

COST OF ILLNESS OF RHEUMATOID ARTHRITIS IN SOUTH INDIA**Vidya Alex^{1*}, Sumitha Cheruvallikattil², Suja Abraham³, Bincy Varghese⁴**

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ABSTRACT

Objective: To perform cost of illness of rheumatoid arthritis in south Indian tertiary care hospital. **Methods:** A prospective, observational study was conducted for a period of 8 months in Rheumatology department of Amrita institute of medical sciences, Kochi. The cost was collected by patient face-to-face interview. **Results:** 200 patients enrolled in our study, 82.5% were females with a mean age group of 52.6 ± 10.136 . The average cost of illness of RA patients in 2013 was estimated as ₹.2229.99(\$34)/month. The direct cost for the current treatment of RA was found to be ₹1929.99 (\$29.43)/month which included the cost of medicine ₹737.49(38.21% of total cost), laboratory cost ₹295.56 (15.31% of total cost), consultation fee ₹122.3027 (6.34% of total cost) and personnel cost ₹316.31 (16.39% of total cost) and transportation cost ₹380.314(19.71% of total cost). Indirect cost

includes lost wages due to disease and is estimated as Rs.300. Methotrexate was the most commonly prescribed DMARD (5.56 % of drug cost). Sulphasalazine consumes about 25.67% of drug cost per month followed by leflunamide (23.12%). Steroids consume about 16.39% of the total cost of drug per month. Cost of NSAIDs comes around 18.78% of the total drug cost per month. **Conclusion:** The study concluded that the burden of RA to the patients is enormous. Medication costs along with transportation cost are the highest contributors to the total expenses incurred by RA patients. Hence it becomes vital to diagnose and control the disease at an early stage to control the economic burden on the patient.

KEY WORDS: Rheumatoid arthritis, DMARDs, Cost of illness.

INTRODUCTION

Rheumatoid arthritis (RA) is an autoimmune disorder characterized by symmetric and erosive synovitis with extra-articular involvement in some cases.^[1] Uncontrolled inflammatory reactions of the disease may lead to joint damage, functional disability, decreased quality of life and increased mortality.^[2] Symptoms of RA vary depending on the degree of inflammation and include joint pain and stiffness, fatigue, anorexia, and low grade fever. Inflammatory reactions in the joints occur commonly in a symmetric manner. RA can also manifest as a systemic autoimmune disease that affects the musculoskeletal, nervous, respiratory, cardiovascular, renal and hematological systems.^[3]

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%.^[4] This indicates that In India there are more than one core patients affected with this devastating disease.

Treatment for RA is aimed at relieving pain, reducing joint swelling, slowing or preventing joint damage and improving physical function and wellbeing. Conventional medicines used for RA include Non steroidal anti-inflammatory drugs (NSAIDs), Disease-modifying anti-rheumatic drugs (DMARDs), biological response modifiers and corticosteroids. 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 healthy diet and reducing emotional stress.^[5]

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.^[5] 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 are due to lost productivity including absence from duties, sick leaves, early retirement etc. Intangible costs are defined as pain and suffering of a patient because of disease and include reduction in physical function, increased psychological distress and reduced social function, which are usually excluded from the pharmacoeconomic studies.^[4,5,6] Cost of therapy is a type of pharmacoeconomic analysis that gives a true picture of the cost implication of a disease condition to the patient and the society.^[7]

Pharmacoeconomics deals with cost and outcome of therapy. The outcome in RA has been described in different studies, mainly in terms of mortality, radiographic changes and functional disability scores.^[8] The most important factors affected by patients are pain or stiffness in joints and increasing economic loss depending up on ability and loss of or changes in employment during the course of RA. Few studies have addressed cumulative disability and outcomes which describes the direct functional loss on patient's lives.^[9, 10, 11]

The result of burden- of – disease studies can be used for prioritizing health policies and justifying the needs for spending on disease prevention, management, and social intervention. As very few such studies have been performed in South India, we carried out a cost of illness study to estimate direct and indirect cost of RA.

