

Weight Gain in Type 2 Diabetes Mellitus Patients Receiving Sulfonylurea Medications at a Tertiary Hospital in Surabaya, Indonesia

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ABSTRACT

Introduction: Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by persistent hyperglycemia. The prevalence of diabetes in Indonesia is 1.5%, although East Java recorded a 2.1% rate in 2013. T2DM medications, such as sulfonylureas, may lead to hypoglycemia and weight gain. This study aimed to investigate the weight gain effects of sulfonylureas in T2DM patients at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia.

Methods: This retrospective cross-sectional study used retrograde anamnesis on 41 T2DM patients receiving sulfonylurea medications for the preceding six months. The data were collected from medical records and interviews with the T2DM patients who received treatment at the Internal Medicine Clinic of Dr. Soetomo General Academic Hospital from January to June 2022.

Results: Most patients were 46–65 years old (73.2%), female (51.2%), and had been diabetic for over 15 years (48.8%). The predominant medications administered to the patients were glimepiride (41.4%) and a combination of glibenclamide 5 mg, metformin 500 mg, and acarbose 100 mg (19.5%). Almost all patients took their medications in the morning before meals (92.6%). The average weight gain was 4.6 kg, with the glibenclamide and metformin combination resulting in a 17% incidence.

Conclusion: T2DM patients who use sulfonylureas generally gain weight and exhibit specific traits, including being middle-aged, female, and diabetic for multiple years. The most commonly used sulfonylureas are glimepiride for monotherapy and glibenclamide for combination therapy with metformin and acarbose. Future research is required to understand weight gain in T2DM patients treated with sulfonylureas more comprehensively.

Keywords: Type 2 diabetes mellitus (T2DM); metabolic disorder; glimepiride; hypoglycemia; weight

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Highlights:

1. This study investigated weight changes in type 2 diabetes mellitus (T2DM) patients receiving sulfonylureas, with a special focus on the emergence of weight gain as a new problem in T2DM management.
2. The importance of this study pertains to its findings regarding weight gain in T2DM patients treated with sulfonylureas, offering additional data that aids in preventing adverse effects of the medications.

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INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder marked by persistent hyperglycemia, which can result from impaired insulin secretion, resistance to peripheral insulin action, or a combination of both factors. In 2015, approximately 415 million adults aged 20 to 79 years had diabetes mellitus, as reported by the International Diabetes Federation (IDF). This poses a global public health burden, with an estimated

increase to 200 million by 2040 (Goyal et al., 2023). In 2008, the National Institute of Health Research and Development reported prevalence rates of 10.25% for impaired glucose tolerance (IGT) and 5.7% for diabetes mellitus across Indonesian provinces (Yuliani et al., 2014). Without preventive measures, the incidence of diabetes mellitus continues to rise each year. Similar to other most populous countries, Indonesia ranks high globally at the fourth place with 8.4 million cases, following India, China, and the United

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States. Data from the 2013 Basic Health Research indicated that the prevalence of diabetes mellitus in Indonesia was 1.5%, whereas in East Java Province, it reached 2.1%. In 2012, the East Java Provincial Health Office reported that diabetes mellitus was the most prevalent condition among the top ten diseases affecting outpatient hospital visits, with 102,399 cases (Martins et al., 2018). Diabetes mellitus is commonly classified into two types: type 1 and type 2. Type 2 diabetes mellitus (T2DM) is one of the most prevalent metabolic disorders worldwide, arising from a combination of damaged insulin secretion by pancreatic β -cells and tissue insensitivity to insulin, which hinders its response (Galicia-Garcia et al., 2020).

Blood glucose level regulation is a pharmacological intervention used to manage blood sugar in T2DM patients, either as monotherapy or as combination therapy. Oral antidiabetic drugs (OADs), such as sulfonylureas, are recognized for their efficacy in controlling blood glucose levels in diabetes mellitus patients (Kalra et al., 2018). According to the diagnostic criteria established by the American Diabetes Association, patients exhibiting a hemoglobin A1c (HbA1C) level of $\geq 6.5\%$, a fasting blood sugar level of ≥ 126 mg/dL, and a two-hour postprandial blood sugar level of ≥ 200 mg/dL after an oral glucose tolerance test, as well as those presenting classic hyperglycemia symptoms or hyperglycemic crisis with a random blood sugar level of ≥ 200 mg/dL, are considered candidates for diabetes mellitus treatment (Kurniawan, 2010; Genuth et al., 2018). However, it does not imply that OAD therapy is without side effects. Sulfonylurea monotherapy is frequently associated with hypoglycemia in T2DM patients. Hypoglycemia in T2DM patients can lead to increased and possibly uncontrollable appetite, resulting in weight gain and an elevated risk of obesity.

