

Medication Adherence in Rheumatoid Arthritis

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ABSTRACT: Rheumatoid arthritis is an autoimmune disease and most common systemic inflammatory disease characterized by symmetrical joint involvement. Rheumatoid arthritis affects around 1 % of the population worldwide and 0.2 to 1.1% population in India. As medication adherence rates remain suboptimal, ranging from 30 to 80%. Improving medication adherence with currently available DMARDs would improve treatment effectiveness and reduce healthcare costs. The aim of the study is to assess the medication adherence in rheumatoid arthritis patients and to measure impact of patient counseling by clinical pharmacist on medication knowledge and medication adherence scores in the patients of rheumatoid arthritis. This was a prospective, interventional, follow up study. In this study, 75 patients were enrolled and fitting into the inclusion exclusion criteria. Medication knowledge was first assessed at the first visit, 1st, 2nd follow up, each at about appropriate intervals. At baseline medication knowledge as assessed with help of medication knowledge Assessment Questionnaire (MKAQ). They were counseled. The results show that there is higher mean medication knowledge score in females when compared to males. But the results also show that adherence to treatment is higher in females when compared to males and there is higher knowledge in the patients with age group of 36-50 years of age, but lesser knowledge in the patients with age group of ≥ 51 years. Moreover adherence to treatment is also higher in the patients with the age between 36-50 years, while is lower in patients of age ≥ 51 years. The results showed that there higher medication knowledge in the patients with higher educational qualification. A study has shown that there is direct correlation between the educational qualification and the knowledge about the disease and its treatment. But the medication adherence of the patients with higher qualifications is less and does not relate with the medication knowledge of the patients. The results of this study reveal that there is a significant improvement in the medication adherence in rheumatoid arthritis patients after intervention by the pharmacist. Pharmacist's efforts can contribute to the optimization of disease management for the patients with Rheumatoid Arthritis thereby helping them to improve their medication adherence and hence in long term quality of life.

KEYWORDS: Medication adherence, Rheumatoid arthritis, Medication knowledge, Patient counseling .

I. INTRODUCTION

Rheumatoid arthritis is an autoimmune disease and most common systemic inflammatory disease characterized by symmetrical joint involvement. Extra-articular involvement including, rheumatoid nodules, vacuities, eye inflammation, neurologic dysfunction, cardiopulmonary disease, lymphadenopathy and splenomegaly are manifestations of the disease. It may result in deformed and painful joints, which can lead to loss of function. Rheumatoid arthritis affects around 1 % of the population worldwide and 0.2 to 1.1% population in India.^{1,2} Rheumatoid arthritis is related to an increased mortality and expected survival of rheumatoid arthritis patient is likely to decrease 3-10 years.³ Depending upon the clinical situation, a realistic goal for every patient with RA is now low disease activity or disease remission.⁴

Despite extensive evidence regarding drug efficacy and the risk of long-term harm from uncontrolled RA, medication adherence rates remain suboptimal, ranging from 30 to 80%.^{4,5} Improving medication adherence with currently available DMARDs would improve treatment effectiveness and reduce healthcare costs.^{6,7} Medication adherence is defined as "the extent to which a patient's behaviour follows medical advice" and whether it relates to taking medication, following a diet, or adopting lifestyle changes. Adherence is usually higher in patients with acute

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conditions compared to those with chronic conditions. Although more effective interventions for improving medication adherence are needed⁸, medication non adherence remains a poorly studied phenomenon.⁹

Good adherence improves the effectiveness of interventions aimed at promoting healthy lifestyles such as diet modification and physical activity also imparts economic benefits by generating direct savings by reduced use of expensive health services needed in cases of disease exacerbation or relapse and indirect savings by enhancement of or preservation of quality of life and social roles of the patient.¹⁰ Medication non adherence can be classified as primary or secondary, both of which are influenced by different factors. Factors of poor Adherence includes Socioeconomic Factors, Healthcare System Factors, Patient-related factors. Consequences of Non adherence leads to Intense relapse, Increased rebound effect may occur when the medication is abruptly discontinued or interrupted. There may be severe adverse effects of discontinuation, Increased risk of toxicity is seen in the over use of medications mainly in drugs with cumulative dynamics and low therapeutic index.

