FACTORS AFFECTING PATIENT ADHERENCE TO PHARMACOLOGICAL THERAPY IN GOUT ARTHRITIS AND HYPERURICEMIA

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ABSTRACT
Background: Pharmacological therapy to reduce serum uric acid levels in gouty arthritis and hyperuricemia patients is essential to prevent gout flare and other hyperuricemia-related morbidities. However, only about 50% of gout arthritis patients adhered to their treatment. Knowing the factors influencing adherence to therapy can be used as a reference for health services to improve adherence. **Objective:** This study aimed to analyze the factors that influenced the patient's adherence to gouty arthritis and hyperuricemia pharmacological therapy. **Methods:** This was an observational study with a cross-sectional approach. Subjects were the patients in Wuryantoro Community Health Center, Wonogiri Regency, diagnosed with gouty arthritis or hyperuricemia due to a disorder in purine metabolism. Sampling was done by a consecutive sampling method. Questionnaires with the related medical record were used to collect the necessary data. Research variables were knowledge, attitudes and behavior, gender, age, occupation, insurance, distance from residence to health care facilities, and adherence to therapy which was in binary. **Results:** Sixty-one percent from a total of 41 respondents were found to be non-adherence to pharmacological therapy. Knowledge, attitudes, and behavior towards therapy, educational level, availability of health insurance, and distance to health facilities were significantly correlated to treatment adherence (p < 0.05). Sex, age, and occupation were not correlated to adherence. **Conclusion:** Factors influencing adherence were knowledge, attitudes and behavior, academic background, insurance, and the distance from residence to health care facilities.
Keywords: Adherence, Gout arthritis, Hyperuricemia, Therapy.

INTRODUCTION

Gout arthritis is an inflammation characterized by repeated acute attacks on the joints with symptoms of redness, tenderness, warmth, and swelling for about 12 hours.[1-3] Based on the latest national prevalence data, it was known that the prevalence of joint disease not due to accidents was 7.3%, of which gout was one of them.[4]

Hyperuricemia, a cause of gouty arthritis, defined as plasma uric acid level above 6.8 mg/dL.[1,2,5] Risk factors known to increase the risk of purine metabolism disorders leading to hyperuricemia have increased in Indonesia. Those risks included a family history of gout, alcohol consumption, kidney failure, obesity, and hypertension.[4,6]

The condition started with underexcretion or overproduction of uric acid, which caused supersaturation of uric acid to precipitate into monosodium urate in the joints as tophi.[1,7] When untreated, crystals could settle in the kidneys as kidney stones cause complications such as nephrolithiasis.[7-9]

With effective treatments, gout attacks can be reduced by regularly taking pharmacological and non-pharmacological therapy.[10-13] These therapies include xanthine oxidase inhibitors such as allopurinol and uricosuric agents.[12] Although treatments of gouty arthritis were found effective, many patients do not adhere to the planned pharmacological therapy. Only about 50% of patients with pharmacologic therapy for gouty arthritis and hyperuricemia adhere to treatment.[14]

Factors influencing long-term therapy have been analyzed in previous studies. Old age, female gender, and insurance ownership positively influence compliance. Older age, female gender, and insurance ownership positively influence adherence, while mental comorbidities negatively impact therapy adherence.[15,16] Other factors such as distance of residence, occupation, and level of education did not affect therapy adherence.[15,17,18]

Guidelines from WHO stated that knowledge of the disease and behavior towards the planned therapy were factors from patients themselves that affect therapy adherence.[19] One of the studies conducted in Indonesia had findings in line with WHO's, where most patients with good knowledge obedient to non-pharmacological therapy for gout arthritis.[20]

Those publications had not shown the factors that influence adherence to pharmacological therapy for gouty arthritis and hyperuricemia, especially in

Dzaki Edmonda Setyawan, Endang Mahati, Nani Maharani

Indonesia. This study aimed to determine the factors influencing adherence to therapy for gouty arthritis and hyperuricemia, which helps health services to know what efforts can be made to ensure adherence to therapy for patients who hold negative factors and become a reference for further research in Indonesia related to the same field.

METHOD

This study had been approved by Health Research Ethics Commission, Faculty of Medicine, Universitas Diponegoro, with the number of 341/EC/KEPK/FK-UNDIP/VII/2021.

