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RELATIONSHIP OF OHA'S TREATMENT RATIONALITY WITH THERAPY TARGETS ACHIEVEMENT IN TYPE II DIABETES MELLITUS PATIENTS

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ABSTRACT

Diabetes mellitus (DM) is the most common condition in Central Java. Irrational use of drugs can cause various problems, including increased disease morbidity and mortality rates, wasted health costs, and the emergence of undesirable effects. Therefore, this study was necessary to assess the rationality of the treatment. The aim was to describe the rationality of OHAs treatment and to achieve therapy targets, and to understand the relationship between OHA treatment rationality and therapy target achievement in patients with type 2 diabetes mellitus at primary health care in Wirosari District, Grobogan Regency. An analytical observational study used a cross-sectional design, purposive sampling, and chi-square test to establish relationships between variables. The rationale for treating OHAs in patients with type 2 diabetes mellitus at primary health care in Wirosari District, Grobogan Regency, is 47.67% rational and 52.33% irrational. Among the samples, 26.7% reached the therapeutic target, whereas 73.3% did not. The rationality of treating OHAs and achieving therapeutic targets was interconnected (p=0.014).

Keywords: HbA1C, rational treatment, therapeutic target, type 2 diabetes mellitus

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder characterized by blood sugar levels exceeding normal limits. According to Riskesdas in 2022, cases of diabetes mellitus in Central Java are the second highest at 10%, and in Grobogan Regency, it reaches 20,677 cases (Dinas Kesehatan Provinsi Jawa Tengah, 2012). Rational therapy is the use of drugs on the condition that the patient receives the drug following clinical needs in adequate doses within a sufficient period, and at the lowest cost. Irrational use of drugs can cause various problems, such as increasing disease morbidity and mortality rates, wasting patient health costs, and the emergence of undesirable effects. The rational use of drugs includes the correct diagnosis, right indication, right type of drug, right dose, method, duration of the drug, right information, and right condition of the patient (Kementerian Kesehatan RI, 2011). Rational treatment for type 2 diabetes mellitus includes the gradual addition of antidiabetic drugs, starting with lifestyle modification and progressing to oral monotherapy, combination therapy, and insulin therapy as needed. Thus, rational treatment is important for achieving and maintaining glycemic control in patients with type 2 diabetes mellitus. The use of evidence-based guidelines, such as the American Diabetes Association (ADA) and Perkumpulan Endokrinologi Indonesia (PERKENI), can help make informed decisions about the most appropriate treatment strategies for individual patients based on their age, body weight, complications, duration of diabetes, life expectancy, and expenses (DeFronzo *et al.*, 2013). In previous research on the rationality of diabetes mellitus treatment, there was an irrational drug use rate of 21.59% (Fatimah, 2021). In addition, research that correlates

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treatment rationality with achieving diabetes mellitus therapeutic targets states a correlation between treatment rationality and temporary glucose control (Yonanda, 2022).

RESEARCH METHODS

The research design was analytical observational, using a cross-sectional method with prospective data collection. Data were collected over 3 consecutive months between January-April 2023. In this study, the chi-square test was used to determine the relationship between variables. Purposive sampling was used. The population of patients with type 2 diabetes mellitus in primary-level health facilities in Wirosari District, Grobogan Regency, is 227. Based on the sample size calculations, the minimum number of samples required was 70. The inclusion criteria for this study were patients who received OHO therapy, patients who used BPJS insurance, and patients who had laboratory data in the form of fasting blood sugar, while the exclusion criteria were patients who used drugs that increased blood glucose, such as long-term steroid use, who had not undergone therapy for 6 consecutive months, and who had undergone a change in therapy during the last 3 months.

The type of data used was primary data in the form of a questionnaire and secondary data in the form of medical records. The questionnaire used in this study was the MARS-5 questionnaire, which contains five question items that assess noncompliance behavior. Each question item was measured using an ordinal scale with values of 1 (always), 2 (often), 3 (sometimes), 4 (rarely), and 5 (never). The level of compliance was categorized into 2, namely high with a score of 25 and low with a score <25. Medical records were used to collect data on the patient characteristics, therapy, and fasting blood sugar levels. The research ethics used in this research were issued by the Research Ethics Commission in the health sector, Faculty of Medicine, Diponegoro University, Semarang with No. 18/EC/KRPK/FK-UNDIP/I/2023.

RESULTS AND DISCUSSION

The sample in this study consisted of 86 patients who were categorized according to several characteristics, such as gender, age, Body Mass Index (BMI), comorbidities, use of Oral Hypoglycemic Agents (OHA), sample HbA1C levels, and compliance.

