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The Effectiveness of Metformin and Glimepiride Therapy on Reducing Blood Glucose Levels in Patients with Diabetes Mellitus

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A B S T R A C T

Diabetes mellitus is a chronic condition that occurs when the pancreas can no longer produce insulin or the body cannot effectively use the insulin it produces. This study aims to determine the effectiveness of metformin and glimepiride in reducing blood glucose levels in diabetes mellitus patients. The study is observational with a cross-sectional retrospective approach, conducted at Puskesmas Balerejo Madiun in February 2024 with a total of 48 respondents. Data analysis was performed using the Mann-Whitney test. Demographic data showed that 25 respondents (52.1%) were female, 28 respondents (58.3%) were aged 36-45 years, 22 respondents (45.8%) had a high school education, 14 respondents (29.2%) were farmers/livestock traders/vendors, and 21 respondents (43.8%) had a normal BMI. The pre-treatment mean fasting blood glucose (FBG) for metformin was 171.96±82.737 and post-treatment was 143.88±58.062. For glimepiride, the pre-treatment mean FBG was 178.21±67.791 and post-treatment was 152.08±63.959

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INTRODUCTION

According to PERKENI (2021), diabetes mellitus is a chronic condition that occurs when the pancreas can no longer produce insulin or when the body cannot effectively utilize the insulin it produces. Diabetes mellitus is a metabolic disorder characterized by elevated blood glucose levels, commonly referred to as hyperglycemia, and is accompanied by symptoms such as frequent urination, increased hunger, and excessive thirst. This condition arises due to abnormalities in insulin secretion, insulin action, or both (PERKENI, 2021).

According to the International Diabetes Federation (IDF) in 2021, an estimated 537 million people aged 20–79 years worldwide were living with diabetes mellitus. Indonesia ranked fifth globally, with approximately 19.47 million individuals affected. Based on the Basic Health Research (RISKESDAS) report, there has been a significant increase in the prevalence of diabetes mellitus in Indonesia, from 6.9% in 2013 to 8.5% in 2018, or approximately 20.4 million people (Kemenkes RI, 2021). The East Java Provincial Health Profile (2022) reported that diabetes mellitus ranked second after hypertension, with a total of 172,917 cases (Dinkes Jatim, 2022).

Diabetes mellitus can lead to chronic complications, which typically emerge after the patient has had the disease for a prolonged period (Maulidya & Oktianti, 2021). Prevention of diabetes mellitus can be achieved by maintaining blood glucose levels close to normal, which involves adhering to regular and consistent medication therapy (Muhaymin & Andini, 2023).

The observable symptoms in individuals with diabetes mellitus include weight loss, polydipsia, polyuria, and polyphagia. Other symptoms may include blurred vision, itching, paresthesia, erectile dysfunction in males, pruritus vulvae in females, and general fatigue (PERKENI, 2021).

The success of therapy in diabetes mellitus patients can be assessed by a decrease in fasting blood glucose levels to within the range of 70–110 mg/dL (Fathurrahman et al., 2023). Indicators of successful diabetes mellitus treatment include controlled blood glucose levels, which may reduce the risk of various acute complications, improve quality of life, and lower diabetes-related morbidity and mortality(Suciati & Alfian, 2022). Treatment success can also be evaluated using both laboratory and clinical data. Laboratory indicators include random blood glucose (RBG), fasting blood glucose (FBG), 2-hour postprandial blood glucose (2h-PPBG), and glycated hemoglobin (HbA1c) (PERKENI, 2021).

A study conducted by Dwiputra et al. (2023) found a significant difference in the effectiveness of metformin and glimepiride in reducing blood glucose levels, with a p-value of <0.05. It was concluded that metformin was more effective in lowering fasting blood glucose compared to glimepiride among outpatient type 2 diabetes mellitus (T2DM) patients at RSD Mangusada Badung

(Dwiputra et al., 2023). However, these findings differ from another study which found no significant efficacy difference between glimepiride and metformin in lowering blood glucose levels among T2DM outpatients at "X" Hospital in Jambi City, with a p-value of 0.933 (p>0.05) (Defirson & Azizah, 2021).

