EFFECTIVENESS OF THE COMBINATION OF METFORMIN AND GLIMEPIRIDE AS A LOWERING OF BLOOD GLUCOSE IN PATIENTS WITH DIABETES MELLITUS AT THE UPTD GEMBONG HEALTH CENTER

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Abstract. According to Riskesdas (2019), the estimated number of Diabetes Mellitus sufferers in Central Java is 652,822 people with a percentage of 83.1%. Diabetes Mellitus can cause various complications of the disease, so it is necessary to monitor blood glucose levels. Pharmacological therapy used to treat Diabetes Mellitus type 2 is the use of oral antidiabetics alone or in combination. Commonly used oral antidiabetics are metformin and glimepiride. This study aims to describe the effectiveness of using oral antidiabetic drugs in lowering blood glucose in Diabetes Mellitus patients. This research is a quantitative study using a cross-sectional design. This research was conducted prospectively by conducting direct monitoring for a period of 3 months from March 2022 to May 2022 at the UPTD Gembong Health Center, Pati Regency. The sampling technique was carried out by purposive sampling and the research instruments used were data collection sheets and medical records. The data obtained was carried out by observing the effectiveness of the use of oral antidiabetic drugs and data analysis. Most cases in this study were in the female sex group (72.8%), aged 51-60 years (50.0%), and housewives (58.3%). The use of combined oral antidiabetic drugs was more with a percentage of 83.3%. The use of oral antidiabetics can reduce blood glucose levels in Diabetes Mellitus patients. Based on these results it can be concluded that the use of oral antidiabetics for outpatients at the UPTD Gembong Health Center, Pati Regency has effectiveness in reducing blood glucose levels in Diabetes Mellitus patients.

Key words: [DM type 2; oral antidiabetics; effectiveness; blood glucose levels]

INTRODUCTION

Diabetes Mellitus (DM) occurs because the body cannot produce insulin properly, so the insulin cannot be used effectively (Sari, 2015). Based on data from the WHO *(World Health Organization)* it is estimated that there are around 8.4 million Indonesians who have diabetes mellitus and will experience an increase in 2030 (Hauri & Faridah, 2019). DM disease in Indonesia in 2015 globally ranked seventh (Ministry of Health, 2018), and based on the *International Diabetes Federation* (IDF) stated that globally in 2019 there were DM sufferers aged 20-79 years around 463 million with a prevalence of 9. 3% (Ministry of Health, 2020). According to the 2019 Riskesdas, the estimated number of DM sufferers in Central Java is 652,822 people with a percentage of 83.1%.

DM can cause various complications of the disease, so it is necessary to monitor blood glucose levels. This aims to keep blood glucose levels maintained, where to maintain blood glucose levels can be delivered medical education related to physical activity (Refdanita & Villya, 2021). Physical activities that are generally carried out by DM patients are walking, running, and exercising (Widodo *et al*., 2016). DM has 2 complications, namely acute complications and chronic complications. Acute complications occur when blood glucose levels decrease and increase in a relatively short time, while chronic complications are caused by abnormalities in the blood vessels which result in coronary heart disease (Meryta et al., *2015*).

DM is included in a lifelong disease, and these conditions can be prevented by adopting a healthy lifestyle such as nutritional therapy and carrying out physical activity accompanied by pharmacological interventions (Jonathan et al., 2019*)*. Pharmacological therapy used to treat type 2 DM is the use of oral antidiabetics alone or in combination. The single oral antidiabetic that was prescribed the most in DM patients was the use of metformin with 26 prescriptions (45%). Metformin is used because it is more effective in lowering the patient's blood glucose compared to other groups (Safitri, 2017). Based on the research by Rahmawaty & Hidayah (2020) it was stated that the use of combined oral antidiabetics was most prescribed with 29 prescriptions (93.5%), namely the use of metformin and glikuidone. Non-compliance of DM patients with medication therapy causes blood glucose levels to be not properly

controlled (Alfian, 2015).

Based on previous research by Septiana & Nurcahyo (2021) it showed that the antidiabetic group that was widely used was the biguanide (metformin) group, with 79 recipes (97.5%). Biguanides are used because biguanide works to reduce blood glucose by around 10-40% by improving glucose transport into muscle cells, reducing glucose production, and reducing glycogenolysis and gluconeogenesis. Based on similar research, shows that the use of a combination of Glimepiride with Pioglitazone as a combination therapy is effective in reducing blood glucose levels in type 2 DM patients (Ulfa & Arfiana, 2020)**.** This shows that pharmacological therapy using oral anti-diabetic drugs can reduce blood glucose levels in patients with DM.