Medication non adherence may be affected by low levels of health literacy, occupations and patient education. These factors may compromise patient understanding of the adverse outcomes from poorly controlled RA. Patients with RA often lack sufficient understanding to make informed health-care decisions.¹¹ In contrast, those with greater appreciation of the risks and benefits of treatment were more likely to accept risk to achieve better outcomes.¹¹ Unfortunately, patient educational interventions usually have limited effectiveness at improving medication adherence.^{12,13,14,24,25}

While many factors influence drug adherence, this research will focus on the effectiveness of existing gender wise, age wise, educational and health literacy interventions targeting medication adherence in patients with RA.

II. MATERIALS AND METHODS

The study was initiated after obtaining permission from Institution's Ethics Committee, Hospital's Administration and taking formal permission of Head of the Department of Clinical Immunology and Rheumatology. The study was conducted for 6 months i.e from June-November. This was a prospective, interventional, follow up study. Patients were enrolled in study based on inclusion and exclusion criteria. Inclusion criteria includes Patients diagnosed with rheumatoid arthritis with or without co-morbidities present in both genders with age above 18yrs. Exclusion criteria includes patients with previous history of rheumatoid arthritis for more than one year. Informed consent was obtained from the patient at the time of enrolment. All the data regarding demographics, treatment and other medical details was collected in a specially designed Patient Data Collection Form.

2.1. Assessment of medication knowledge:

Medication knowledge was first assessed at the first visit, 1st follow up, 2nd follow up, each at about appropriate intervals. At baseline medication knowledge was assessed with help of medication knowledge Assessment Questionnaire (MKAQ). They were counseled verbally. Later during the 1st follow up MKAQ was again asked, they were counseled and followed.

2.2. Assessment of medication adherence:

At baseline, medication adherence of the patient was assessed by using Medication Adherence Assessment Questionnaire. Patients were also enquired about the reasons for not adhering to the medication regimens. Patients were administered with same Medication Adherence Assessment Questionnaire to reassess their medication adherence at subsequent follow ups. Hence the impact of pharmacist mediated patient counseling on medication knowledge and medication adherence of the patient was determined.

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III. RESULTS

3.1.DEMOGRAPHIC DETAILS OF PATIENTS ENROLLED IN THE STUDY:

Details of patients enrolled in the study:

In this study, 75 patients were enrolled and fitting into the inclusion exclusion criteria into study. the Out of 60 patients, 36 patients (48%) successfully completed the study, and 39patients were drop outs (52%).

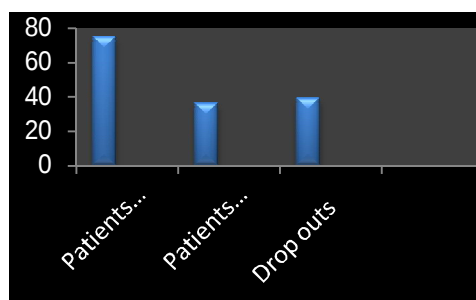


Figure 1: Patients study chart

Table 1: Demographic details of the patients enrolled in the study:

	No. of patients	Percentage
No. of patients enrolled drop out	39	52%
Patient completed the study (second follow up)	36	48%

- **Gender-wise distribution of patients(n=75):**Out of total 75 patients enrolled in the study, 49 patients were female patient, 26 were male patients. Out of 75 patients, 24 female patients (32%) and 12 male patients (16%) completed the study. 25 females and 14 males were dropouts.

Table 2: Gender-wise distribution of patients

	No. of patients	Percentage
Male patients	26	34.6%
Female patients	49	65.4%

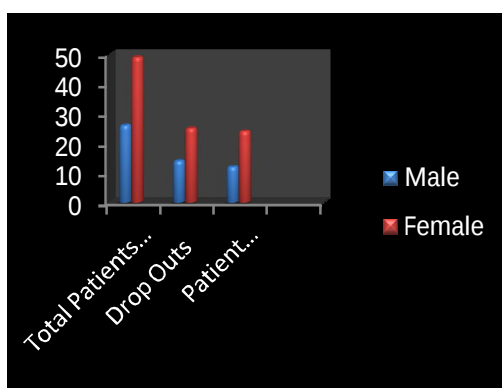
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Figure 2: Gender-wise distribution of patients:



- **Age-wise distribution (n=75):** Out of 75 patients, 20 patients (26.6%) were between the age group of 18-35 years of age. 38 patients (50.6%) were between the age group of 36-50 years and 17 patients (22.6%) were aged more than or equal to 51 years.

