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Cost effectiveness analysis of rheumatoid arthritis outpatient at a hospital in bandung

Oskar Skarayadi[1], Wita Anggraeni[2], Pudjiastuti Kartidjo[3], Andri Reza Rahmadi[4], Suci Nar Vikasari[5*]

[1,2,3,5],Pharmacy Department, Universitas Jenderal Achmad Yani , Cimahi, Indonesia

[4]Division *of* Rheumatology, Department of Internal Medicine,*Dr.* Hasan Sadikin *General Hospital. Bandung, Indonesia*

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ABSTRACT

Rheumatoid arthritis is a chronic systemic autoimmune disease of the joints with unknown etiology. treatment therapy is carried out to reduce the symptoms of inflammation, one of which is by using methylprednisolone and methotrexate. treatment is carried out in the long term. this study aims to analyze the cost-effectiveness of combined methylprednisolone in rheumatoid arthritis patients. the study used a retrospective descriptive analytic design. the data were taken from 31 outpatient medical records in hasan sadikin hospital from january 2017-december 2018. the research data included the das28 score, doctor visit fees, medical expenses, and laboratory fees. cost-effectiveness analysis is done by calculating the average cost effectiveness ratio (acer) and incremental cost effectiveness ratio (icer). the results showed 17 patients using methylprednisolone+methotrexate, 6 patients using methylprednisolone+sulfasalazine, 1 patient using methylprednisolone+cyclosporine, 2 patients using methylprednisolone+methotrexate+chloroquine, 3 patients using methylprednisolone+chloroquine+cyclosporine and 2 patients using methylprednisolone+chloroquine. the lowest acer value was obtainedwhen the combination of methylpredisolone+chloroquine was rp. 453,716 per effectiveness with an icer value of rp. 11,686 per effectiveness. this study concludes that the combination of methylprednisolone + chloroquine is the most effective therapy compared to other combinations of methylprednisolone.

Corresponding Author:

Suci Nar Vikasari
Pharmacy Department,
Universitas Jenderal Achmad Yani
Jl. Terusan Jend. Sudirman, Cimahi, 40531, Indonesia,
Email: suci.vikasari@lecture.unjani.ac.id

INTRODUCTION

Rheumatoid arthritis (R.A.) is an autoimmune disease characterized by recurrent inflammation of the joints. Long-term treatment for R.A. results in intermittent R.A. symptoms. The goal of rheumatoid arthritis (R.A.) treatment is to reduce the severity of joint damage, deformity, and joint shape changes that can lead to disability and even premature death (Radu & Bungau, 2021).

The prevalence of R.A. patients in Indonesia is not known with certainty, but it is estimated to increase by 0.5–1.0% per year (Hidayat et al., 2021). According to the 2018 Riskesdas data, R.A. patients are categorized as having joint disorders. Most patients in Indonesia are over 45 years old, and women have the highest risk of common diseases (Badan Penelitian dan Pengembangan Kesehatan, 2019).

Because of its long-term chronic course and safety, it must be treated immediately with immunomodulatory drugs. Disease-modifying antirheumatic drugs (DMARDs) like Methotrexate, Sulfasalazine, and Hydroxychloroquine can delay the progression of the disease (Gholami et al., 2021). Selecting R.A. medications that are effective, efficient, safe, and have few adverse effects in patients with R.A. is becoming difficult; deciding on these treatments demands a variety of factors in terms of both quality and cost (Hidayat et al., 2021).

DAS-28 is a well-known technique for distinguishing patients in remission (Haridoss et al., 2021; Hejrati et al., 2020; Ma et al., 2020). Based on the mean DAS-28 scores, we classified disease activity as remission, low, moderate, or high and performed a subgroup analysis to discover the EQ-5D values associated with disease activity (Haridoss et al., 2021). DAS-28 is determined using four variables: the number of tender joints (0-28), the number of swollen joints (0-28), the patient's global health status on a visual analogue scale (VAS) of 0-10, and the measurement of acute phase reactants (either erythrocyte sedimentation rate (ESR) or C-reactive protein) (CRP) (Dissanayake et al., 2022).