Based on the aforementioned background, the researcher is interested in investigating "The Effectiveness of Metformin and Glimepiride Therapy on Reducing Blood Glucose Levels in Patients with Diabetes Mellitus".

LITERATURE REVIEW

According to the study conducted by Dwiputra (2023), the majority of participants were male, totaling 59 respondents (61.5%), with the highest age distribution in the 65–74 year group (34 respondents, 35.4%). Additionally, 52 respondents (54.2%) had a family history of type 2 diabetes mellitus (T2DM), and 39 respondents (40.6%) had a body mass index (BMI) of 25–29.9, classified as overweight or obese. In the first month of therapy, the average fasting blood glucose (FBG) level with metformin was lower at 141.45 mg/dL compared to glimepiride, which had an average FBG of 146.60 mg/dL. In the second month, metformin also showed a lower average FBG of 131.37 mg/dL compared to 136.87 mg/dL for glimepiride. By the third month, the average FBG for metformin was again lower at 124.06 mg/dL compared to 129.79 mg/dL for glimepiride. The results indicated that metformin monotherapy was effective in reducing fasting blood glucose levels in 36 patients (75%), whereas glimepiride monotherapy was effective in 25 patients (52.1%). A statistically significant difference was found in the effectiveness of metformin and glimepiride in lowering blood glucose levels, with a p-value of <0.05 (Dwiputra et al., 2023).

In a separate study by Hisyam (2023), the fasting blood glucose (FBG) levels of patients before receiving metformin therapy ranged from 94 to 306 mg/dL, with an average of 163 mg/dL. After three months of metformin therapy, FBG levels ranged from 62 to 259 mg/dL, with an average of 148 mg/dL. However, this study found no statistically significant difference in the control of fasting blood glucose (ΔFBG) among patients treated with metformin, combination therapy, or glimepiride. This conclusion was supported by the statistical analysis showing a significance value of 0.575, which is greater than the threshold of 0.05, indicating no meaningful difference in glucose control between the three treatment groups (Hisyam, 2023).

METHODOLOGY

The type of research used in this study was observational with a retrospective cross-sectional approach. Secondary data were collected from the medical records of diabetes mellitus patients from the year 2024. Data collection was conducted using purposive sampling. The inclusion criteria were: patients diagnosed with diabetes mellitus who were undergoing outpatient treatment at Balerejo Public Health Center, Madiun; aged over 18 years; and patients using single-dose metformin or glimepiride therapy. The exclusion criteria included unreadable medical records, patients who were referred to other facilities, and patients who had died. Data collection involved reviewing laboratory results of fasting blood glucose (FBG) levels. FBG levels were then re-evaluated after three months of metformin or glimepiride therapy at Puskesmas Balerejo, Madiun. This study was conducted at Balerejo Public Health Center, Madiun in February 2024. A total of 48 respondents were included in the sample. Data were analyzed using the Mann–Whitney U test to determine the effectiveness of metformin and glimepiride therapy in reducing blood glucose levels in patients with diabetes mellitus.

RESEARCH RESULT

Demographic Characteristics of Diabetes Mellitus Patients

Based on the collected data, the majority of respondents were female (25 respondents, 52.1%) and male (23 respondents, 47.9%). The largest age group was 36–45 years old (28 respondents, 58.3%), followed by 46–55 years (13 respondents, 27.1%) and 26–35 years (7 respondents, 14.6%). In terms of educational background, 22 respondents (45.8%) had completed senior high school, 8 respondents (16.7%) had completed junior high school, 8 respondents (16.7%) had tertiary education, 7 respondents (14.6%) had completed elementary school, and 3 respondents (6.3%) had no formal education.

Regarding occupation, the distribution was as follows: 14 respondents (29.2%) were farmers, livestock breeders, or traders; 12 respondents (25.0%) were civil servants; 7 respondents (14.6%) were housewives; 6 respondents (12.5%) were in other occupations; 5 respondents (10.4%) were private employees; and 4 respondents (8.3%) were entrepreneurs.