Table 3: Age-wise distribution of patients

Age	No. of patients	Percentage
18-35yrs	20	26.6%
36-50yrs	38	50.6%
≥51yrs	17	22.6%

- **Social Habits:** Out of 75 patients, 13 patients (17.4%) had habit of smoking & 10 patients (13.4%) had habit of alcohol while 52 patients had no such social habits.

Table 4: Habit of Alcohol intake and Smoking in patients

	No. of patients	%
Alcoholic	10	13.4%
Smoking	13	17.4%

- **Education level wise distribution of the patients:** Out of 75 patients, 22 patients (29.4%) had completed their diploma or degree level education. 18 patients (24%) were Inter. 27 patients (36%) had education level less than 10th standard, while only 8 of the patients (10.7%) were illiterate.

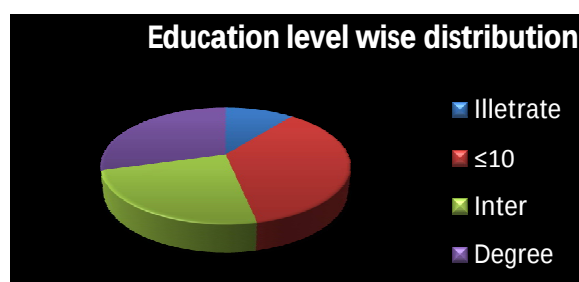
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Figure 3: Education level wise distribution of the patients



3.2.COMPARISON OF THE MEAN MEDICATION KNOWLEDGE SCORE OF PATIENTS:

Mean medication knowledge score was assessed at baseline, first follow up and second follow up. It was observed that there was significant improvement in the mean medication knowledge score of the patients at each follow ups ($p < 0.001$). Mean score increased from 11.74 at baseline to 29.63 at first follow up and 45.58 at second follow up.

Table 5: Comparison of the mean medication knowledge score of patients at baseline and first follow up

Mean baseline score $\pm$ SE	Mean first follow up score $\pm$ SE	Difference of means	p- value
11.74 $\pm$ 2.562	29.63 $\pm$ 1.542	17.89	<0.001

Table 6: Comparison of the mean medication knowledge score of patients at first follow up and second follow up

Mean first follow up score $\pm$ SE	Mean second follow up score $\pm$ SE	Difference of Means	p- value
29.63 $\pm$ 1.542	45.58 $\pm$ 1.265	15.95	<0.001

Table 7: Comparison of the mean medication knowledge score of patients at baseline and second follow up

Mean baseline score $\pm$ SE	Mean second follow up score $\pm$ SE	Difference of means	p- value
11.74 $\pm$ 2.562	45.58 $\pm$ 1.265	33.84	<0.001

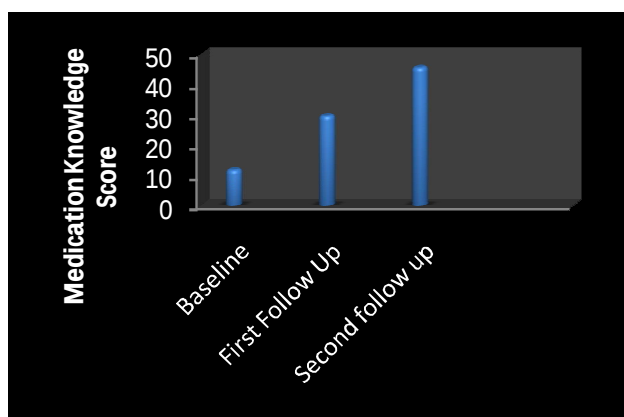
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Figure 4: Overall comparison of mean Medication Knowledge Score (0-50)



COMPARISON OF THE MEAN MEDICATION ADHERENCE SCORE OF PATIENTS (score= 0-8)

Mean medication adherence score was assessed at baseline, first follow up and second follow up. It was observed that there was significant improvement in the mean medication adherence score of the patients at each follow ups ($p < 0.001$). Mean score increased from 4.273 at baseline to 5.727 at first follow up and 6.709 at second follow up.