Hardin & Jacobs (2023) have indicated that glibenclamide, which belonged to the sulfonylurea class, had side effects, such as weight gain. Furthermore, a meta-analysis has demonstrated that sulfonylureas are linked to weight gain ranging from 2.01 to 2.3 kg, making them not recommended for T2DM patients with obesity (Apovian et al., 2019). These side effects must be carefully considered, as they can pose health risks if left unaddressed. Uncontrolled weight gain due to sulfonylurea use may lead to new problems, such as obesity, high blood pressure, high cholesterol, abnormal blood lipid levels, and insulin resistance. These issues may have broad societal implications, particularly in Indonesia. Oral antidiabetic drugs are not considered the first-choice therapy for managing T2DM. The primary intervention often overlooked in diabetes mellitus management is lifestyle changes, including maintaining a healthy diet and engaging in physical exercise. Therefore, the use of sulfonylureas necessitates monitoring and, importantly, primary intervention in the form of lifestyle changes. In Indonesia, particularly in Surabaya, there is still limited information regarding weight gain profiles in T2DM patients undergoing sulfonylurea therapy. According to the aforementioned issues, the researchers aimed to investigate the weight gain effects of sulfonylurea therapy in T2DM patients.

METHODS

This descriptive study was conducted using a retrospective cross-sectional design with primary data (Aranaz-Andrés et al., 2017). The research performed retrograde anamnesis on T2DM patients undergoing sulfonylurea therapy at the Internal Medicine Clinic of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, over the last six months. The

data were collected from medical records and interviews with a total of 41 T2DM patients who received treatment from January to June 2022 (Bai et al., 2014). The inclusion criteria were T2DM patients above 18 years old who received sulfonylureas, either as monotherapy or in combination with other medications that do not affect body weight, as well as those with T2DM accompanied by other diseases that do not affect body weight. The exclusion criteria were patients consuming medications with appetite-suppressing effects, patients diagnosed with malignancy that did not affect body weight, and patients with dietary disorders. Those with mental disorders such as depression, thyroid gland disorders, and infectious diseases that do not affect body weight were also excluded from this study. Data obtained from the medical records and interviews with the T2DM patients were compiled. The data from medical records contained information on the patients' age, sex, duration of diabetes, duration of sulfonylurea use, and physical exercise habit. Subsequently, the data were descriptively analyzed and presented in tables and diagrams.

RESULTS

Table 1 presents the sample distribution of the T2DM patients across diverse age groups, with an overall average age of 58.7 years and a standard deviation of 9.4 years. This study focused on patients aged 18 and above. Among the 41 T2DM patients, the predominant age group was 46 to 65 years, comprising 30 individuals (73.2%). The data revealed an absence of patients between the ages of 18 and 25 years (0%). In addition to the patients' age, the data also presented a distribution of sex among the T2DM patients receiving sulfonylureas. Out of the 41 patients, 20 were male (48.8%) and 21 were female (51.2%). Another aspect of the patient profiles presented in the table is the duration of T2DM. The majority of the population had suffered from T2DM for more than 15 years, comprising 20 patients (48.8%). The smallest group had been affected by T2DM for less than a year, comprising one patient (2.4%). The average duration of patients suffering from T2DM was 13.9 years with a standard deviation of 6.5 years. The majority of the T2DM patients, 14 individuals (34.2%), had consumed sulfonylureas for more than 15 years, whereas only one patient (2.4%) had a duration of sulfonylurea use of less than a year. The subsequent aspect of the patient profiles pertained to physical exercise, with 16 patients (39%) regularly exercising and 25 patients (61%) not exercising regularly.

Medication profiles of type 2 diabetes mellitus patients

Table 2 presents data on the medication profiles of T2DM patients receiving sulfonylureas at the Outpatient Unit of Internal Medicine, Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, from January to June 2022. It was found that the patients only used three types of sulfonylureas: gliclazide, glibenclamide, and glimepiride. The most frequently administered medication for T2DM therapy was glimepiride, which was used by 17 patients (41.4%), whereas gliclazide was the least used medication, administered to 11 patients (26.8%). Other oral antidiabetic drugs were used in conjunction with sulfonylureas as combination therapy. In the gliclazide group, six patients (14.6%) were administered the sulfonylurea medication at a dose of 80 mg, along with metformin 500 mg and pioglitazone 15 mg. Meanwhile, only one patient (2.4%) received gliclazide 60 mg and acarbose 100 mg. In the glibenclamide group, eight patients (19.5%) were administered the sulfonylurea medication at a dose of 5 mg, alongside metformin 500 mg and acarbose 100

mg. Simultaneously, one patient (2.4%) was administered glibenclamide 5 mg in conjunction with metformin 500 mg, while another patient (2.4%) received glibenclamide 5 mg, metformin 500 mg, acarbose 100 mg, and pioglitazone 15 mg. In the glimepiride group, the majority of the patients received the sulfonylurea medication at a dose of 4 mg combined with metformin 500 mg and acarbose 100 mg, with a total of four patients (9.8%). Some patients also used medications other than oral antidiabetic drugs, which was still consistent with the inclusion criteria of this study. Specifically, one patient each (2.4%) used either atorvastatin 20 mg, lisinopril 5 mg, or nifedipine 30 mg.