This study was observational with a cross-sectional approach conducted at the Wuryantoro Community Health Center, Wonogiri Regency. The scope of this research was in Medical Pharmacology, Internal Medicine, and Public Health Sciences.

All patients diagnosed with purine metabolism disorders in the area of Wuryantoro Public Health Center were the target population. However, the accessible population was patients who visited in October 2021. The research subjects were patients diagnosed with gouty arthritis or hyperuricemia classified as purine metabolism deficiency. The sample was taken by consecutive sampling, and questionnaires with related medical records were used to take the necessary data. The sample size of this study was 41. Respondents over the age of 18 years and diagnosed with purine metabolism disorders were included in the study.

The independent variables included were knowledge, attitudes and behavior, gender, age, occupation, insurance, and distance from residence to health care facilities. Knowledge variable was measured with Gout Knowledge Questionnaire (GKQ), while attitudes and behavior were measured with Beliefs and Behavior Questionnaire (BBQ).[21-23] The dependent variable was therapy adherence which was known by measured good in Morisky Medication Adherence Scale 8 Items (MMAS-8) questionnaire, normal in plasma uric acid level, and had no acute attack for the last month.[24] The said questionnaires were used as primary data sources, while the rest of the variable data were taken from related medical records. All of the variables were in binary.

The questionnaires were first tested for validity and found that all questions were valid for the data to be used in the analysis. The data were then analyzed univariately and bivariate. Univariate analysis was used to describe the distribution of variables in the sample, while bivariate analysis was used to find the correlation between two variables using Fischer's Exact Test.

RESULTS

Based on primary and secondary data, the data distribution was obtained as shown in Table 1 and Table 2. In October 2021, 44 patients with inclusion criteria agreed to participate in the study. Three of them did not complete the questionnaire, so that 41 respondents were obtained and analyzed. The MMAS-8, BBQ, and GKQ questionnaires have been tested for validity, and all questions were valid.

Adherence to therapy, which was then referred to as definitive adherence, was categorized as adherent if the MMAS-8 score was six or higher, there was no history of relapse in the past month, and normal uric acid levels. Uric acid levels were stated normal if < 7.2 mg/dL for men and < 6.0 mg/dL for women. Attitudes and behavior are categorized as good if the BBQ score was greater than 19, while knowledge was considered sufficient if the GKQ score was 7.8 or higher. The margin of the elderly category was > 45 years while the young age was younger than 45 years. Distance of residence measured from health service place > 2km was distant while < 2km was nearby.

Of 41 respondents, 25 (61.0%) did not comply with the treatment. There were 27.3% male respondents with high uric acid levels (7.2 mg/dL or higher), while 46.7% female respondents with high uric acid levels (6.0 mg/dL or higher). As many as 31.7% of respondents behaved poorly, and none complied. Of the 24 respondents (58.5%) with less knowledge, there are 12.5% that obeyed. There are no obedient respondents among respondents who did not graduate from elementary school.

The bivariate analysis results between the independent and dependent variables of "definitive compliance" can be seen in Table 2. Computing the 2×2 table was carried out using the Fisher's Exact Test for the calculated correlation.

The one-pointed correlation on attitudes and behavior towards compliance was obtained with a significance value of $p<0.001$. One-pointed correlation between knowledge and adherence was found to have a significant value of $p<0.001$.

Dzaki Edmonda Setyawan, Endang Mahati, Nani Maharani

Table 1. Data Distribution of Dependent Variable

Variable	Category	Count	Percentage*
Therapy adherence (MMAS-8)	Adhere	13	31.7%
	Does not adhere	28	68.3%
Uric acid level	High	17	41.5%
	Normal	24	58.5%
Morbidity	Relapsed	21	51.2%
	Recessed	20	48.8%
Definitive adherence	Adhere	16	39.0%
	Does not adhere	25	61.0%

Description:
*Percentage from the total of 41 respondents.