Table 8: Comparison of the mean medication adherence score of patients at baseline and first follow up

Mean baseline score $\pm$ SE	Mean first follow up score $\pm$ SE	Difference of means	p- value
2.73 $\pm$ 0.355	4.56 $\pm$ 0.205	1.83	<0.001

Table 9: Comparison of the mean medication adherence score of patients at first follow up and second follow up

Mean first follow up score $\pm$ SE	Mean second follow up score $\pm$ SE	Difference of means	p- value
4.56 $\pm$ 0.205	5.24 $\pm$ 0.135	0.68	<0.001

Table 10: Comparison of the mean medication adherence score of patients at baseline and second follow up

Mean baseline score $\pm$ SE	Mean second follow up score $\pm$ SE	Difference of means	p- value
2.73 $\pm$ 0.355	5.24 $\pm$ 0.135	2.51	<0.001

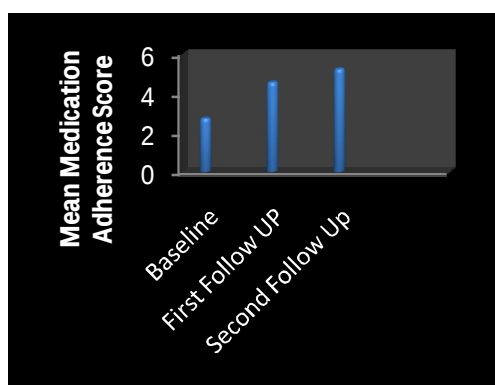
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Figure 5: Overall comparison of Mean Medication Adherence Score (0-8):



3.3.BARRIERS TO MEDICATION ADHERENCE:

Various barriers medication adherence were identified by the pharmacist. 20 patients mentioned. Busy daily schedule as a reason of forgetting the medication, 15 mentioned fear of becoming dependent to medication as a barrier. 6 patients mentioned high cost, 04 patients mentioned fear of side effects, and 05 mentioned confusion in schedule as a reason for non-adherence.

Table 11: Barriers to medication adherence

Barriers for medication adherence	Reported by Number of patients	Percentage of patients
Busy in daily schedule	20	55.6
High cost of drugs	06	16.7
Fear of side effects	04	11.2
Confusion in schedule	05	13.9
Belief that medication is not effective	03	8.4
Fear of becoming dependent	15	41.7

3.4.CORRELATION BETWEEN MEAN MEDICATION KNOWLEDGE SCORE AND MEDICATION ADHERENCE SCORE:

It showed that as the Medication knowledge increases, there is increase in medication adherence score at each follow up. This shows that as there is improvement in medication knowledge, there is improvement in medication adherence score.

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Table 12: Correlation between mean medication knowledge score and mean medication adherence score

	Baseline score	First follow up score	Second follow up Score
Mean medication knowledge score	11.74	29.63	45.58
Mean medication adherence score	2.73	4.56	5.24

DEMOGRAPHY OF THE PATIENT AND MEAN MEDICATION KNOWLEDGE AND ADHERENCE SCORES:

Demographic details of all the patients were analyzed to assess the medication knowledge and medication adherence in each group at each visits. Medication knowledge and adherence scores were compared gender-wise, age-wise, and educational qualification wise to check the impact of demographic factors on the medication knowledge and medication adherence.