Table 1. Demographic profiles of type 2 diabetes mellitus patients receiving sulfonylureas at the Internal Medicine Outpatient Unit of Dr. Soetomo General Academic Hospital from January to June 2022

Variables	n	%
Age (years)		
18–25	0	0
26–45	2	4.8
46–65	30	73.2
>65	9	22
Average±SD	58.7±9.4	
Sex		
Male	20	48.8
Female	21	51.2
T2DM duration (years)		
<1	1	2.4
1–5	4	9.8
6–10	7	17
11–15	9	22
>15	20	48.8
Average±SD	13.9±6.5	
Duration of SU use (years)		
<1	1	2.4
1–5	5	12.2
6–10	11	26.8
11–15	10	24.4
>15	14	34.2
Physical exercise habits		
Yes	16	39
No	25	61

Notes: SD=standard deviation; SU=sulfonylurea

Sulfonylurea intake profiles of type 2 diabetes mellitus patients

Table 3 displays data on the administration of sulfonylureas in T2DM patients at the Internal Medicine Outpatient Unit of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, from January to June 2022. The administration of sulfonylureas was categorized according to the timing of intake, frequency of intake, and duration of the medication use by the T2DM patients. It was observed that the majority of the patients, totaling 38 individuals (92.6%), consumed sulfonylureas before meals. Only one T2DM patient (2.4%) took the medication during meals. Regarding the frequency of intake, most of the T2DM patients, comprising 32 patients (78%), took sulfonylureas once a day. None of the T2DM patients (0%) consumed the medication three times a day.

Weight profiles of type 2 diabetes mellitus patients

Table 4 presents data on the weight profiles of T2DM patients receiving sulfonylureas at the Internal Medicine Outpatient Unit of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, from January to June 2022. The data revealed that most of the T2DM patients,

including 29 individuals (70.7%), experienced weight gain, with an average increase of 3.7 kg and a standard deviation of 3.7 kg. Additionally, seven patients (17.1%) experienced weight loss, with an average decrease of 15.1 kg and a standard deviation of 18.1 kg. The smallest group consisted of five patients (12.2%) who did not exhibit any increase or decrease in weight.

Table 2. Medication profiles of type 2 diabetes mellitus patients undergoing sulfonylurea therapy at the Internal Medicine Outpatient Unit of Dr. Soetomo General Academic Hospital between January and June 2022

Variables	n	%
SU types		
Gliclazide	11	26.8
Glibenclamide	13	31.8
Glimepiride	17	41.4
OADs		
Gliclazide 60 mg + acarbose 100 mg	1	2.4
Gliclazide 60 mg + metformin 500 mg	3	7.3
Gliclazide 80 mg + metformin 500 mg + acarbose 100 mg	6	14.6
Gliclazide 80 mg + metformin 500 mg + pioglitazone 15 mg	1	2.4
Glibenclamide 5 mg + metformin 500 mg	1	2.4
Glibenclamide 5 mg + metformin 500 mg + acarbose 100 mg	8	19.5
Glibenclamide 5 mg + metformin 500 mg + pioglitazone 15 mg	3	7.3
Glibenclamide 5 mg + metformin 500 mg + acarbose 100 mg + pioglitazone 15 mg	1	2.4
Glimepiride 1 mg + metformin 500 mg + pioglitazone 15 mg	1	2.4
Glimepiride 2 mg + metformin 500 mg	3	7.3
Glimepiride 2 mg + pioglitazone 30mg	1	2.4
Glimepiride 2 mg + metformin 500 mg + pioglitazone 15 mg	1	2.4
Glimepiride 3 mg + metformin 500 mg	1	2.4
Glimepiride 3 mg + metformin 500 mg + acarbose 100 mg	1	2.4
Glimepiride 3 mg + metformin 500 mg + pioglitazone 15 mg	1	2.4
Glimepiride 4 mg + acarbose 100 mg	1	2.4
Glimepiride 4 mg + metformin 500 mg + acarbose 100 mg	4	9.8
Glimepiride 4 mg + metformin 500 mg + acarbose 100 mg + pioglitazone 15 mg	3	7.3
Administration of OADs		
OADs and atorvastatin 20mg	1	2.4
OADs and lisinopril 5 mg	1	2.4
OADs and nifedipine 30mg	1	2.4
OAD monotherapy	38	92.7

Notes: SU=sulfonylurea; OAD=oral antidiabetic drug.

Table 3. Sulfonylurea intake profiles of type 2 diabetes mellitus patients at the Internal Medicine Outpatient Unit of Dr. Soetomo General Academic Hospital from January to June 2022

Variables	n	%
Timing of intake		
Before meals	38	92.6
During meals	1	2.4
After meals	3	7.3
Frequency of intake		
Once a day	32	78
Twice a day	9	22
Three times a day	0	0

Table 4. Weight profiles of type 2 diabetes mellitus patients receiving sulfonylureas at the Internal Medicine Outpatient Unit of Dr. Soetomo General Academic Hospital in January-June 2022

Variables	n	%	Average±SD
Weight			
Increase	29	70.7	3.7±3.7
Decrease	7	17.1	15.1±18.1
Constant	5	12.2	

Note: SD=standard deviation.