Table 2. Analysis Test Results for Independent Variable

Factors	Category	Definitive Adherence Adhere	Does not	Percentage*	Correlation Significance** One-way	Two-way	Coefficient Correlation[b]
Attitudes and behavior (BBQ)	Good	16	12	68.3%	< 0.001[a]	< 0.001[a]	0.545
	Inadequate	0	13	31.7%			
Knowledge (GKQ)	Sufficient	13	4	41.5%	< 0.001[a]	< 0.001[a]	0.646
	Insufficient	3	21	58.5%			
Gender	Woman	13	17	73.2%	0.287	0.478	0.146
	Man	3	8	26.8%			
Age	Elderly	9	18	65.9%	0.241	0.332	0.162
	Young	7	7	34.1%			
Academic background	Passed elementary school	16	17	80.5%	0.011[a]	0.014[a]	0.394
	Did not pass elementary school	0	8	19.5%			
Occupation	Occupied	8	15	56.1%	0.379	0.748	0.098
	Unoccupied	8	10	43.9%			
Insurance	Insured	16	16	78.0%	0.006[a]	0.007[a]	0.424
	Uninsured	0	9	22.0%			
Distance from residence	Distant	3	17	48.8%	0.002[a]	0.004[a]	0.481
	Near	13	8	51.2%			

Description:
* Percentage from the total of 41 respondents.
**Computed with *Fisher's Exact Test* correlated with definitive adherence for 2×2 table.
[a]Significant for Confidence Interval 95% ($p < 0.05$)
[b]Coefficient Correlation computed with Phi-Correlation

Dzaki Edmonda Setyawan, Endang Mahati, Nani Maharani

DISCUSSION

Based on Table 1 regarding the distribution of research data, 25 of 41 respondents (61.0%) did not comply. Many articles on gout were motivated by the low adherence to therapy for gouty arthritis patients. It was mentioned in a previous study that adherence to therapy for gout patients was only 47%, so special attention was needed regarding patient compliance when undergoing pharmacological therapy for gouty arthritis and hyperuricemia.[14] Among the sample, there are 30 (73.2%) female respondents. According to global data, the prevalence of gout shows differences between races, but men tend to have a higher prevalence than women.[25] According to the same data, Asia had contrasting prevalence data differences between countries. The cause of the dominance of women in this research sample may be due to the tendency to seek treatment, level of compliance, occupation, or other reasons not discussed in this study. However, as discussed below, there was no significant correlation between patient gender on adherence to pharmacologic therapy for gouty arthritis and hyperuricemia. The number of patients with insurance reached 32 (78.0%), mainly from JKN BPJS PBI or Non-PBI insurance. This insurance in Indonesia was an obligation for all Indonesian citizens.[26,27]

The influencing factors have been marked as ([a]) in the significance column in Table 2. These factors include attitudes and behavior, knowledge, latest education level, insurance, and distance between their residence to healthcare facilities. In contrast, the factors that are not significant include gender, age, and occupation of the patient. All of the significant factors affect both in one direction and in two directions.

The correlation of attitudes and behavior with treatment adherence has been previously investigated on non-pharmacological therapy adherence. A significant two-way correlation (p = 0.010) was found in this study between the two variables. However, the dependent variable of therapeutic adherence in question was non-pharmacological therapy in the form of changes in the patient's lifestyle conveyed through education.[28]

The pharmacological therapy used in the study was long-term for chronic diseases of purine metabolism disorders. Previous studies with the same therapeutic characteristics, namely long-term pharmacological therapy, one of which was tuberculosis (TB) therapy. Long-term pharmacological therapy in patients with TB has been studied repeatedly and shows different results even with the same variables. It has been shown that there was no correlation between attitudes and behavior with therapy adherence in previous studies.[29] However, in the discussion, it was mentioned that several previous studies have debated the correlation. It was concluded that the difference in correlation between the two variables was due to other factors, including the respondent's background. Each of the studies mentioned used an accessible population originating from one area or one health care agency.