Figure 6: Gender wise comparison of the mean medication knowledge of patients at baseline, first follow up and second follow up

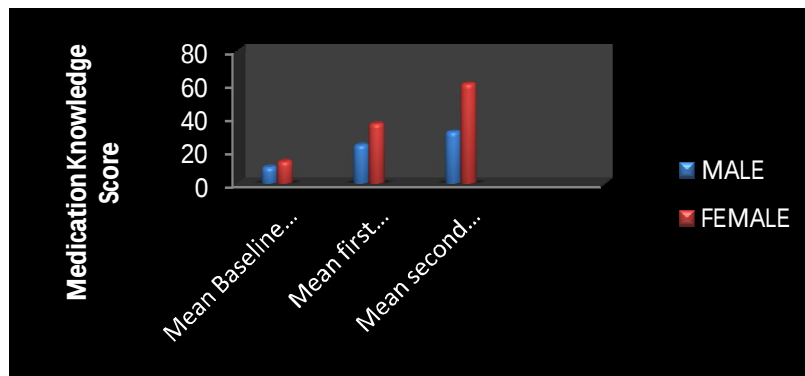


Figure 7: Gender wise comparison of the mean medication adherence of patients at baseline, first follow up and second follow up

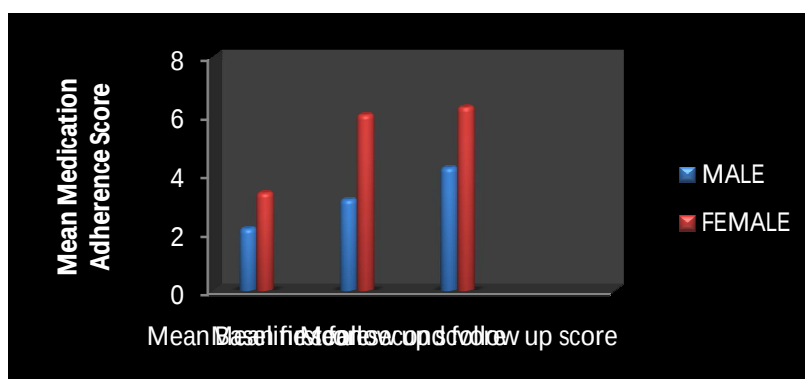


Figure 8: Age-wise comparison of mean medication knowledge and adherence scores

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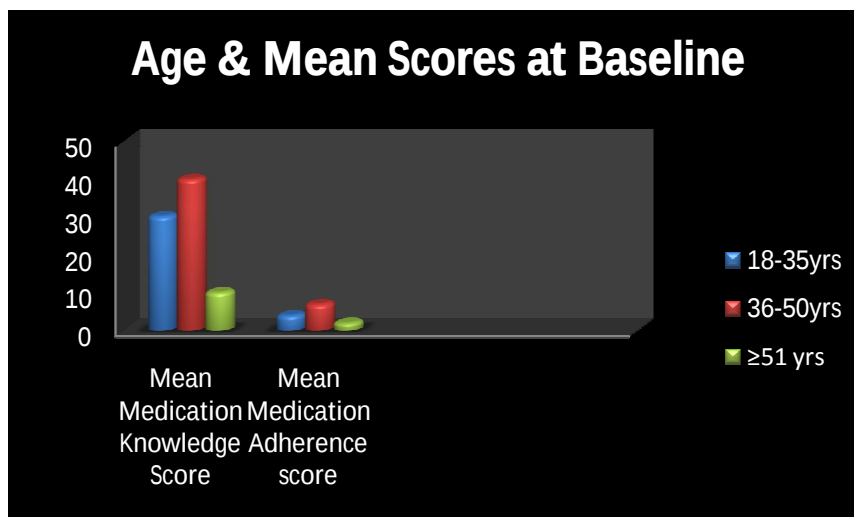


Table 13: Educational status-wise comparison of the mean knowledge of patients at baseline

Education	Illiterate	≤10	Inter	Degree
Mean baseline score ± SE	15.16 ± 2.113	23.61 ± 2.451	37.24 ± 1.657	43.52 ± 4.513

Table 14: Educational status-wise comparison of the mean adherence of patients at baseline

Education	Illiterate	≤10	Inter	Degree
Mean baseline score ± SE	3.264 ± 0.534	2.685 ± 0.416	2.753 ± 0.285	3.627 ± 0.325

IV. DISCUSSION

Gender-wise distribution of patients:

Total of 26 male patients and 49 female patients were enrolled into the study as per the study inclusion and exclusion criteria. Out of these, 12 males and 24 females completed the study. There were 14 dropouts in males and 25 drop outs in female due to lost to follow up. The results show that the number of females (65.4%) affected with rheumatoid arthritis is about double times higher than males (34.6%).