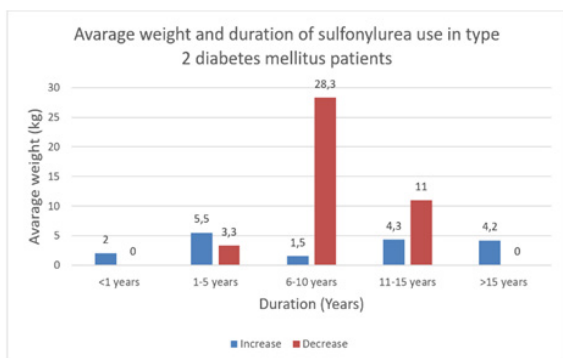


Figure 1. Average weight changes and sulfonylurea use duration in type 2 diabetes mellitus patients at the Internal Medicine Outpatient Unit of Dr. Soetomo General Academic Hospital from January to June 2022

Figure 1 illustrates the data regarding the average weight fluctuations and the duration of sulfonylurea use in T2DM patients at the Internal Medicine Outpatient Unit of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, from January to June 2022. Patients with a duration of sulfonylurea use ranging from one to five years exhibited the highest weight gain, with an average increase of 5.5 kg, in comparison to those with shorter or longer usage durations. Patients who consumed sulfonylureas for six to ten years exhibited minimal weight gain, with an average increase of 1.5 kg. On the other hand, this group demonstrated the most severe weight loss, with an average decrease of 28.3 kg. Those who were on sulfonylureas for less than a year and for more than 15 years did not experience weight loss.

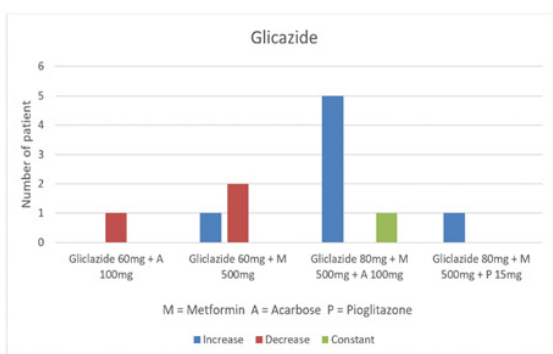


Figure 2. Weight profiles of type 2 diabetes mellitus patients undergoing gliclazide therapy at the Internal Medicine Outpatient Unit of Dr. Soetomo General Academic Hospital in January-June 2022

Figure 2 displays the weight profiles of T2DM patients who received gliclazide therapy at the Internal Medicine Outpatient Unit of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, during the period from January to June 2022. The patients who experienced weight gain were mostly found in the group that consumed gliclazide 80 mg, metformin 500 mg, and acarbose 100 mg, comprising five individuals (12.1%). No weight gain (0%) was found in the group that received gliclazide 60 mg and acarbose 100 mg. The majority of patients experiencing weight loss were found in the group consuming gliclazide 60 mg and metformin 500 mg, amounting to two individuals (4.8%).

In addition, only one patient (2.4%), belonging to the group that ingested gliclazide 80 mg, metformin 500 mg, and acarbose 100 mg, did not experience any weight gain or loss.

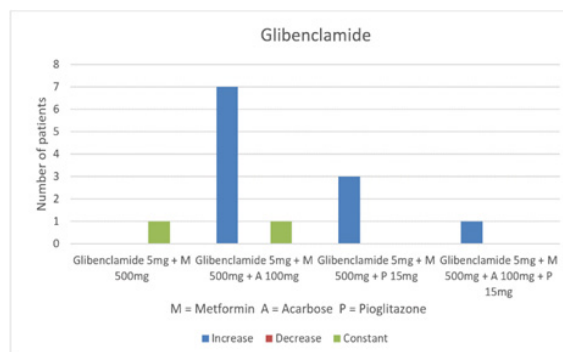


Figure 3. Weight profiles of type 2 diabetes mellitus patients receiving glibenclamide therapy at the Internal Medicine Outpatient Unit of Dr. Soetomo General Academic Hospital between January and June 2022

Figure 3 presents the weight profiles of T2DM patients who received glibenclamide therapy at the Internal Medicine Outpatient Unit of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, from January to June 2022. Patients receiving a combination of glibenclamide 5 mg, metformin 500 mg, and acarbose 100 mg showed the highest incidence of weight gain, with a total of seven patients (17%). The least incidence of weight gain was observed in the group of patients receiving glibenclamide 5 mg, metformin 500 mg, acarbose 100 mg, and pioglitazone 15 mg, with only one patient (2.4%). On the other hand, merely two patients had constant weight, comprising one individual who consumed glibenclamide 5 mg and metformin 500 mg (2.4%) and another individual (2.4%) who was administered glibenclamide 5 mg, metformin 500 mg, and acarbose 100 mg.