Based on the description above, it is necessary to carry out research related to the description of the effectiveness of using oral antidiabetic drugs as a lowering of blood glucose in DM patients at the UPTD Gembong Health Center, Pati Regency. This study aims to describe the effectiveness of using oral antidiabetic drugs in lowering blood glucose in DM patients.

METHODS

This research is a quantitative study using a cross-sectional design. This research was conducted prospectively by conducting direct monitoring for a period of 3 months from March 2022 to May 2022 at the UPTD Gembong Health Center, Pati Regency, Central Java Province. The sampling technique was carried out by purposive sampling with inclusion criteria including patients diagnosed with DM > 1 year old, patients aged > 40 years, outpatient type 2 DM patients with or without comorbidities, patients receiving single or combined oral antidiabetic drugs, patients receiving willing to provide information directly or indirectly. The research instrument used in this study was medical record data collection sheets with documentation techniques or medical record data from Diabetes Mellitus patients undergoing treatment and supported using ADA *(American Diabetes Association)* in 2018. The steps taken in this study included:

a. Research Ethical Due Diligence (Ethical Clearance)
   The Ethical Clearance for this research was submitted to the Health Research Ethics Commission at Muhamadiyah University, Purwokerto, and recommendations for research implementation were issued in March 2022 with No. KEPK/UMP/19/III/2022.
b. Medical Record Data
   Data collection was carried out by recording the required data in the form of the name, age, gender, diagnosis, administration of single or combined oral antidiabetic drugs, length of treatment, blood sugar levels at the time, and also a history of allergies.
c. Monitoring Blood Glucose Levels
   Monitoring of blood glucose levels was carried out directly from the beginning of the study to the end of the study by providing data collection sheets to patients. The data collection sheet includes the patient's name, age, sex, diagnosis, occupation, length of treatment, history of allergies, medication received, blood glucose levels at any time, and some questions about the consumption of drugs and food or drinks containing sugar.
d. Observation of Drug Effectiveness
   The observation was carried out by assessing the effectiveness of the use of oral antidiabetic drugs based on data in recorded medical records and the results of monitoring blood glucose levels on informed consent.
e. Data analysis
   The data obtained was analyzed using SPSS (Statistical Product and Service Solution) version 25 using a univariate test, namely a frequency test to see patient characteristics and an overview of the effectiveness of using oral antidiabetic drugs.

RESULTS AND DISCUSSION

Research conducted at UPTD Gembong Health Center to find out the effectiveness of the use of oral

antidiabetic drugs showed results that can be seen in 3 parts, including:

Patient Characteristics

Patients who met the inclusion criteria at the UPTD Gembong Health Center during the March-May 2022 period were 36 patients. The characteristics of the patients in this study can be broken down as follows:

a. Gender

Patient characteristics based on age group can be seen in Table 1. Based on the gender grouping in this study, the patients most affected by Diabetes Mellitus (DM) were female patients at 72.8% (26 patients), compared to the male population. male by 27.2% (10 patients). This is due to the lack of physical activity carried out, often consuming excessively sweet foods and drinks. Eating and drinking excessively and exceeding the amount needed by the body can trigger diabetes mellitus (Zulfh & Muflihatin, 2020).

Table 1. Distribution of DM patients by gender

Gender	Number of Patients	Percentage (%)
Man	10	27,2
Woman	26	72,8
Total	36	100

The results of the research shown in Table 1 are in line with the research of Fitriani & Barus (2019) which stated that the prevalence of DM in women is higher than in men because the composition of fat in the body in women is more than in men, causing women are overweight so that it can pose a risk of obesity.

b. Age

Based on the age grouping of type 2 Diabetes Mellitus patients in this study, patients who suffered the most from the disease occurred at the age of 51-60 years at 50.0%. Vulnerable age 51-60 including in old age. This can happen because as you get older, body functions also decrease, old age causes the function of organs in the body to decrease. Increasing age can also affect physical activities carried out it can result in abnormal glucose metabolism in the body (Muhasidah *et al.*, 2019). The results can be seen in Table 2.