Age-wise distribution of patients:

Out of 75 patients, 50.6% patients belonged to the group of age 38- 50 years, while only 26.6% patients were between the age group of 18-35 years. Boey ML et al. had studied the patterns of disease in rheumatoid arthritis patients. Study had revealed that there is more number of patients in the age group of > 50 years.¹⁵ Another study by Remus CR et al. had suggested that mean age of onset of rheumatoid arthritis is 50years.¹⁶

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Social habits in patients:

Out of 55 patients enrolled in the study, only 13.4% patients had the habit of alcohol and 17.4% had smoking habit. The parameters of social habits like smoking was determined as some recent studies have shown positive relation between this social habit and risk of developing arthritis. Of several environmental factors that predispose people toward developing rheumatoid arthritis, smoking has been found to be the main risk factor and a strong gene-environment interaction between smoking and shared epitope alleles for ACPA-positive patients has been shown in previous studies.¹⁷

On the contrary a recent finding has shown that drinking alcohol was associated with a significantly lower risk of developing rheumatoid arthritis. And the more alcohol was consumed, the lower the risk of rheumatoid arthritis. Among those who drank regularly, the quarter with the highest consumption were up to 50% less likely to develop the disease compared with the half who drank the least.¹⁸

Educational level of the patients:

It is very much essential to determine the educational levels in the patients as the strategies to counsel the patient depends on their educational background. The simplicity of language to be used and the approach toward the counseling depends on the patient's understandability. Moreover these parameters also help to correlate the medication knowledge levels and the medication adherence levels of the patients. Medication knowledge and adherence might be influenced by the educational qualifications of the patients.

In this study, Out of 75 patients, 22 patients (29.4%) had completed their diploma or degree level education. 18 patients (24%) were Inter. 27 patients (36%) had education level less than 10th standard, while only 8 of the patients (10.7%) were illiterate.

Medication Knowledge Score:

A Medication Knowledge Assessment Questionnaire was adopted from a study carried out by Sathvik BS et al.¹⁹ The questionnaire was obtained from the research article by the above mentioned authors, titled "Medication Knowledge of Hemodialysis patients and influence of clinical pharmacist provided education on their knowledge". It consisted of 4 questions to assess the knowledge of patient regarding their Medications.

Studies have shown that pharmacist's counseling can have statistically significant impact on the medication knowledge of the patients. Study by Ponnusankar S et al. had shown that pharmaceutical care improves medication knowledge and in turn medication adherence.²⁰ Barlow JH had shown that there is the need for education in rheumatoid arthritis patients.²¹ Another study by Abourazzak F et al. showed that knowledge of patients is improved after provision of education programs. Such education programs also reduce patient's anxiety and improve their treatment adherence.²² Baseline results of our study too indicate that there is requirement of counseling the patients regarding their treatment as there is very low level of knowledge regarding their diseases.

Medication adherence score:

The results of our study show that there is poor medication adherence in the patients with rheumatoid arthritis at baseline. After counseling, there is significant improvement in the medication adherence of the patients. There is direct correlation of Medication Knowledge with Medication Adherence in the patients. With the improvement in medication knowledge, there is improvement in medication adherence.

Many studies have shown that medication adherence in the rheumatoid arthritis patients range from 30-98 %. Same was seen in our study where there was huge difference in adherence patterns of the patients. Few patients had very high

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medication adherence score, while few had very low medication adherence score leading to high variability. Many patients felt that complexity of regimens lead to forgetfulness and hence non-adherence. Some patients mentioned busy schedule as a reason for forgetting to take their medications. Most patients used to forget their once weekly doses of DMARDs. To overcome this barrier, patients were systematically counseled the importance of taking their drugs and the precautions being taken (laboratory parameters monitoring) to prevent side effects of the drugs.

A study by Garcia PL et al. had shown that financial cost of medication can also lead to non-adherence. Similar reason was given by few patients who could not take few DMARDs owing to their high costs.