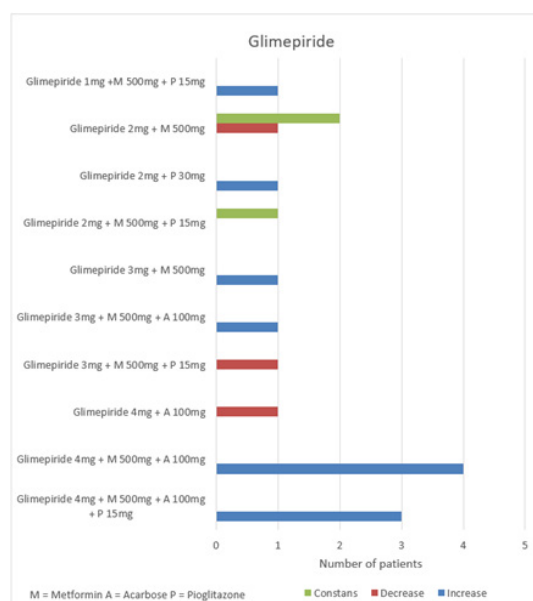


Figure 4. Weight profiles of type 2 diabetes mellitus patients receiving glimepiride therapy at the Internal Medicine Outpatient Unit of Dr. Soetomo General Academic Hospital between January and June 2022

Figure 4 illustrates the weight profiles of T2DM patients undergoing glimepiride therapy at the Internal Medicine Outpatient Unit of Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, from January to June 2022. In patients receiving a combination of glimepiride 1 mg, metformin 500 mg, and pioglitazone 15 mg, only one individual (2.4%) experienced weight gain. Among patients receiving a combination of glimepiride 2 mg and metformin 500 mg, two individuals (4.9%) maintained a constant weight, whereas an individual (2.4%) experienced weight loss. There was one patient (2.4%) who gained weight in each group that consumed the following combinations: (1) glimepiride 2 mg and pioglitazone 30 mg; (2) glimepiride 3 mg and metformin 500 mg; and (3) glimepiride 3 mg, metformin 500 mg, and acarbose 100 mg. A patient (2.4%) who was administered glimepiride 2 mg in conjunction with metformin 500 mg and pioglitazone 15 mg had constant weight. Weight loss was observed in a patient (2.4%) who received glimepiride 3 mg, metformin 500 mg, and pioglitazone 15 mg, as well as in an individual administered with a combination of glimepiride 4 mg and acarbose 100 mg. In addition, weight gain was also noted in four patients (9.8%) who received a combination of glimepiride 4 mg, metformin 500 mg, and acarbose 100 mg, as well as in three individuals (7.3%) who were administered a combination of glimepiride 4 mg, metformin 500 mg, acarbose 100 mg, and pioglitazone 15 mg.

DISCUSSION

Type 2 diabetes mellitus patients receiving sulfonylureas categorized by age groups

This study collected research samples at Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, from January to June 2022. The findings indicated that the T2DM patients consuming sulfonylureas were predominantly in the 46–65 age group (73.2%), with no research subjects in the 18–25 age group (0%). Data on the patients' age were presented as averages and standard deviations in this study, although alternative representations, such as medians, can also be used. The findings of this study are similar to those of prior research conducted in Denpasar, Indonesia, specifically at Bali Mandara Regional General Hospital, Wangaya Regional General Hospital, and Puri Raharja General Hospital, where 59 (73.8%) out of 80 samples were between 46 and 65 years old, with no samples in the 18–25 age group (Wikannanda et al., 2023).

A previous study conducted by Reddy et al. (2022) revealed that all countries examined exhibit an 80% increase in the prevalence of T2DM, predominantly affecting individuals between the ages of 45 and 64 years. T2DM usually emerges later in life as a consequence of obesity during adolescence, which is currently on the rise. T2DM in adults is anticipated to be more common over the next two decades. One of the unmodifiable risk factors for T2DM, influencing its occurrence, is age above 45 years (Utomo et al., 2020). At this age, the body begins to undergo degenerative processes, such as the decline in pancreatic beta cell function and insulin secretion. Older adults are also more susceptible to obesity and an increase in visceral fat levels, which raises the risk of developing diabetes mellitus. Furthermore, the American Diabetes Association (2022) asserts that the risk of T2DM increases with age. An increased accumulation of abdominal fat, resulting in central obesity, is responsible for the increased risk of T2DM in older adults.

Patients with type 2 diabetes mellitus receiving sulfonylureas categorized by sex

The results of this study indicated that among T2DM patients receiving sulfonylureas, 48.8% were male, while 51.2% were female. Therefore, the majority of the research subjects were female. This aligns with prior research carried out by Wikannanda et al. (2023), who found that out of 80 samples, 41 (51.2%) were female. Another study conducted by Komariah & Rahayu (2020) revealed similar findings, indicating that 81 patients (60.4%) were female. This might be attributed to women's higher body mass index, rendering them more susceptible to diabetes (de Ritter et al., 2020). Consequently, women exhibit a greater concern about undergoing health examinations in comparison to men. Sex categories are considered a risk factor for diabetes mellitus. Women are more vulnerable to diabetes mellitus due to a comparatively less healthy lifestyle than men. Additionally, elderly women are more likely to be unemployed compared to men, and post-menopausal conditions are more prone to arise due to hormonal processes (Rita, 2018).

The findings of this study contrast with those of a separate study involving 590 T2DM patients (Ali et al., 2023). Of the total, 310 subjects (52.5%) were male, while 280 individuals (47.5%) were female. The average age for men and women was 57.46 ± 14.93 and 50.38 ± 14.85 , respectively. Prior research conducted at Divari Medical Center, Manokwari, Indonesia, presented data indicating that prescriptions for anti-diabetic drugs were predominantly given to men, amounting to 32 prescriptions (52.94%) (Taborat, 2022). However, Isnaini & Ratnasari (2018) determined that sex categories do not have a significant effect on the prevalence of T2DM cases, as evidenced by a p-value of 0.63. Furthermore, sex categories may not affect blood sugar level fluctuations in T2DM patients, as both men and women have an equal risk of suffering from the disease. Blood sugar levels in diabetic patients may vary by sex due to other influencing factors (Boku, 2019).