Pharmacoeconomics is the health economics discipline that compares a specific intervention's costs and benefits to a similar alternative. Given the goal of maximizing value for patients, healthcare payers, and society in the face of increasingly restricted resources, this analysis is crucial. New healthcare interventions (drugs, medical equipment, or services) are generally more expensive than existing ones (Tonin et al., 2021). Since drugs have become essential in medicine, more attention is paid to issues such as biosimilars, cost-effectiveness, and pricing control (Gholami et al., 2021). Cost-effectiveness analysis (CEA) is one of the globally most widely utilized forms of economic evaluation. I.S.P.O.R. defines cost-effectiveness analysis (CEA) as a comparison of interventions addressing costs in monetary units and outcomes stated in quantitative non-monetary health units (e.g., reduced mortality or morbidity, symptom-free days gained, cases prevented, patients improved, life years gained) (Tonin et al., 2021).

Savitri et al., (2019) evaluated the effectiveness of DMRAD medications using the DAS-28 to determine the efficacy of their therapy. The study concludes that, despite the majority of patients getting methylprednisolone alone or in combination with other D.M.R.A.D.s, methotrexate alone remains the most effective method for avoiding remission and minimizing adverse effects. Another study conducted by Achmad et al. (2020) found that A.R. patients still need adherence to methotrexate therapy to achieve remission and the effectiveness of methotrexate therapy adherence through DAS-28.

CEA studies of RA patients have been carried out in several countries such as Canada, Netherlands, Canada, UK, USA, Thailand and Germany. In research it is known that the use of traditional DMRAD is more cost-effective than the use of biological DMARDs (Benucci et al., 2011). The CEA study on the use of prednisone to prevent morning stiffness showed that the use of modified release prednisone was more cost effective than the use of intermediate released prednisone (Dunlop et al., 2013). Evaluation of the cost-effectiveness of using prednisone in RA patients over 65 years of age for two years shows that low-dose prednisolone is more cost-effective than placebo (Hartman et al., 2022). Until now there has been no publication regarding CEA using methylprodisolone alone or in combination with DMARD drugs to prevent recurrence in RA patients in Indonesia. Based on this background and study, the purpose of this study is to determine the cost of drug use and identify the most cost-effective alternative to provide R.A. patients with an overview of optimally effective and cost-effective drug administration.

RESEARCH METHOD

The research was conducted in R.S.U.P. Dr. Hasan Sadikin, Jawa Barat, Indonesia. The ethics and law committee RSUP. Dr. Hasan Sadikin approved the study. The number of ethics approval was No.LB.02.01/X.6.5/38/2019. This research is a retrospective descriptive study applying a cross-sectional design. The preliminary study was conducted on patients using single methylprednisolone.

The inclusion criteria were outpatient R.A. patients in the period January 2017–December 2018, patients aged 16–64 who received combination methylprednisolone therapy, new patients who had not received therapy with a total of 2-3 visits, treatment for at least three months, and a DAS28 value > 2.6.

The data taken were direct medical costs from hospital perspective. The direct medical cost was defined as room stay charges, cost of laboratory tests, medicine, service fee, and a total payment based on the hospital perspective (Faridah et al., 2022). Patients and cost data whose medical records were incomplete, missing, or unclear were taken out of the study. The standard costing method was used to calculate the unit costs of medical services (Chatterjee et al., 2013).

Data from outpatient medical records were collected from January 2017 to December 2018. Number, gender, and age were among the patient characteristics collected. The DAS28 score provides information about the efficacy of therapy (Disease Activity Score 28). Based on DAS28 value data, a cost-effectiveness analysis is performed by calculating the average cost-effectiveness ratio (ACER) value and then the incremental cost-effectiveness ratio (ICER). The DAS28 score is a validated index of R.A. disease activity that consists of calculations of tenderness in 28 joints (TJC28) and swelling in 28 joints (SJC28), E.S.R. (blood sedimentation rate), and a global health score (G.H.) measured at 100 mm VAS. The average cost divided by the effectiveness yields the ACER The ICER was calculated by comparing the difference in therapy costs to the difference in effectiveness.

RESULTS AND DISCUSSIONS

The outpatient of R.A. at R.S.U.P. Dr Hasan Sadikin from January 2017 to December 2018 was 480 patients. The selection of patients to be analyzed further showed that 31 patients met the inclusion criteria. The number of patients occurred because most patients visited more than three times in three months. Based on the management of R.A., adaptation to therapy in R.A. patients will occur within 1–3 months of administration of the preparation, and after that, the patient is categorized as having remission(Aletaha & Smolen, 2018). The analysis of patient characteristics distinguished by age and gender table 1 shows the findings of the patient characteristics analysis. The age classification of patients in this study was based on a modification of the Central Bureau of Statistics (BPS) productivity classification, which divided productive age into three categories: 0-14 years, 15-64 years, and >65 years (Goma et al., 2021)