A study by Hill J et al. had shown that there is significant improvement adherence to treatment in the rheumatoid arthritis after educational interventions. The participants in the study had initial adherence of 76% which gradually increased to 85% over a period of six months, with provision of patient counseling at predetermined intervals.²³

Gender wise comparison of medication knowledge and medication adherence:

The results show that there is higher mean medication knowledge score in females when compared to males. But the results also show that adherence to treatment is higher in females when compared to males, which may be due to various reasons like more disease activity in females when compared to males, which necessitates them to be compliant to the therapy.

Age-wise comparison of medication knowledge and medication adherence:

The results show that there is higher knowledge in the patients with age group of 36-50 years of age, but lesser knowledge in the patients with age group of ≥ 51 years. Moreover adherence to treatment is also higher in the patients with the age between 36-50 years, while is lower in patients of age ≥ 51 years. This shows that age may be an important factor affecting medication knowledge as well as adherence.

Educational status wise comparison of medication knowledge and medication adherence:

The results showed that there higher medication knowledge in the patients with higher educational qualification. A study has shown that there is direct correlation between the educational qualification and the knowledge about the disease and its treatment. But the medication adherence of the patients with higher qualifications is less and does not relate with the medication knowledge of the patients.

V. CONCLUSION

The results of this study reveal that there is a Significant improvement in the medication adherence in rheumatoid arthritis patients after intervention by the pharmacist. Study revealed that there are various factors affecting the adherence in patients like busy daily schedule, high costs of drugs, fear of side effects, confusion in schedule, fear of becoming dependent on medication, and belief that medication is not effective. As we can see that most of these identified factors are due to inadequate knowledge about the medicines. If counselled appropriately, pharmacist can bring about major change in the adherence related attitude of the patients. There is definite relationship between the medication related knowledge and medication adherence. Hence improving the medication knowledge can lead to greater awareness and hence better medication adherence. The results at baseline showed that there are fewer adherences to treatment as well as less knowledge in patients regarding their medications. As the drug therapy is mainstay of rheumatoid arthritis, it is very much essential to educate patients regarding their medications to improve their knowledge about the medications.

Pharmacist's efforts can contribute to the optimization of disease management for the patients with Rheumatoid Arthritis thereby helping them to improve their medication adherence and hence in long term quality of life.

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VII. LIMITATIONS OF STUDY

The major limitation of this study was inability to implement randomized Controlled design. To obtain more accurate results and estimate the impact of pharmacists counseling on medication knowledge and medication adherence, randomization of the patients in test and control group is more appropriate. A crossover randomized study conducted for longer period of time could provide more specific results, but due to shorter duration of the study period, this could not be done.