Durations of type 2 diabetes mellitus in patients consuming sulfonylureas

The data in this study, which were obtained from medical records, included information about the durations of patients' suffering from T2DM. The majority of the patients, specifically 20 individuals (48.8%), had suffered from diabetes mellitus for over 15 years. This is in line with prior research conducted by Simanjuntak & Simamora (2020), who utilized various classifications of suffering durations. The findings indicated that the respondents had suffered from T2DM for multiple years, predominantly more than five years. In contrast, another study, presenting data only in the form of averages and standard deviations, indicated that the suffering durations for diabetes mellitus patients were 2.07 ± 0.72 years in men and 1.88 ± 0.66 years in women (Ali et al., 2023).

Patients who have suffered from diabetes mellitus for more than ten years, especially the elderly, have a diminished quality of life, particularly in physical aspects, social relationships, independence, and social participation. Independence and social relationships in diabetes mellitus patients tend to diminish each year due to the debilitating effects of the disease. Furthermore, after more than ten years of suffering from diabetes mellitus, there is a high likelihood of limitations in functional capacity, as well as pain and discomfort. This may negatively impact

daily activities, increasing feelings of sadness, social isolation, and fear of death. Additionally, the reduction in independence and decision-making ability can affect self-esteem, leading to a lack of health awareness. This ultimately reduces the ability for self-care and potentially results in the emergence of unaddressed health problems related to T2DM (Pelawi & Fauzia, 2022).

Durations of sulfonylurea use in type 2 diabetes mellitus patients

This study demonstrated that the majority of the T2DM patients, amounting to 14 patients (34.2%), had consumed sulfonylureas for over 15 years. Prior research reported by Purwakanthi et al. (2020) revealed that the predominant durations of diabetes mellitus drug use were more than a year to three years as well as more than five years, with 30 individuals in each duration category. Other participants disclosed that 16 individuals had utilized diabetes mellitus medications for more than five years, 15 individuals for less than a year, and 10 individuals for a duration ranging from more than three years to five years. The findings indicate similarities with the data obtained in this study. Findings from a study conducted at the Enemawira Community Health Center in Sangihe Islands Regency, Indonesia, differ slightly from this study, as the data indicated that most patients had been on medication for less than five years, amounting to 48 patients (75%) (Bidulang et al., 2021).

The duration of treatment corresponds directly to the duration of suffering from diabetes. Patients diagnosed with diabetes should receive prompt treatment according to the four pillars of diabetes care. An increase in plasma insulin levels is considered the cause of weight gain, leading to the utilization of glucose and other metabolic fuels. The duration of diabetes has a significant relationship with a patient's lifespan, quality of life, and management of T2DM. Prolonged suffering from T2DM diminishes quality of life, complicating diabetes management and making it more difficult to handle (Pelawi & Fauzia, 2022).

Exercise habits of type 2 diabetes mellitus patients receiving sulfonylureas

This study presents data on the physical exercise habits of T2DM patients who were on sulfonylurea therapy. The majority of the patients, comprising 25 individuals (61%), did not engage in any form of exercise. This contrasts with an earlier study where 84.2% of the respondents engaged in regular exercise and achieved the targets of diabetes mellitus management (Karamoy & Dharmadi, 2019). Meanwhile, 15.8% of the respondents exercised irregularly and failed to reach the targets of diabetes mellitus management. Prior research indicated that 49 elderly individuals did not engage in physical exercise, while 29 demonstrated an exercise habit (Rita, 2018). In 2015, a predominant proportion of respondents in the working area of the Nanggalo Community Health Center, Padang, Indonesia, demonstrated an absence of physical exercise habits (62.8%). Similarly, another study conducted by Nasution et al. (2021) revealed that 82.6% of the case group exhibited insufficient physical activity, whereas the control group engaged in physical activity at a rate of 60.9%.

Although physical exercise habit may be a crucial variable, several other factors could possibly explain why the majority of T2DM patients in this study lacked such habit. The majority of the elderly individuals claimed to be too lazy to exercise and preferred sitting at home rather

than participating in health-professional-led exercises. They were unaware that infrequent exercise could lead to diabetes mellitus (Rita, 2018). This study mostly involved patients of advanced age, predominantly within the age group of 46–65 years, followed by those above 65 years old. According to the World Health Organization, advanced age is classified as follows: ages 45 to 60 as middle age; ages 60 to 75 as elderly; ages 75 to 90 as old; and ages above 90 as very old (Sabilla et al., 2020).