MATERIALS AND METHODS

The study was prospective and observational. It was carried out on outpatients at the Rheumatology department of Amrita Institute of Medical Sciences (AIMS), Kochi for a period of 8 months (February 2013 to September 2013). The Institutional Ethics Committee approval was obtained before the commencement of the study and it conforms to the provisions of the World Medical Association's Declaration of Helsinki. All patients were diagnosed according to the 2007 ACR/EULAR classification criteria for rheumatoid arthritis.^[12, 13] Those patients who were above the age 18 and were diagnosed to have RA and were on treatment at least for a period of 6 months in AIMS were selected. Patients with age < 18 years, special group population having psychiatric problems, or hearing impairment and non co-operative and freshly diagnosed patients were excluded from the study.

This study was mainly done to estimate the economic burden of RA. So the treatment or management cost of comorbidities was not included in this study. Only direct and indirect cost for the management of RA was taken in to consideration. The study was conducted on patient perspective. Sociodemographic characteristics such as age, gender, marital status, employment status, education status, and disease duration were collected by patient face-to-face interview. Information was collected from patients and physicians and from medical records. The cost of medicines was obtained from the bill of pharmacy from where they purchase medicines, so that cost to patients can be measured. In addition the cost of diagnostic tests was obtained from the laboratory of the hospital. The indirect cost included 2 parts in this study. First, for RA patients, the cost of work absenteeism and premature retirement were calculated. Second, for the family members of RA patients,

only costs of the work absenteeism were calculated. Other costs such as intangible, opportunity costs were not considered in the study. All these costs were added up for each patient and for all the patients to obtain the total. The average cost per patient was then calculated and recorded.

Different direct and indirect cost are shown in the table no.1

Table No 1: Different direct and indirect cost.

Direct Cost	
Direct medical cost	Direct non-medical cost
Cost of medicines	Transportation cost
Laboratory cost	Cost of food
Consultation fees	Personal cost
Indirect Cost	
Productivity loss of patients	
Productivity loss of family members	

Statistical analysis was performed using SAS 9.1.3. Descriptive statistics were used for demographics, clinical variables and cost. Results were expressed as frequencies, percentages, means and standard deviation.

RESULTS

Patient demographics

In total, 200 patients were consecutively enrolled in this study. 165 were females and 35 were males. The percentage of females was 82.5 and those of males were 17.5. This study shows a predominance of RA for females. The male-Female ratio was found to be 1:5. Majority of the patients belong to the age group of 51-60. The youngest patient was 23 years old and the oldest was of 79 years. The mean age group was found to be 52.6 ± 10.89 . None of our population was illiterate. Majority had an education till intermediate or post high school diploma 68 (34%) and 51 patients were graduates. The lowest level of education was till middle school. 11% of the population had education only till this level. 25% had an education at the level of high school. Only 4.5% of the population had a professional education. Occupational status shows that 132 (66%) of the patient population consists of house wives. This was followed by professionals (10%), patients who retired from their services (7.5%), patients who worked for daily wages (6.5%), patients with desk job (3%) and the unemployed population consists of 2% of the study population. Duration of the disease extends from over less than one year to more than 20 years. The time span of the

disease was less for 127 patients, about 0-5 years. Only 9 patients had duration greater than 20 years. 34 patients were suffering the disease for about 6-10 years. 19 patients had the disease for about 11-15 years and 11 of them had the disease for time period of 16-20 years.

Table 2: Demographics of study participants.

Demographic Variables	
Age, years	52.6±10.89
Sex, % Females	82.5
Married, %	90
Duration in years	
0-5	63.5
6-10	17
11-15	9.5
16-20	5.5
>20	4.5
Education Level %	
Middle school certificate	11
High school certificate	25
Intermediate or post high	34
Graduate	25.5
Professional degree	4.5
Occupation %	
Desk job	3
House wives	66
Daily wages	6.5
Professionals	10
Retired	7.5
Student	0.5
Unemployed	2

Current system of Treatment

Table3: Total number of patients taking drugs for the treatment of RA.