Based on **Table I**, it was found that the majority of the sample was women (83.72%), while the proportion of men was only 16.28%. Basic health research in 2018 also stated that more women than men were diagnosed with diabetes mellitus (Balitbang Kemenkes RI, 2018). In this study, the majority of samples were in the elderly category (≥60 years), amounting to 51.16%, pre-elderly (45-59 years) amounting to 46.51%, while the other 2.33% fell into the adult category (19-44 years). This is caused by aging, which results in a decrease in insulin sensitivity and the body's ability to metabolize glucose (Trisnawati and Setyorogo, 2013).

Most of the samples (63,95%) in this study had a normal BMI (18.5-25.0). This is because DM patients have a high glucose content in their urine, and glucose is wasted in the urine in high quantities. This causes calories to be wasted, resulting in weight loss (Sasongko *et al*. 2018). The majority of the participants in this study did not have comorbidities (83.72%), while the remaining 16.28% had comorbidities in the form of hypertension. Hypertension is one of the most common complications caused by suffering from diabetes mellitus (Lee *et al*., 2017). Hyperglycemia can increase blood pressure by increasing the circulating fluid volume. An increase in circulating fluid volume occurs when the body has excess blood sugar levels, which causes an increase in extracellular osmotic pressure so that water will come out of the tissues to reduce the difference between extracellular and intracellular osmotic pressure. This can cause an increase in cardiac output and blood pressure. In addition, long-term hyperglycemia can lead to hyperinsulinemia. Hyperinsulinemia is a condition in which excessive insulin levels can increase sodium reabsorption in kidney tubules, thereby causing high blood pressure (Ohishi, 2018).

The majority of samples in this study (63.95 %) had a normal BMI (18.5-25.0). This is because DM patients have a high glucose content in their urine; therefore, a large amount of glucose is wasted in the urine. This causes calories to be wasted, resulting in weight loss (Sasongko *et al*. 2018). The majority of the participants in this study did not have comorbidities (83.72%), while the remaining 16.28% had comorbidities in the form of hypertension. Hypertension is one of the most common complications caused by suffering from diabetes mellitus (Lee *et al*., 2017). Hyperglycemia can increase blood pressure by increasing the circulating fluid volume. An increase in circulating fluid volume occurs when the body has excess blood sugar levels, which causes an increase in extracellular osmotic pressure so that water will come out of the tissues to reduce the difference between extracellular and intracellular osmotic pressure. This can cause an increase in cardiac output and blood pressure. In addition, long-term hyperglycemia can lead to hyperinsulinemia. Hyperinsulinemia is a condition in which excessive insulin levels can increase sodium reabsorption in kidney tubules, thereby causing high blood pressure (Ohishi, 2018).

Table I. Sample Characteristics

Characteristics	Number of Samples (n)	Percentage (%)
Gender		
Men	14	16,28%
Women	72	83,72%
Age		
Mature (19-44 years old)	2	2,33%
Pre-elderly (45-59 years old)	40	46,51%
Erlderly (≥60 years old)	44	51,16%
BMI		
Heavily skinny (<17,0)	1	1,16%
Light skinny (17,0-18,4)	2	2,33%
Normal (>27,0)	55	63,95%
Light obese (25,1-27,0)	17	19,77%
Heavily obese (>27,0)	11	12,79%
Comorbidities		
Hipertension	14	16,28%
No comorbidities	72	83,72%
OHA's Use		
Metformin	13	15,12%
Glimepiride	36	41,86%
Glibenclamide	7	8,14%
Metformin-Glimepiride	30	34,88%
HbA1C Levels Pre-treatment		
<7	36	41,86%
7-7,49	11	17,79%
7,5-9	17	19,77%
>9	22	25,58%
HbA1C Levels Post-treatment		
<7	41	47,67%
7-7,49	9	10,47%
7,5-9	15	17,44%
>9	21	23,42%
Compliance		
High	39	45,35%
Low	47	54,65%

In the profile of drug use, the most frequently used OHO was the use of a single OHO in the form of glimepirid (41.86%) and the use of a combination of OHO and metformin-glimepiride (34.88%). The choice of single or combination therapy can be based on cost, effectiveness, allergy history, contraindications, side effects, and drug availability at health facilities (PERKENI, 2021). Glimepiride is said to be more effective than glibenclamide in controlling glycemic and lipid profile disorders. Glibenclamide has been reported to cause hypoglycemia in up–20-30%, whereas glimepiride has been reported to cause hypoglycemia in only 2-4%. This is because glibenclamide has a longer half-life than glimepirid (Brunton *et al*., 2008). Therefore, glimepiride is preferred over glibenclamide, even though it belongs to the same group.

Based on **Table I,** it was found that the majority of the samples had HbA1C levels <7 both pre-(41.86%) and post-treatment (47.67%). HbA1C levels in this study were not obtained directly, but were obtained from the conversion of average fasting blood sugar levels for 3 consecutive months. This is because HbA1C levels are not always checked every month, and at the sampling site for this study, HbA1C levels were checked every 6 months. In this study, pre- and post-treatment HbA1C levels were observed, and the initial HbA1C level was used to determine the provision of further therapy, whereas post-treatment HbA1C levels were used to evaluate the achievement of therapy targets (PERKENI, 2021).