Types of medication administered to type 2 diabetes mellitus patients

The results of this study revealed that glimepiride was the predominant sulfonylurea administered to the T2DM patients, totaling 17 patients (41.4%). This is consistent with earlier research conducted by Taborat (2023), who observed that the most frequently prescribed oral antidiabetic was glimepiride, accounting for 41 prescriptions (39.05%). Other medications administered to patients in the study included metformin with 39 prescriptions (37.14%), galvus with 18 prescriptions (17.14%), gliquidone with 5 prescriptions (4.76%), and glibenclamide with 2 prescriptions (1.91%). However, in another study conducted by Jonathan et al. (2019), gliquidone emerged as the most commonly used sulfonylurea, received by 8 (7%) to 15 (13%) patients, with the frequency peaking in February and declining in December. Gliclazide was administered to two (1.7%) to seven (6.1%) patients, while glimepiride was prescribed to fewer than five patients (5%). The findings of this study are corroborated by prior research, which demonstrated the pattern of oral antidiabetic drug use in outpatient T2DM patients at a hospital in Gianyar, Indonesia. The most common type of sulfonylureas used by the patients was glimepiride (22.22%), administered at a dose of 2 mg once a day (Sujayanti & Kurnianta, 2022).

Glimepiride is a second-generation sulfonylurea that received approval from the U.S. Food and Drug Administration (FDA) in 1995 for treatment of patients with T2DM. This group of drugs primarily increases insulin secretion by pancreatic beta cells, with strong hypoglycemic effects and a reduction in microvascular complications (Soelistijo et al., 2021). Glimepiride is considered safe for use in patients with cardiovascular comorbidities, as it does not affect the ischemic condition of cardiac myocytes or the ischemic responses that limit heart tissue damage (Trerattanavong & Tadi, 2023). In this study, data on the administration of oral antidiabetic drugs indicated that the majority of the research subjects, totaling eight patients (19.5%), received a combination therapy of glibenclamide 5 mg, metformin 500 mg, and acarbose 100 mg.

In a prior study conducted at Bandung City Regional General Hospital in Bandung, Indonesia, the average usage of the metformin-gliclazide-pioglitazone combination was reported in three to six patients (2.6–5.2%), whereas the metformin-gliclazide-acarbose combination was used by one to seven patients (0.9–6.1%). The study also revealed that the combination of metformin-gliquidone-pioglitazone was most commonly used in February, March, May, and July. From August to December, the combination of metformin-gliclazide-acarbose was used most frequently. The two most prevalent combinations recorded in January were metformin-gliquidone-pioglitazone and metformin-glimepiride-pioglitazone, each consumed by three patients (2.6%). In April, the combination of metformin-gliclazide-acarbose was most commonly used (Jonathan et al., 2019).

In another study conducted by Yuswantina & Dyahariesti (2018), the combination of glimepiride and metformin was used most frequently, with 25 patients accounting for 40.32% of the samples. The two prior studies did not present data on the dosages of the combined oral antidiabetic drugs used. Despite that, the studies indicated differences in the most frequently used combined oral antidiabetic drugs. The use of these antidiabetic drugs aligns with the guidelines for T2DM therapy released by the Indonesian Society of Endocrinology (Soelistijo et al., 2021). As recommended by the guidelines as well as by Rejeski et al. (2012), the management of T2DM can begin with changes to a healthy lifestyle. One option for monotherapy is the administration of oral antidiabetics. However, if a single oral antidiabetic is insufficient for controlling blood sugar levels, the alternative is to combine several oral antidiabetics (Annisa et al., 2021; Widiyari et al., 2021). The combination therapy of biguanide and sulfonylurea is regarded as the most suitable for this alternative option. Its therapeutic effect is expected to improve, resulting in reduced blood sugar levels. The synergistic effects of sulfonylurea and biguanide enable their usage as a combination (Wang & Perri, 2018; Ganesan et al., 2023).

Patients with T2DM in this study also consumed medications other than oral antidiabetic drugs, as long as they met the inclusion criteria. One patient (2.4%) used atorvastatin 20 mg, a statin-type anti-hyperlipidemic agent. In addition, one patient (2.4%) used an angiotensin-converting enzyme (ACE) inhibitor, lisinopril 5 mg, for hypertension and angina. Meanwhile, another patient (2.4%) consumed a calcium channel blocker, nifedipine 30 mg, for hypertension. A total of 38 patients (92.7%) solely consumed oral antidiabetic drugs. This differs from prior research conducted by Murwati & Murtisiwi (2021) at dr. Soediran Mangun Sumarso Regional General Hospital, Wonogiri, Indonesia, where the most common class of antidiabetic drugs was sulfonylurea, as demonstrated by 162 samples (19.64%). The predominant types of medications were glimepiride, with 143 samples (17.33%), and angiotensin receptor blockers (ARBs) (19.03%), specifically irbesartan, with 142 samples (17.21%). The ACE inhibitor used was imidapril, as shown by two samples (0.24%). The predominant calcium antagonist or calcium channel blocker used by the respondents was amlodipine, with 81 samples (9.82%), followed by nifedipine, with 18 samples (2.18%). Meanwhile, diltiazem was the least used, with only two samples (0.24%). In the anti-hyperlipidemia group, most respondents consumed simvastatin, although only shown in two samples (0.24%). Out of 138 total respondents in a study conducted by Wijaya et al. (2015), 133 patients (96.38%) solely received oral antidiabetic drugs in the therapy for diabetes mellitus. Simultaneously, 60 patients (43.47%) used additional drugs, specifically for hypertension, while two patients (1.45%) used antianginal drugs, and 38 individuals (27.53%) were administered additional antihyperlipidemic drugs. However, the study simply did not specify the types of drugs used in each group.