Table 2. Distribution of DM patients by age

Age	Number of Patients	Percentage (%)
40-50	5	16,7
51-60	18	50.0
≥ 61	13	33,3
Total	36	100

The results of this study are in line with the research of Yulianti *et al.* (2014) which states that type 2 Diabetes Mellitus patients are most common at the age of 41-60 years, namely 72.5% of 50 patients. This is because the vulnerable aged 41-60 years are included in the elderly category so the metabolism in the body will decrease. This will affect changes in diet and physical activity undertaken.

c. Profession

The grouping of patient characteristics based on the profession can be seen in Table 3.

Table 3. Distribution of DM patients by profession

Work	Number of Patients	Percentage (%)
Housewife (IRT)	20	58,3
Farmer	12	30,6
Laborer	3	8,3
Retired	1	2,8
Total	36	100

Based on the table above, shows that of the 36 patients with Diabetes Mellitus Type 2 whose data were collected for the most occupations, namely 20 patients were housewives (58.3%), 12 patients were farmers (30.6%), 3 patients were laborers (8.3%), and 1 patient retired (2.8%). This research is in line with research conducted by Muhasidah *et al.,* (2019), based on research conducted on average the most jobs were housewives (IRT) (49.3%) as many as 70 patients. This is because housewives tend to be less in physical activity.

d. Length of Treatment

The duration of drug use in type 2 Diabetes Mellitus patients undergoing outpatient care was 1-2 years (25%), 3-4 years (47.2%), 5-6 years (27.8%) and the most was 3- 5 years as much (47.2%). These results can be seen in Table 4.

Table 4. Distribution of DM patients based on length of treatment

Length of Treatment	Number of Patients	Percentage (%)
1-2 yrs	9	25
3-4 yrs	17	47,2
5-6 yrs	10	27,8
Total	36	100

e. Comorbidities

The grouping of patient characteristics based on the associated disease can be seen in Table 5.

Table 5. Distribution of DM patients based on comorbidities

Concomitant Diseases	Number of Patients	Percentage (%)
With Comorbidities (Hypertension)	7	19,4
No Comorbidities	29	80.6
Total	36	100

Based on the table above, it can be seen that the comorbidities in type 2 Diabetes Mellitus patients at the UPTD Gembong Health Center, Pati Regency, namely hypertension (19.4%) in 7 patients. This research is in line with research conducted by Safitri (2017) with co-morbidities, namely hypertension. Because hypertension is more common than other comorbidities. Hypertension can cause pancreatic beta cells to be insensitive to insulin, which can lead to insulin resistance.

Use of oral antidiabetic

Patients at UPTD Gembong Health Center as many as 36 patients received oral antidiabetics, either alone or in combination. The single oral antidiabetic given was glimepiride, while the combination given was metformin with glimepiride. The use of oral antidiabetics can be seen in Table 6.

Table 6. Use of oral antidiabetics in DM patients at UPTD Gembong Health Center

Administered oral antidiabetic drugs	Number of Patients	Percentage (%)
Single Glimepiride	6	16,7
Combination Metformin + Glimepiride	30	83.3
Total	36	100

Based on the above table it can be seen that in 36 patients with Type 2 Diabetes Mellitus whose data were collected for Single ADO as much as 16.7% were 6 patients who were given Glimepiride, while for Combination ADO as many as 83.3% were 30 patients who were given Metformin in combination with Glimepiride. The use of Glimepiride is a single therapy. After all, Glimepiride is a class of sulfonylureas, including a class of drugs that are often used because Glimepiride works by increasing insulin secretion. This research is in line with research that has been conducted by Syarifuddin *et al* (2021), which obtained the results using the single most widely used oral antidiabetic (ADO), namely

glimepiride. Glimepiride belongs to the sulfonylurea class which is often used in patients with type 2 Diabetes Mellitus who have normal weight and who have never experienced ketoacidosis or a condition that occurs when the body cannot convert glucose into energy. Glimepiride tends to have mild side effects (Dipiro *et al* ., 2015). The use of a single oral antidiabetic (ADO) is given if you have normal blood glucose levels, and the administration of combined oral antidiabetics is given if a single drug does not give results even though you have applied dietary factors and adopted a healthy life (Hauri & Faridah, 2019).