Based on Body Mass Index (BMI), 21 respondents (43.8%) had a normal BMI (18.5–22.9 kg/m²), 19 respondents (39.6%) were overweight (23–29.9 kg/m²), 6 respondents (12.5%) were underweight (<18.5 kg/m²), and 2 respondents (4.2%) were classified as obese (≥30 kg/m²).

Table 1. Demographic Characteristics of Diabetes Mellitus Patients

Demografi	f	%
Sex		
Male	23	47.9
Female	25	52.1
Age Group (years)		
26–35	7	14.6
36–45	28	58.3
46–55	13	27.1
Education Level		
No formal education	3	6.3
Elementary school	7	14.6
Junior high school	8	16.7
Senior high school	22	45.8
Tertiary education	8	16.7
Occupation		
Unemployed / Housewife	7	14.6
Farmer / Breeder / Trader	14	29.2
Entrepreneur / Self-employed	4	8.3
Private sector employee	5	10.4
Civil servant	12	25.0
Others	6	12.5
Body Mass Index (BMI)		
Underweight (<18.5 kg/m^2)	6	12.5
Normal (18.5–22.9 kg/m^2)	21	43.8
Overweight (23–29.9 kg/m^2)	19	39.6
Obese (≥30 kg/m^2)	2	4.2

Blood Glucose Levels in Patients with Diabetes Mellitus

Based on the collected data, the total sample consisted of 48 respondents, with 24 respondents assigned to the metformin group and 24 to the glimepiride group. The mean fasting blood glucose (FBG) level in the metformin group before treatment was 171.96 ± 82.737 mg/dL, and after treatment it decreased to 143.88 ± 58.062 mg/dL. In the glimepiride group, the pre-treatment mean FBG level was 178.21 ± 67.791 mg/dL, and the post-treatment value was 152.08 ± 63.959 mg/dL. The minimum and maximum pre-treatment FBG levels in the metformin group were 87 mg/dL and 445 mg/dL, respectively, while post-treatment values ranged from 85 mg/dL to 289 mg/dL. In the glimepiride group, the pre-treatment FBG levels ranged from 87 mg/dL to 332 mg/dL, and post-treatment levels ranged from 84 mg/dL to 300 mg/dL.

Tabel 2. Blood Glucose Level

Drug	FBG	N	Mean	Median	SD	Minimum	Maximum
Metformin	FBG pre	24	171.96	138.00	82.737	87	445
	FBG post	24	143.88	122.50	58.062	85	289
Glimepirid	FBG pre	24	178.21	168.50	67.791	87	332
	FBG post	24	152.08	134.50	63.959	84	300

Effectiveness of Diabetes Mellitus Drug Therapy

In this study, the effectiveness of metformin and glimepiride therapy in reducing fasting blood glucose (FBG) levels in patients with diabetes mellitus was analyzed using the Wilcoxon test. The results of the Wilcoxon test in Table 3 indicate that both metformin and glimepiride therapies are effective in reducing fasting blood glucose (FBG) levels, as shown by the p-value of 0.000 ($p < 0.05$) for each treatment. Furthermore, the Mann–Whitney test was used to compare the effectiveness between the two drugs. The analysis showed no significant difference in the effectiveness of metformin versus glimepiride in reducing FBG levels, with a p-value of 0.781 (>0.05).

Tabel 3. Effectiveness of Metformin and Glimepiride Therapy

Drug	N	*Sig. (wilcoxon)*	*Sig. (mann-whitney)*
Metformin	24	0.000	0.781
	24		
Glimepirid	24	0.000	
	24		

DISCUSSION

Based on the 2021 guidelines by the Indonesian Society of Endocrinology (PERKENI), laboratory tests for diagnosing diabetes and prediabetes include the following criteria:

Table 4. Laboratory Tests to Diagnose Diabetes and Prediabetes Include Criteria

	HbA1c (%)	Fasting Blood Glucose (mg/dL)	2-Hour Post-Oral Glucose Tolerance Test (OGTT) Plasma Glucose (mg/dL)
Diabetes	≥ 6,5	≥ 126	≥ 200
Pre-Diabetes	5,7 – 6,4	100 – 125	140 – 199
Normal	< 5,7	70 – 99	70 – 139

Diabetes mellitus can lead to chronic complications, which generally appear after a prolonged duration of the disease (Maulidya & Oktianti, 2021). These complications can be prevented by maintaining optimal blood glucose levels. According to PERKENI (2021), normal blood glucose levels include fasting blood glucose (FBG) at 70–99 mg/dL, 2-hour postprandial glucose (2h-PPG) at 70–139 mg/dL, and hemoglobin A1c (HbA1c) at <5.7%. Controlling diabetes mellitus by maintaining blood glucose near normal levels can be achieved through regular and consistent therapy(Muhaymin & Andini, 2023).

Table 5. Classification of Antihyperglycemic Agents (PERKENI, 2021)

Drug Class	**Main Mechanism of Action**	**Common Side Effects**	**HbA1c Reduction (%)**
Biguanide	Reduces hepatic glucose production and increases insulin sensitivity	Dyspepsia, diarrhea, lactic acidosis	1.0 – 1.3
Thiazolidinedione	Increases insulin sensitivity	Edema	0.5 – 1.4
Sulfonylurea	Increases insulin secretion	Weight gain, hypoglycemia	0.4 – 1.2
Glinide	Increases insulin secretion	Weight gain, hypoglycemia	0.5 – 1.0
Alpha-glucosidase inhibitor	Delays glucose absorption	Flatulence, soft stools	0.5 – 0.8

DPP-4 inhibitor	Enhances insulin secretion and inhibits glucagon secretion	Nausea, vomiting	0.5 – 0.9
SGLT-2 inhibitor	Inhibits glucose reabsorption in the distal tubules	Urinary and genital infections	0.5 – 0.9

Metformin, classified under the biguanide class, lowers blood glucose levels by reducing hepatic glucose production, decreasing intestinal glucose absorption, and increasing insulin sensitivity. Therefore, metformin is effective in reducing both fasting and postprandial blood glucose levels. Metformin also plays a role in the management of polycystic ovary syndrome (PCOS) by reducing insulin levels, which leads to a decrease in luteinizing hormone and androgen levels (Corcoran & Jacobs, 2023). Glimepiride, a sulfonylurea, acts on ATP-sensitive potassium channels on pancreatic beta-cell membranes, causing iatrogenic depolarization by preventing potassium efflux. This depolarization activates voltage-dependent calcium channels, increasing intracellular calcium concentration and triggering insulin exocytosis into the bloodstream. The released insulin binds to cell membrane receptors, inducing GLUT-4 expression and glucose uptake into cells, thereby lowering blood glucose levels (Trerattanavong & Tadi, 2023).

CONCLUSIONS AND RECOMMENDATIONS

The results of this study showed that the mean fasting blood glucose (FBG) level in the metformin group decreased from 171.96 ± 82.737 mg/dL (pre-treatment) to 143.88 ± 58.062 mg/dL (post-treatment). In the glimepiride group, the mean FBG level decreased from 178.21 ± 67.791 mg/dL (pre-treatment) to 152.08 ± 63.959 mg/dL (post-treatment). The minimum and maximum FBG values in the metformin group were 87 mg/dL and 445 mg/dL (pre-treatment), and 85 mg/dL and 289 mg/dL (post-treatment), respectively. In the glimepiride group, the minimum and maximum values were 87 mg/dL and 332 mg/dL (pre-treatment), and 84 mg/dL and 300 mg/dL (post-treatment), respectively. Statistical analysis indicated that both metformin and glimepiride therapies were effective in reducing fasting blood glucose levels (p-value = 0.000, which is < 0.05). However, the results also showed that there was no significant difference in the effectiveness of metformin and glimepiride therapies in lowering FBG levels among patients with diabetes mellitus (p-value = 0.781, which is > 0.05).

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