Sulfonylurea usage in type 2 diabetes mellitus patients

This study presents data on the administration of sulfonylureas, indicating that the majority of the T2DM patients, comprising 38 patients (92.6%), ingested the medications before meals. In prior research, data on drug usage profiles in health centers around the eastern area of Surabaya, Indonesia, supported the findings of this study,

revealing that glibenclamide was most frequently taken by diabetes mellitus patients before meals (76.04%) (Wijaya et al., 2015b). Sulfonylureas are absorbed in the intestine following oral administration, albeit in different amounts and times. The absorption and biological availability of each sulfonylurea vary. Hyperglycemia can reduce sulfonylurea absorption by damaging intestinal motility, which in turn reduces the absorption of all oral drugs. The same principle also applies to food intake. As a result, sulfonylureas should be taken 30 minutes before meals for easier absorption (Costello et al., 2023).

Regarding the frequency of intake, the majority of the patients in this study took sulfonylureas once a day, accounting for 32 individuals (78%). This is supported by data from earlier research, where 72.93% of the patients ingested glibenclamide at an interval of 24 hours or once daily (Wijaya et al., 2015b). Moreover, it was found that the most common instance of simultaneous intake involved three different types of drugs at once, occurring primarily in the morning (34.06%). Data from another study differ from this study, indicating that metformin and sulfonylurea were generally prescribed twice a day (84.4%) to patients receiving oral combination therapy (Akrom et al., 2019). Sulfonylureas are given once or twice a day because they have prolonged biological effects. Due to receptor interactions and active metabolite formation, the biological effects of sulfonylureas often last longer than the plasma half-life. These biological effects may even last for more than 24 hours (Costello et al., 2023).

Weight fluctuations in type 2 diabetes mellitus patients

The data obtained from this study indicated that weight gain predominantly occurred in T2DM patients treated with a sulfonylurea, in the form of glibenclamide 5 mg, in combination with metformin 500 mg and acarbose 100 mg, as represented by seven individuals (17%). Khairinnisa et al. (2020) conducted an observational study revealing that using a combination of sulfonylureas and metformin led to hypoglycemia in 29.3% of cases. Most of the study subjects, accounting for 70 patients (60.3%), had a normal body mass index (BMI). This might be attributed to significant weight loss, a common issue in diabetes mellitus, and dietary intervention. The use of sulfonylureas may lead to weight loss and BMI reduction by up to 3 kg over one year in diabetes mellitus patients. The direct metabolic effects of sulfonylureas occur in adipocytes expressing specific receptors. Their activation increases intracellular Ca²⁺ levels, which stimulate lipogenesis. On another note, hunger may arise as a symptom of hypoglycemia. Since increased insulin levels in the blood and excessive calorie intake can lead to weight gain, diabetes mellitus patients receiving sulfonylureas should be routinely monitored, as indicated by the aforementioned data (Confederat et al., 2016). Weight gain is common with sulfonylurea usage and is almost a constant consequence of the treatment, albeit to a lesser severity compared to insulin administration. This side effect poses harmful effects, especially in relation to chronic diseases such as diabetes mellitus, where weight control is the main goal of treatment (Costello et al., 2023).

This study included a comprehensive exploration of sulfonylurea therapy, specifically glibenclamide, gliclazide, and glimepiride, in combination with other antidiabetics and the incidences of weight gain in T2DM patients. However, this study has several limitations. Firstly, it employed a descriptive research method, presenting data in the form of variable comparisons without conducting a

detailed analysis of their interrelationships. Secondly, there were instances of incomplete patient medical records, which might have affected the comprehensiveness of this study. Lastly, the scarcity of prior research focusing on the weight of T2DM patients using oral antidiabetic drugs from the sulfonylurea class suggests a gap in existing literature, highlighting the need for further exploration in this specific area.

CONCLUSION

This study concludes that the majority of T2DM patients treated with sulfonylureas are middle-aged women who have been diabetic for a decade and a half. Glimepiride is the most commonly used sulfonylurea for monotherapy. For combination therapy, glibenclamide is the most frequently consumed, alongside metformin and acarbose. T2DM patients consuming sulfonylureas predominantly experience weight gain, although some patients may exhibit decreased or constant weight. Improved medical records and further research are necessary to acquire a more comprehensive understanding of weight gain in T2DM patients treated with sulfonylurea.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest in this study.

ETHICS CONSIDERATION

This study received ethical clearance from the Health Research Ethics Committee of Dr. Soetomo General Academic Hospital, under reference number 1735/101/4/X/2022, on March 2, 2023.

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AUTHOR CONTRIBUTION

GDPR conceptualized and designed the study, analyzed and interpreted the data, drafted the article, provided administrative, technical, and logistic support, and collected and assembled the data. JHP and RS conceptualized and designed the study, analyzed and interpreted the data, drafted the article, critically revised the article for important intellectual content, provided study materials, and gave final approval of the article. RW contributed to the critical revision of the article for important intellectual content and provided final approval of the article.

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