In this study, the MARS-5 questionnaire, consisting of five question items, was used to assess patients compliance, consisting of 5 question items, and validity and reliability tests were carried out. The questionnaire had a p-value <0.001 for the five question items and a Cronbach's alpha value of 0.948. Based on these results, the questionnaire used was declared valid because it had a p-value <0.05, and reliable because it had a Cronbach's alpha value >0.6 (Burhan Bungin, 2009; Ghozali, 2018). As shown in **Table I**, it was found that 54.65% of the sample had low compliance, while 45.35% had high compliance. Compliance is said to be high if the total score obtained is 25 (Alfian and Putra, 2017). Treatment compliance influences the achievement of therapy targets. With high compliance, therapy targets can be achieved (Firdiawan *et al*., 2021).

Table II. The Rationality of Treating Oral Hypoglycemic Agents

Treatment Rationality	Right	Not Right	Total
Right Indication	100%	0%	100%
Right Patient	100%	0%	100%
Right Dose	100%	0%	100%
Right Drug	47,67%	52,33%	100%

The rationality of treatment was assessed based on the right indication, patient, drug, and dose. The correct indication is the appropriateness of treatment based on the diagnosis made by the doctor. Appropriate for patients is treatment based on contraindications, history of allergies, and comorbidities. Appropriate medication refers to the appropriateness of administering medication based on interactions, side effects, and therapeutic guidelines. The correct dosage is the appropriateness of administering medication based on dose, time, and frequency (Kementerian Kesehatan RI, 2011).

Table III. The Achievement of Therapeutic Targets

Achievement of Therapeutic Targets	Number of Samples (n)	Percentage (%)
Achieved	23	26,7%
Not achieved	63	73,3%
Total	86	100%

As shown in **Table III**, 73.3% of the samples did not reach the therapy target. This can be caused by the patient's non-compliance with medication because diabetes mellitus is a chronic disease that requires continuous, appropriate therapy (Hartanti, 2019). The Chi-Square test was used to analyze the relationship between the variables, rationality of treatment, and achievement of therapy targets.

Table IV. Relationship of Oral Hypoglycemic Agents Treatment Rationality and Achieving Therapeutic Targets

Treatment Rationality	Achievement of Therapeutic Target		Total	P Value
	Not achieved	Achieved		
Irrational	38	7	45	0,014
Rational	25	16	41	
Total	63	23	86	

A relationship was found between the rationality of OHO treatment and the achievement of therapy targets (p = 0,014). These results are consistent with previous research that correlates treatment rationality with achieving therapeutic targets for diabetes mellitus, which shows a relationship between treatment rationality and achieving therapy targets (Yonanda, 2022).

There were 63 samples that did not reach the therapy target **Table IV**. Three samples initially had HbA1C levels >9 and did not undergo rational treatment but experienced a decrease in HbA1C levels post-treatment. This may be caused by factors that were not observed in this study, such as physical activity and dietary regulation, which are also factors that influence therapeutic targets. According to PERKENI 2021, physical activity can be useful for maintaining body fitness, losing weight, and improving insulin sensitivity, thereby improving blood glucose control. Furthermore, diet can be used to control blood glucose levels in patients with DM. The diet for patients with DM is adjusted according to each patient's calorie and nutritional needs, and the administration is adjusted based on the meal schedule, type, and amount of calorie content (PERKENI, 2021).

A limitation of this study is that it did not include patients who had just received therapy. It is hoped that future research will include patients who have just received therapy so that assessments can be carried out simultaneously. In this study, the therapy monitoring indicator used was not the HbA1C value resulting from laboratory examination, but the HbA1C value converted from the average fasting blood glucose for 3 consecutive months. Because the 3-month average fasting blood sugar results are an alternative if HbA1C examination cannot be performed and does not accurately reflect the actual HbA1C value, it would be better to conduct further research using therapy monitoring indicators in the form of HbA1C laboratory examination results. In this study, one indicator could not be seen, namely, the combination of insulin with OHO, which should be administered to patients with HbA1C >9. This is because this drug combination can only be seen in advanced health facilities; therefore, in this study, those with HbA1C >9 were categorized as irrational. Therefore, primary-level health facilities are expected to be able to refer patients with HbA1C >9 to advanced health facilities.

CONCLUSION

Oral hypoglycemic therapy at the Wirosari District Primary Health Center, Grobogan Regency, is mostly irrational, and the therapy target in patients with type II diabetes mellitus cannot be achieved. There is a correlation between the rationality of oral hypoglycemic treatment and the achievement of therapeutic targets.

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