Table 1.R.A. Patients Characteristics

Characteristic	Number Of Patients	Percentage (%)
Age		
15-25	2	6,45
26-35	9	9,67
36-45	5	16,12
46-55	13	41,93
56-64	2	6,45
Gender		
Men	6	19,35

Women	25	80,65

According to the study results, most R.A. patients were between the ages of 46 and 55. The majority of R.A. patients are female. R.A. is a chronic autoimmune disease primarily affecting women(Xu & Wu, 2021). The R.A. disease can affect individuals of any race. It is approximately 2.5 times more common in women than in men. This risk may increase with age. Because of the hormonal factors that influence this disease, most R.A. patients are female. Because of a disturbance in the body's hormonal balance (estrogen), the incidence of R.A. is higher in women, particularly in fertile women. Estrogen is a female hormone that can modulate immune function, which is why most rheumatoid arthritis patients are female (Romo-garcía et al., 2020). The primary objective of RA treatment is to prevent clinical remission. According to several experts, the frequency of remission is obtained through treatment. Clinical remission is the absence of symptoms and signs of disease activity in inflammatory disease. Even though relief from inflammation cannot be found in all affected joints, the swelling of the joints in a single finger can go into remission (Hidayat et al., 2021).

Management RSUP. Dr Hasan Sadikin Bandung recommends chloroquine, methotrexate, sulfasalazine, and leflunomide as the standard therapies for RA. Bridging therapy is a treatment that bridges the time gap between the administration of a DMARD and the clinical response. In this study, methylprednisolone was used as bridging therapy in the initial DMARD prescribing because it has a rapid effect on joint pain and swelling, reduces patient complaints while waiting for the 4–16-week D.M.A.R.D. effects, and helps prevent recurrence or remission (Gestel et al., 1995; Hidayat et al., 2021; Iwami et al., 2022). In this study, 31 patients with R.A. who were diagnosed between January 2017 and December 2018 met the inclusion criteria. Table 2 depicts the process of treating R.A. patients at R.S.U.P. Dr. Hasan Sadikin Bandung, including methylprednisolone in combination with other drug therapies in addition to its use at the beginning of treatment.

Table 2. Patterns of methylprednisolone and other drug use patients with R.A

Drugs	Number of patients	Percentage (%)
MP + MTX	17	54,83
MP + SFZ	6	19,35
MP + SP	1	3,22
MP+MTX+KK	2	6,45
MP+KK+SP	3	9,67
MP+KK	2	6,45

Note : MP= Methylprednisolone, MTX = Methotrexate, SFZ= Sulfasalazine, SP= Cyclosporine KK=Chloroquin,

The most common combination of methylprednisolone is methotrexate, which has the potential to reduce joint damage, maintain joint function, and ultimately reduce joint pain. Methylprednisolone is used to treat inflammation of the joints, while prednisone decreases R.A. patients' treatment costs and boosts their productivity (Hidayat et al., 2021). Based on the effectiveness of R.A. therapy using single methylprednisolone and its combination, it was determined that single methylprednisolone (M.P.) could reduce the DAS28 value by 17.68%. According to an evaluation of the effectiveness of R.A. therapy using a single dose of methylprednisolone and its combination, a single dose of methylprednisolone (M.P.) could lower the DAS28 value by 17.68%. Meanwhile, methylprednisolone and methotrexate (MP+MTX) can reduce DAS28 levels by 19.54%, while methylprednisolone and sulfasalazine (MP+SFZ) can lower DAS28 levels by 22.77%. DAS28 values can be reduced by 38.35% with methylprednisolone, methotrexate, and chloroquine (MP+MTX+KK) (Savitri et al., 2019). Consequently, this drug

combination has the lowest ACER value, where the lower the ACER value, the better or more cost-effective the treatment (Karaeng et al., 2021).

Long-term R.A. treatment is required to prevent remission. The cost of treatment for R.A. patients in remission is higher treatment (Hidayat et al., 2021). The cost-effectiveness analysis is performed by calculating the cost of treatment from the standpoint of health workers. The total direct medical costs, which include medical expenses, laboratory costs, and doctor visits, are calculated. The cost of examining the erythrocyte sedimentation rate (ESR) as a marker of inflammation and a positive R.F. is the cost of the laboratory used (rheumatoid factor). The total average cost is calculated by adding the costs of the drug and the doctor's visit. Table 3 shows the medical expenses.