The use of an oral antidiabetic (ADO) combination of Metformin and Glimepide as a combination therapy is because Metformin can be used as a single drug or in combination, Metformin is included in the Biguanid class. Metformin has a way of working by reducing glucose production in the liver. Metformin has side effects, namely in the form of cramps in the patient's stomach, watery stools, and a feeling of cramps in the stomach, causing a feeling of bloating (Hasdianah, 2012). Metformin works by suppressing hunger in sufferers. Glimepiride, which belongs to the Sulfonylurea group, works by increasing insulin secretion. Metformin and Glimepiride can be used as combination drugs because Metformin and Glimepiride complement each other's actions (Gumantara & Oktarlina, 2017).

This research is in line with research conducted by Maulidya & Oktianti (2021) the most widely used combination oral antidiabetic, namely the combination of Metformin and Glimepiride (38%). Metformin and Glimepiride have mutually reinforcing ways of working and Metformin and Glimepiride have a synergistic effect so that the 2 Biguanid and Sulfonylurea drug classes affect insulin sensitivity.

Effectiveness of oral antidiabetic use

The effectiveness of using oral antidiabetic drugs was obtained by 15 patients who were controlled (38.9%) and those who were not controlled were obtained by data for (61.1%) as many as 21 patients. The most controlled patients were the use of combined oral antidiabetics, namely the use of Metformin combined with Glimepiride (31.2%) in 13 patients. 2 patients were using the single oral antidiabetic Glimepiride (1.95%). In this study, many patients had uncontrolled transient blood glucose levels. From the data obtained, only 15 patients had controlled glucose levels, while 21 patients were not controlled. These results can be seen in Table 7.

Table 7. Effectiveness of using oral antidiabetics as a lowering of blood glucose levels in DM patients at UPTD Gembong Health Center

Information	Number of Patients	Percentage (%)	Drug Type	Number of Patients	Percentage of Decreased Blood Glucose Levels During (%)
Controlled	15	38,9	Glimepiride	2	5,19
			Metformin + Glimepiride	13	33,71
Not controlled	21	61,1	Glimepiride	5	14.55
			Metformin + Glimepiride	16	46.55
Total	36	100			100

Increased blood glucose levels in patients with Diabetes Mellitus are caused by less physical activity in Diabetes Mellitus patients because increasing age can also affect the physical activity carried out. Eating patterns that are not as recommended can cause an increase in blood glucose levels in patients with Diabetes Mellitus because they consume lots of sugar and foods that contain lots of sugar. A good diet can also affect blood glucose levels by eating according to recommendations, consuming enough fiber, and reducing excessive sugar consumption (Rasdianah et al., 2016).

The control of blood glucose levels in type 2 diabetes mellitus patients is due to patient compliance factors in taking diabetes mellitus medication. The more obedient diabetes mellitus patients are in taking oral antidiabetics (ADO), the more controlled their blood glucose levels will be. Based on data taken at the UPTD Gembong Health Center, Pati Regency, many patients are disobedient in taking oral antidiabetic drugs due to activities carried out or forgetting to take oral antidiabetics so that blood glucose levels in type 2 diabetes mellitus patients are uncontrolled (Fandinata & Darmawan, 2020).

According to research conducted by Zulfh & Muflihatin (2020), many patients are controlled because patients are compliant with taking medication. Glucose levels can be controlled because of the factors

of gender and also the disease and also other drugs, and because of the medication adherence factor of DM patients. The high patient compliance in controlling blood glucose levels in patients with diabetes mellitus can also affect blood glucose levels to be more controlled.

According to research conducted by Hauri & Faridah (2019), the use of combined oral antidiabetics that is used to increase the effectiveness of therapy of oral antidiabetic drugs used which are intended to be used as lowering blood glucose levels in patients with type 2 diabetes mellitus used is Metformin in combination with glimepiride as much as 61% as many as 36 patients. The mechanism of action of biguanide 47 (metformin) is to increase beta-cell insulin secretion. The sulfonylurea group (glimepiride) can be combined because the biguanide group has a strong mechanism of action for each drug.

CONCLUSION

Patients with DM at the UPTD Gembong Health Center, Pati Regency, were mostly female (72,8%), aged 51-60 years (50,0%), and housewives (58,3%). The use of oral antidiabetics for outpatients at the UPTD Gembong Health Center, Pati Regency has effectiveness in reducing blood glucose levels in DM patients. The use of oral antidiabetic drugs in outpatients showed controlled blood glucose levels in 15 patients (38,9%) and those that were not controlled in 21 patients (61,1%).

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