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REFERENCES

1. Chandrasekaran AN, Radhakrishna B. Rheumatoid Arthritis and connective tissue disorders: India and South-East Asia. *Bailliere's Clinical Rheumatology*;9(1):45-57;1995.
2. Alamanos Y, Drosos AA. Epidemiology of adult Rheumatoid Arthritis. *Autoimmunity Reviews*;4:130-6; 2005.
3. B. J. F. van den Bemt, H. E. Zwikker, and C. H. M. van den Ende, "Medication adherence in patients with rheumatoid arthritis: a critical appraisal of the existing literature," *Expert Review of Clinical Immunology*, vol. 8, no. 4, pp. 337–351, 2012.
4. J. A. Singh, D. E. Furst, A. Bharat et al., "2012 update of the 2008 American College of Rheumatology recommendations for the use of disease-modifying antirheumatic drugs and biologic agents in the treatment of rheumatoid arthritis," *Arthritis Care & Research*, vol. 64, no. 5, pp. 625–639, 2012.
5. B. J. F. van den Bemt, F. H. J. van den Hoogen, B. Benraad, Y. A. Hekster, P. L. C. M. van Riel, and W. van Lankveld, "Adherence rates and associations with nonadherence in patients with rheumatoid arthritis using disease modifying antirheumatic drugs," *Journal of Rheumatology*, vol. 36, no. 10, pp. 2164–2170, 2009.
6. K. P. Krueger, B. G. Felkey, and B. A. Berger, "Improving adherence and persistence: a review and assessment of interventions and description of steps toward a national adherence initiative," *Journal of the American Pharmacists Association*, vol. 43, no. 6, pp. 668–679, 2003.
7. E. Sabat e and World Health Organization, *Adherence to Long-Term Therapies: Evidence for Action*, World Health Organization, Geneva, Switzerland, 2003.
8. M. A. Blum, D. Koo, and J. A. Doshi, "Measurement and rates of persistence with and adherence to biologics for rheumatoid arthritis: a systematic review," *Clinical Therapeutics*, vol. 33, no. 7, pp. 901–913, 2011.
9. P. Butow and L. Sharpe, "The impact of communication on adherence in pain management," *Pain*, vol. 154, Supplement 1, pp. S101–S107, 2013.
10. Sabate E. Editor. *Adherence to long term therapies: evidence for action*. Geneva: World Health Organization. [online] 2003 [cited on 12 Nov 2009].
11. M. Ho, B. Lavery, and T. Pullar, "The risk of treatment. A study of rheumatoid arthritis patients' attitudes," *British Journal of Rheumatology*, vol. 37, no. 4, pp. 459–460, 1998.
12. K. Niedermann, J. Fransen, R. Knols, and D. Uebelhart, "Gap between short- and long-term effects of patient education in rheumatoid arthritis patients: a systematic review," *Arthritis Care & Research*, vol. 51, no. 3, pp. 388–398, 2004.
13. H. L. M. Brus, M. A. F. J. Van De Laar, E. Taal, J. J. Rasker, and O. Wiegman, "Effects of patient education on compliance with basic treatment regimens and health in recent onset active rheumatoid arthritis," *Annals of the Rheumatic Diseases*, vol. 57, no. 3, pp. 146–151, 1998.
14. R. P. Riemsma, E. Taal, J. R. Kirwan, and J. J. Rasker, "Patient education programmes for adults with rheumatoid arthritis: benefits are small and short lived," *British Medical Journal*, vol. 325, no. 7364, pp. 558–559, 2002.
15. Boey ML, Tan KT, Lee KS, Fong KY, Feng PH. Patterns of disease in rheumatoid arthritis. *Singapore Medical Journal* 1987 Feb;28(1):23-7.
16. Ramos-Remus CR, Sierra-Jimenez G, Skeith K, Aceves-Avila FJ, Russell AS, Offer R, et al. Latitude gradient influences the age of onset in rheumatoid arthritis patients. *Clinical rheumatology* 26:1725-8;2007.
17. K  llberg H, Jacobsen S. Drinking alcohol cuts risk of developing rheumatoid arthritis 2008 Jun 5.
18. Pool AJ, Axford JS. The effects of exercise on the hormonal and immune systems in rheumatoid arthritis. *Rheumatology* 2001;40:610-4
19. Ponnusankar S, Surulivel RM, Anandamoorthy N, Suresh B. Assessment of impact of medication counselling on patients' medication knowledge and compliance in an outpatient clinic in South India. *Patient Education and counselling*;54:55-60;2004.
20. Barlow JH, Cullen LA, Rower IF. Comparison of knowledge and psychological well-being between patients with a short disease duration (< 1 year) and patients with more established rheumatoid arthritis (> 10 years duration). *Patient education and counselling* 38:195-203; 1999.
21. Abourazzak F, Mansouri LE, Huchet D, Lozac'hmeur R, Hassouni NH, Ingels A, et al. Long term effects of therapeutic education for patients with rheumatoid arthritis. *Joint Bone Spine* 76:648-53;2009.
22. Joseph Dipiro, *Pharmacotherapy-A Pathophysiologic Approach*, "Rheumatoid Arthritis" Pg No: 1505-1518.
23. Hill J, Bird H, Johnson S. Effect of patient education on adherence to drug treatment for rheumatoid arthritis: a randomized controlled trial. *Ann Rheum Dis*;60:869-75;2001.
24. R. A. Elliott, "Poor adherence to medication in adults with rheumatoid arthritis: reasons and solutions," *Disease Management and Health Outcomes*, vol. 16, no. 1, pp. 13–29;2008.
25. B. J. F. van den Bemt and W. G. J. M. van Lankveld, "How can we improve adherence to therapy by patients with rheumatoid arthritis?" *Nature Clinical Practice Rheumatology*, vol. 3, no. 12, p. 681;2007.