Drug	No. patients involved	% patients involved
Methotrexate	175	87.5
Sulfasalazine	100	50
Leflunamide	51	25.5
Hydroxychloroquine	151	75.5
Deflazacort	52	26
Methyl prednisolone	23	11
Etoricoxib	13	6.5
Diclofenac gel	5	2.5

During the current treatment, all the patients were prescribed with DMARDs which is the main stay for the treatment for RA. Methotrexate was the most commonly prescribed DMARD (87.5%). Other DMARDs such as hydroxychloroquine (75.5%), sulphasalazine

(50%) and leflunamide (25.5%) were also prescribed. NSAIDs and steroids were next treatment options. Frequently used NSAID was Etoricoxib (6.5%) and 2.5% of patients were prescribed with diclofenac gel. 37% of patients prescribed with steroids. Deflazacort was the commonly used corticosteroids. Other medicines such as folic acid, proton pump inhibitors, calcium supplements, ursodeoxycholic acid were also given to patients. 51.5% of patients were on PPI's. 44% of the study population was given calcium supplements. Folic acid was given in conjugation with methotrexate.

Frequently used combination drugs for RA

Table 4: Frequently used combination drugs for RA.

Combinations	No. of patients	% of patients involved
1 DMARDs	15	7.5
2DMARDs	51	25.5
3DMARDs	67	33.5
1 DMARDs+ steroid	7	3.5
2DMARDs+ steroid	42	21
1DMARDs+ NSAID	12	6
1DMARDs+ steroid+ NSAID	6	3

The most frequently used combination of drug was 3 DMARDs i.e., Methotrexate+Sulfasalazine+Leflunamide. 33.5% of the study group was prescribed with 3 DMARDs. 25.5% of the patients were prescribed with 2 DMARDs. A combination of 2 DMARDs and a steroid was the 3rd choice. 21% were prescribed with this combination.

Cost of illness

Table 5: Cost of illness of 200 RA patients.

Cost components	Total cost/month (rupees)	% of total direct cost
Drug	737.49	38.21
Laboratory test	295.56	15.31
Consultation fees	122.3027	6.34
Transport	380.314	19.71
Food	78.0157	4.04
Personal cost	316.31	16.39
Total direct cost	1929.99	86.54
Indirect cost	300.00	13.45
Total cost of disease	2229.99	100

Direct cost components include cost of medicines, cost of diagnostic test, cost of health professionals time, transportation cost and other personnel expenses. Total average direct cost per month for the treatment of RA was found to be Rs.1929.99. Major Part of total cost was

covered by medicines and followed by transportation cost. Indirect cost due to productivity losses of patients were estimated as Rs.300. The average cost of illness of RA patients in 2013 was estimated as Rs.2229.99/month.