Meanwhile, adherence to long-term pharmacological therapy in chronic non-communicable diseases has also been investigated in at research. It was stated in an article review regarding the factors influencing adherence to long-term pharmacological therapy for hypertension that perception to illnesses and therapy, fear of side effects, and lack of understanding or knowledge were factors of the patients who were assessed by the questionnaires in this study that were following WHO guidelines.[19,20]

Knowledge was an essential factor because gout arthritis was a disease that is poorly controlled even though the available therapies are effective.[30] An experimental study found that patients who attended the "school for gout" had more knowledge, thereby increasing therapy adherence and the patient's quality of life. Regarding the explanation in the correlation of patient attitudes and behavior towards adherence to previous therapy, the correlation of knowledge has been investigated for several similar pharmacological therapies. One of these studies was the relationship between knowledge of HIV/AIDS patients and adherence to long-term antiretroviral therapy, which was found to be significant.[31,32]

The academic background was found to affect compliance. This finding differed from previous studies that found no clear relationship between academic background and therapy adherence.[15,18] This finding was possible because there might be an indirect relationship between the patient's last education level and the knowledge of patients with Gout, where knowledge has been shown to affect adherence. Because of this, there was a possibility that the significance of academic background with therapy adherence was due to intellectual factors, exposure to information, or ease of understanding

Dzaki Edmonda Setyawan, Endang Mahati, Nani Maharani

the concept of disease related to the level of education that the patient can achieve. However, this relationship needs to be further correlated to patient knowledge due to differences in findings with previous publications.

The distance from the patient's residence to the place of health care was correlated to adherence. This correlation was not in line with previous publications that showed no relationship between mileage to treatment establishment and adherence to non-pharmacological therapy in the United States.[17] However, a research in Indonesia showed a significant correlation between distance from health services to residents in pharmacological therapy.[33] The findings of the study were in line with the findings of this study which may be supported by several factors such as geographic access, types of transportation available, barriers, and distances that need to be covered.

The finding that gender had no significant effect was in line with the findings of previous studies regarding factors that influence long-term therapy adherence. In that study, the findings from previous studies that the effect of gender in various scenarios was not significant, except for the treatment of heart disease which found that women were significantly more obedient.[15]

Patients with the age of > 45 years were found to be more adhered to treatment in previous publications, but this finding was not consistent in all diseases.[15,34] This age range might not well-represent the cognitive and psychological aspects of the patients, therefore, it is not correlated with the adherence to therapy. Based on a review of several studies, only the very young and the very elder age have significant negative correlation with therapy adherence. Thus, it is necessary to conduct further research on the patient's age with a numerical or ordinal scale so that the correlation factor on adherence to pharmacological therapy can be described in detail.

Consistent with published review articles, occupation was found to affect therapy adherence.[15] Drug preparations in pharmacological therapy for gouty arthritis and hyperuricemia are in tablet form. It should be possible to take practical tablets with a dose of just one drink per day, making the correlation between busyness and non-adherence to therapy less significant. Based on previous research, it was also found that the occupation had a p-value = 0.097, so that there was no significant correlation between occupation and medication adherence in patients with chronic Inflammatory Bowel Disease (IBD).[35]

Insurance as an influential factor has been proven by a qualitative study provided by rheumatologists in treatment adherence of rheumatic arthritis patients. The study stated that one of the factors that helped improve adherence to therapy was having insurance.[36] In long-term treatment, the bill for expensive and prolonged drug costs can be reduced by insurance. As discussed in the correlation of patient occupation with therapy adherence, socioeconomic factors have a less direct influence on the availability of treatment for patients. Owning an insurance should be advised by healthcare services to patients with long-term pharmacological therapy.

Identifying the factors which influences adherence is important to emphasize appropriate education for patients undergoing pharmacological therapy for gouty arthritis and hyperuricemia. For example, if it was found that a patient did not graduate from elementary school, or the distance from where he lives was more than 2 km, the health care worker can emphasize education to increase the knowledge, attitudes, and behavior of the patient so that the patient will be obedient to treatment.

CONCLUSION

Factors influencing therapy adherence include attitudes and behavior, knowledge, last education level, insurance, and residence distance, which were found significant in both one and two-tailed correlations. In contrast, the factors that have no effect include gender, age, and the patient's occupation.

ETHICAL APPROVAL

Ethical Clearance was issued by the Health Research Ethics Commission, Faculty of Medicine, Diponegoro University under number 341/EC/KEPK/FK-UNDIP/VII/2021.

CONFLICTS OF INTEREST

The authors declared no conflict of interest.

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AUTHOR CONTRIBUTION

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Dzaki Edmonda Setyawan, Endang Mahati, Nani Maharani

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