Patients receiving standard hospital therapy with MP+MTX incur medical costs of Rp. 206,597, Rp. 161,750 with MP+KK, and Rp. 28,417 with M.P. + MTX + K.K., according to the findings. The most expensive direct medical treatment is the combination of MP+SP, which costs Rp. 838,650. The cost-effectiveness analysis uses the difference between the cost and the effect (the average cost-effectiveness ratio, or ACER). The main therapy compared in this study was the use of single-dose methylprednisolone. Table 3 displays the calculation results.

Table 3. Cost analysis, Average Cost Effectiveness Ratio (ACER) and Incremental Cost Effectiveness Ratio (ICER) in R.A. Patients

Therapy	Direct Medical Cost				Effectivity (%)(Savitri et al., 2019)	ACER (Rp)	ICER
	Drug Cost (Rp)	Doctor Visit Cost (Rp)	Lab Cost (Rp)	Total (Rp)			
MP	5.900	30.000	123.750	159.650	17,68	902.997	-
MP + MTX	52.847	30.000	123.750	206.597	19,54	1.057.302	2.524.032
MP + SFZ	339.943	30.000	123.750	493.693	22,77	2.168.173	6.562.720
MP + SP	684.900	30.000	123.750	838.650	31,93	2.626.526	4.764.912
MP+MTX+KK	127.667	30.000	123.750	281.417	38,35	733.812	589.100
MP+KK+SP	380.150	30.000	123.750	533.900	8,07	6.615.861	-3.894.380
MP+KK	8.000	30.000	123.750	161.750	35,65	453.716	11.686

Note : MP= Methylprednisolone, MTX = Methotrexate, SFZ= Sulfasalazine, SP= Cyclosporine KK=Chloroquin,

The patients who got a combination of M.P. and K.K. had the lowest ACER value, Rp. 453,716. Patients with a combination of MP+SP+KK therapy had the highest ACER value of Rp. 6,615,861.Based on an analysis of the cost-effectiveness relationship, it was discovered that the lower the ACER value, the more cost-effective the therapy choice.(Citraningtyas et al., 2018) It was found that the MP+KK combination was more cost-effective in treating people with R.A. than other combination therapies. Figure 1 depicts the cost and effectiveness of the utilized therapy.

Table 4. Cost-Effectiveness Diagram of Drug Combinations over a single Methylprednisolone

Effectivity - Cost	Lower Cost	Equal Cost	Higher Cost
Low Effectivity	A	B	C MP+KK+SP

	D	**E**	**F**
Equal Effectivity			
	G	**H**	**I**
Higher Effectivity			MP+MTX MP+SFZ MP+SP MP+MTX+KK MP+KK

Note : MP= Methylprednisolone, MTX = Methotrexate, SFZ= Sulfasalazine, SP= Cyclosporine KK=Chloroquin

The results showed that the combination of M.P., K.K., and S.P. was in column C, which was the most common area. Even though the MP+MTX, MP+SFZ+MP+SP, MP+KK, and MP+MTX+KK combinations are all in column I, ICER calculations will be used to do more research. It was determined that the MP+KK combination was a cost-effective alternative to other combination therapies in treating R.A. patients. Figure 1 depicts the cost and effectiveness of the utilized therapy. The results indicated that the MP+KK+SP combination was located in column C, the predominant region. Even though the combinations MP+MTX, MP+SFZ+MP+SP, MP+KK, and MP+MTX+KK are located in column I. The ICER value is obtained for cost-effectiveness analysis by comparing the difference between the cost of therapy and the difference in effectiveness, where the total cost of R.A. patients is variable, the DAS28 value is the effectiveness, and the ICER value is obtained from this comparison. The ICER is used to calculate the additional cost of each increase in the effectiveness of therapy (Citraningtyas et al., 2018). The results of the ICER calculation can be seen in table 3. The results of the ICER calculation show that the lowest ICER value is the MP+KK combination of Rp. 11,686 - The highest ICER value in the MP+SFZ combination is Rp. 6,562,720. This ICER value shows that the MP+KK combination is more effective and cheaper than other combinations. In this study, negative ICER results were obtained in the MP+KK+SP combination due to the very low effectiveness of the drug compared to the high cost. If an ICER is obtained with a negative value, the drug should not be used in therapy (Mahony, 2020).

CONCLUSION

Based on retrospective analysis of total direct medical costs and the effectiveness of the DAS28 score reduction, the combination of methylprednisolone and chloroquine is the most cost-effective therapy compared to the combination of methylprednisolone with other drugs. Therefore, to determine the total cost of RA patients, it is necessary to carry out concurrent follow-up research on the total indirect cost using the interview method in several study sites.

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