Etanercept	10 (52.7%)
Rituximab	4 (21%)

DMARDs – Disease modifying antirheumatic drugs; NSAIDs - Non-steroidal anti-inflammatory drugs

DISCUSSION

According to this study, the average cost of illness of a patient with RA was estimated to be in the range of 2406/month to 2858/month in the year 2021. Monitoring of clinical variables can be considered necessary to determine the effectiveness of the treatment and to rule outside effects. In this study most of the patients were professionals, so the cost due to loss of productivity was less and covered 13.45% of the cost of illness. The same result observed in the cost analysis of RA in China conducted by Chuanhui et al showed direct cost covers 10% of the total cost of illness. [11] A study conducted by Shini et al showed the cost of RA per month to be 107.29 which is less than ours. [12] This may be due to cost variation among institutions. Professionals with long-standing RA or depending on adaptations that assist their professional duties could increase the cost. In the study conducted by Peter Tug well et al in USA and Canada, they found that DMARDs were the most prescribed category of drugs. [13] The similar finding was also observed in both our study and the study conducted by Shini et al., in Kerala.

In India, very few pharmacoeconomic studies have been conducted in the area of RA. A study conducted in India, by Agarwal et al estimated the average total cost of drug treatment was 999 ± 76 INR per month and the average monthly cost of rheumatoid arthritis was estimated to be 623 ± 31 INR per month. [14]

Table 4: Cost variation among drugs for rheumatoid arthritis

Drug	Dosage form	Dose & frequency	Maximum Cost(INR)/unit	Minimum Cost(INR)/unit	Cost ratio	Cost-variability (%)	Monthly cost of medicines (INR)
Methotrexate	Tablet	2.5 mg once wkly	60.55	14	4.32	332.5	16.8-72.66
	Tablet	5 mg once wkly	71	34	2.09	108.9	27.2-56.8
	Tablet	7.5 mg once wkly	100	47.2	2.12	111.9	18.9-40
Hydroxychloroquine sulfate	Tablet	200 mg BD	68	40	1.7	70.0	240-408
Sulfasalazine	Tablet	500 mg BD	65.09	39.06	1.67	66.6	234.36-390.54
Leflunomide	Tablet	10 mg BD	105.28	80	1.32	31.6	240-315.84
	Tablet	20 mg BD	205.39	160	1.28	28.4	480-616.2
Azathioprine	Tablet	50 mg OD	115.8	58.5	1.98	98.0	175.5-347.4
Prednisolone	Tablet	5 mg TDS	156	10	15.6	1460	60-936
	Tablet	10 mg TDS	72.2	8.62	8.38	737.6	25.86-216.6
	Tablet	20 mg TDS	102	17.2	5.93	493	25.8-153
Methylprednisolone	Tablet	8 mg OD	58.8	21.4	2.75	174.80	64.2-176.4
	Injection	40mg/1ml	123.81	46.98	2.64	163.50	93.96–247.62
Deflazacort	Tablet	6 mg BD	171	77	2.22	122	462-1026
Hydrocortisone	Tablet	10 mg	NR	NR	NR	NR	NR
Hydrocortisone	Injection	100mg/2ml	NR	NR	NR	NR	NR
Diclofenac	Tablet	50 mg BD	90	10.2	8.82	782.40	61.2-540
Aceclofenac	Tablet	100 mg BD	90	7.5	12	1100	45-540
Etoricoxib	Tablet	60 mg OD	92	54	1.70	70.40	162-276
	Tablet	90 mg OD	134.5	69.5	1.94	93.50	208.5-403.5
Indomethacin	Capsule	25 mg BD	40.92	11	3.72	272	66-245.52
Ibuprofen	Tablet	400 mg BD	16	10.92	1.47	46.50	65.52-96
Naproxen	Tablet	500 mg BD	138	28	4.93	392.90	168-828
Adalimumab	Injection	40 mg/0.4 ml every other wk	27,475	25,000	1.09	9.90	50,000-54,950
Etanercept	Injection	50 mg once wkly	NR	NR	NR	NR	NR
Rituximab	Injection	500 mg/50 ml	NR	NR	NR	NR	NR

wkly – weekly; wk-week

Table 5: Mean monthly cost of various drugs for rheumatoid arthritis

Drug class	Mean minimum monthly cost (INR)	Mean maximum monthly cost (INR)
DMARDs	179.09	280.93
Corticosteroids	121.97	459.27
NSAIDs	110.89	418.43
Biological agents	50,000	54,950