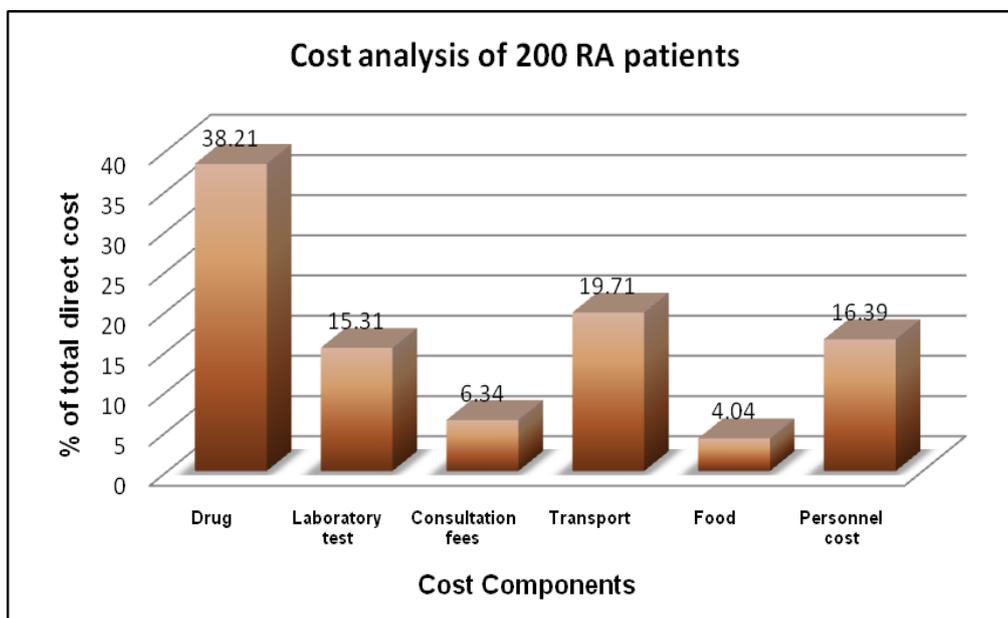


Fig. 1. Cost Analysis of RA Patients.

Table 6: Total cost/month medicines used in treatment of RA.

Medicine	No. patients involved	% patients involved	Unit price (₹)	Cost of drug/month (₹)	% drug cost per month
Methotrexate	175	87.5	25.5	102	5.24
Sulfasalazine	100	50	8.33	499.8	25.67
Leflunamide	51	25.5	15	450	23.12
Hydroxychloroquine	151	75.5	7	210	10.78
Deflazacort	52	26	9	270	13.87
Methyl prednisolone	23	11	1.64	49.20	2.52
Etoricoxib	13	6.5	5	300	15.41
Diclofenac gel	5	2.5	65.60	65.60	3.37

Among the DMARDs unit cost was high for methotrexate but the monthly cost was high for sulphasalazine. This is because methotrexate is prescribed on a once weekly basis while sulphasalazine is taken twice a day. Sulphasalazine consumes about 25.67% of drug cost per month followed by leflunamide (23.12%). Steroids consume about 16.39% of the total cost of drug per month. Cost of NSAIDs comes around 18.78% of the total drug cost per month.

DISCUSSION

According to this study, the average cost of illness of patient with RA was estimated to be ₹ 2229.99/month in 2013. In detail, direct cost accounted for 86.54% of the total cost, slightly

higher than indirect cost. Out of which 38.21% was consumed by cost of medicine, Laboratory tests was covered by about 15.31%, consultation fee 6.34%, transportation and food 23.75%. Early diagnosis and treatment can reduce disease progression and hence the cost. The transportation cost varied among individuals due to distance travelled and mode of transportation. Monitoring of clinical variables was necessary to determine the effectiveness of the treatment and to rule out side effects. ESR, CBC, LFT, RFT and CRP were done at timely intervals. They varied with disease intensity and duration. In this study most of the patients are unemployed housewives, so indirect cost due to loss of productivity is less and covers 13.45% of cost of illness. The same result observed in societal cost analysis of RA in China conducted by Chuanhui et al shows indirect cost covers 10% of total cost of illness.^[14] In a study revealed by Shini et al showed lab monitoring cost of RA per month to be ₹107.29 which is than ours.^[15] This may be due to cost variation among institutions. Housewives with long standing RA or depending on adaptations which assist their daily house hold duties could increase personal cost. Study conducted by Peter Tug well et al in USA and Canada, they found that DMARDs were most commonly prescribed category of drugs.^[16] The same was observed in study conducted by Shini et al., in Kerala and also in our study.^[15]

There are very less pharmacoeconomic studies conducted in India in the area of RA. In a study conducted in India, by Sukhpreet et al estimated the average total cost of drug treatment was ₹999±76 per month. The average monthly direct cost of rheumatoid arthritis was estimated to be ₹623±31. The average indirect cost was found to be ₹368±62 per month.^[17] 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 that the economic burden of RA to be \$1.64 billion in 1992-93, half of which is 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.^[18] In our study the total cost of disease was \$21.85 per month. Indian GDP per capita income for the year 2013 was about Rs.182000 which means on an 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 is spend for the treatment of RA per year.

The treatment cost differs in different countries. In UK, the average annual medical cost was reported to range from £ 3575 to £ 3638 in a study by N J Cooper et al.^[19] where as in Australia it was about £ 893 as reported by Lapsey et al.^[8] The out pocket expenditure in

Germany was found to be £ 417.20 per year which accounted for 15.3% of total direct cost.^[20] The Gross Domestic Product in UK was 41,220 US dollars in 2000. RA patients in UK spend only 7.61% of their per capita income for treatment. While in Australia only about 1.79% of their per capita income is needed for treatment of RA. Germany per capita GDP income was 42,540 US \$ and 0.85% of per capita income is spending 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, that is about 225.41\$ per month.^[21] The result of US based study showed the mean total annual direct medical cost for RA patient 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 patient who was not taking biological was \$ 6,164 Per month cost was calculated as \$513.66.^[22] This is higher than our direct cost which is about \$35.95 per month. The discrepancy of annual cost of RA might be due to the difference in health care systems, referral practices, financing, GDP, and methodologies of studies between India and other countries.

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. About as 91, 51,500 people or even more may be suffering from Rheumatoid Arthritis. A direct cost of Rheumatoid Arthritis may be about ₹17.66 billion annually. Government need to initiate massive, intensive and sustainable public programs to improve policy on Rheumatoid Arthritis among others because of enormous cost associated with its therapy and increasing prevalence rate which will further contribute the cost problems and affect productivity. Patient with lower income could afford sufficient therapy and thereby experience more impairment of work ability, resulting in lower income and higher cost of illness.

Functional disability has been constantly found strongly associated with increased indirect costs, as also demonstrated in our study, suggesting that preserving patients' function is an effective approach to 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.^[23] 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 providing early and aggressive treatment may increase the short-term costs, but

would improve the chances of remaining in work for those who are of working age, and thus, generate long-term productivity gains for the economy.^[24] It is of great importance that public policy decision in the future be underpinned by a thorough consideration of the costs of RA and the potential benefits of the services.

Main limitation of our study was its duration due to which we could not assess the cost effectiveness analysis and toxicity analysis. Since our study involves direct interview of the patient, recall bias is a potential limitation of the study. Certain costs are strictly based on patient's recollection. The changes in value of money are not taken into consideration. The cost of medicine is obtained from the pharmacy billing counter of the study center. The final value is obtained after the discount that is availed to the patient. This value may be different in different center.

CONCLUSION

The study concluded that the burden of RA to the patients is huge. The direct cost such as cost of medicines consumes a major proportion of the Cost of illness. The Indirect cost such as loss of wages due to sick leave was less. This was due to the fact that severity of disability was less in most of the study population. Almost all of the patients had a history of past treatments such as Ayurveda and Homeopathy. A very few patients had consulted a Rheumatologist in the past. Hence, early referral to a rheumatologist can control the disease and its progression. This can be effectively incorporated by government initiatives like medical check up camps, educational campaign etc. This study is expected to serve as useful material to improve our understanding of the burdens of patients with RA in India and as a good reference for developing health related policies in the future. Certain insurance policies and reimbursement schemes can reduce the burden on the patient. Further population based, prospective research is necessary for a detailed analysis of changes in the COI according to changes in the functional status of patients with RA. Currently, a new therapy approach, which includes early and aggressive intervention, new drugs, such as biologic agents and combinations of drugs, has been shown effective and safe in postponing and slowing disease progression, thereby it has the potential to reduce costs by restoring productivity in the long run.

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