DMARDs – Disease modifying antirheumatic drugs; NSAIDs - Non-steroidal anti-inflammatory drugs

The cost was less compared to our study as it was conducted in a government setting and also due to inflation. Van Haselen et al analyzed the economic burden of RA to be $1.64 billion, half of which was lost production. The total direct cost for 89 OP patients was found to be $10,060 including consultation fee (29% of total cost), drug (22% of the total cost), diagnostic cost, and others. [15] In our study the total cost of the disease was $21.85 per month. Indian GDP per capita income for the year 2020 was about Rs.182000 which means on average each person is earning only about Rs.15166 per month. So according to our study, a person with RA spends about 13.59 % of his income for the treatment of RA per year. The treatment cost differs in different countries. In the UK, the average annual medical cost was reported to range from £ 3575 to £ 3638 in a study by N J Cooper et al. [16] whereas in Australia it was about £ 893 as reported by Lapsey et al. [17] The out-pocket expenditure in Germany was found to be £ 417.20 per year which accounted for 15.3% of total direct cost.[17] The Gross Domestic Product in the UK was 41,220 US dollars in 2000. RA patients in the UK spend only 7.61% of their per capita income on treatment. While in Australia only about 1.79% of their per capita income is needed for the treatment of RA. Germany's per capita GDP income was 42,540 US $ and 0.85% of per capita income is spent on the treatment of RA. A study conducted in Japan by Tanaka E et al estimated the annual average outpatient cost was US $2705 per patient, which is about 225.41$ per month. [18] The result of a US-based study showed the mean total annual direct medical cost for RA patients was $9,519 in 2001. Medicine cost was $6,324(66% of the total), while hospitalization cost was only $1,573(17%). Approximately 25% of patients received biological therapy. The mean total annual direct cost for the patient who was not taking biological was $ 6,164. Per month cost was calculated as $513.66. [19] This is higher than our direct cost which is about $35.95 per month. The disparity in the annual cost of RA in India and other countries may be due to differences in their healthcare systems, financing, GDP, referral procedures, and study methodologies.

With an average cost of 2229.99 per month per patient, given a prevalence rate of about 0.75% in our country and with an estimated population of 1.21 billion. There

may be as many as 91,51,500 people who are suffering from rheumatoid arthritis. Rheumatoid arthritis may have an annual direct cost of around 17.66 billion. Due to the significant financial burden associated with its treatment and the rising prevalence rate of the condition, which may exacerbate the condition and affect productivity, the government needs to launch extensive, comprehensive, and sustainable public programs to improve policy on the condition. Patients with lesser incomes may not afford sufficient treatment, which may lead to greater workability impairment, resulting in higher costs of illness and lower income. As shown in our study, functional disability has consistently been found to be strongly correlated with higher indirect costs, indicating that maintaining patients' function is a successful strategy for restoring productivity. Furthermore, it is well recognized now that early diagnosis and aggressive treatment, especially by rheumatologists, can limit disease progression and restore patients' function. [20] However, despite many rheumatologists having embraced these tenets and altered their therapeutic approach, the diagnosis and treatment of patients with recent onset RA are often delayed because of limited access to rheumatological care services. Although aggressive therapy may enhance the short-term costs but would also enhance the possibility of staying in work for those who are of working age, and thus, create long-term productivity gains for the economy. Future public policy decisions must be supported by a thorough consideration of RA costs and the potential benefit of services. Early referral to a rheumatologist may control the condition and its progression. This can be effectively incorporated by government initiatives like medical checkup camps, educational campaigns, etc.

The main limitation of our study was its duration due to which we could not assess the cost-effectiveness analysis and toxicity analysis.

CONCLUSION

Our study concludes that RA imposes a tremendous burden on the patients. The direct cost such as cost of medicines consumes a major proportion of the cost of illness (COI). This study aims to serve as a useful resource for better understanding of the burden of RA patients in India and as a good reference for the formulation of future health-related policies. Certain insurance policies and reimbursement schemes can reduce the burden on the patient. For a thorough investigation of changes in the COI based on changes in the functional status of individuals with RA, additional population-based prospective studies are required. New therapeutic approaches, including early and aggressive interventions, new drugs such as biologics, and drug combinations, are now proving to be effective and safe in slowing disease progression, as a result, there is potential for cost savings by restoring productivity in the long term.

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Ethical approval: The study was approved by the Institutional Review Board

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