Profile of Hypoglycemia Incidence in Type 2 Diabetes Mellitus Patients with Sulfonylurea Therapy

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Abstract

Over 10 million adults of Indonesian people have Type 2 Diabetes Mellitus (T2DM), the country ranks seventh globally in terms of diabetes cases. Effective blood glucose control is crucial, especially when using medications like Sulfonylurea to avoid the risk of hypoglycemia. This study was conducted to evaluate hypoglycemia incidence in T2DM patients on sulfonylurea therapy.

The focus of this research is on the population of samples who have experienced symptoms of hypoglycemia. The results show that the prevalence of T2DM patients with SU therapy who have experienced symptomatic hypoglycemia is 62.0% (31/50 sample). Out of these 31 individuals, 51.61% are women. The majority of them is early elderly age group (46-55 years) (35.48%). Most of them have completed high school education (45.16%). Among them, 64.52% are unemployed, and 58.06% come from within Surabaya. The majority of them use glimepiride therapy (64.52%), and the most commonly used combination therapy is glimepiride + 1 combination of oral diabetes medication (54.84%). The most common comorbidity is heart disease (28.21%). Most of them attribute the symptoms of hypoglycemia to skipping meals (48.39%) and occurring at irregular times (45.16%). The average fasting plasma glucose (FPG) level for the total sample is 130.44 mg/dl, and patients that using single SU therapy have lower FPG levels than patients on combination therapy.

In conclusion, the incidence of hypoglycemia due to SU therapy remains significantly high, emphasizing the need for specific efforts to ensure the safety of therapy while maintaining its effectiveness.

Keywords: Diabetes Mellitus; Hypoglycemia; Sulfonylurea

1. Introduction

Diabetes mellitus is a serious chronic disease with significant complications that impact the quality of life of individuals, and it is one of the major health problems in Indonesia. With more than 10 million adults in Indonesia diagnosed with Type 2 Diabetes Mellitus (T2DM), Indonesia ranks seventh globally in the number of diabetes mellitus patients[1]. In 2009, the International Diabetes Federation (IDF) estimated that around 7.3 million people were suffering from T2DM, and by 2017, this number had increased to 10.3 million, with 7.3 million of them undiagnosed[2]. The data from the Ministry of Health (2018) through the Basic Health Research (Riskesdas) indicates that the prevalence of diabetes mellitus in Indonesia, based on doctor diagnoses in patients aged ≥15 years, increased from 1.5% in 2013 to 2% in 2018. Meanwhile, the prevalence based on elevated glucose levels rose from 6.9% in 2013 to 8.5% in 2018. It can be concluded that only 25% are aware that they have diabetes mellitus[3].

T2DM arises due to insulin resistance in muscle and liver cells, as well as the inability of pancreatic beta cells to function properly. The consequence is hyperglycemia, which, if not addressed, can lead to dangerous complications affecting the blood vessels and nervous system, such as neuropathy[4]. Uncontrolled blood glucose levels in T2DM patients require comprehensive management to prevent such complications. The overall goal of diabetes management is to improve the quality of life for T2DM patients, outlined in three key points: short-term goals to address complaints and reduce the risk of acute complications, medium-term goals to inhibit the development of microangiopathy and macroangiopathy complications, and ultimate goals to reduce DM morbidity and mortality. Achieving these objectives involves comprehensive control of blood glucose, blood pressure, weight, and lipid profiles through a combination of a healthy lifestyle and pharmacological therapy [4]. Effective blood glucose control is crucial in T2DM therapy, not only to achieve sufficient glycemic control but also to mitigate the risk of severe hypoglycemia, especially with the use of Sulfonylureas (SUs), glinides, or insulin. Severe hypoglycemia poses significant challenges to T2DM therapy, impacting cardiovascular

function, cognitive health, and mortality. The fear of hypoglycemia itself can lead to inadequate and inefficient therapy[5]. According to medical records from outpatient DM patients at the Karang Rejo Tarakan Health Center during January-April 2017, SUs were the second most frequently used diabetes medication after metformin (Biguanide), accounting for 35.71% [6]. A Nested Case-Control study found that, overall, among 692 patients treated with SUs, 130 patients (19%) experienced at least one episode of hypoglycemia during SU therapy in the hospital [7].

Knowledge about self-monitoring, signs and symptoms of hypoglycemia, and how to manage it is crucial for individuals with diabetes mellitus (DM). Therefore, education becomes a primary focus in efforts to improve the quality of life for DM patients and is an essential component of holistic DM management[4]. Based on research conducted at the internal medicine clinic of the Sultan Syarif Mohamad Alkadrie Regional General Hospital from October 2014 to November 2015, the results from 105 respondents showed that only 49 (46.7%) had a good level of knowledge regarding the risk factors for hypoglycemia in DM [8].

Based on the information provided, RSUD Dr. Soetomo needs to have its own data on the profile of hypoglycemia incidents in patients with diabetes mellitus. This data is essential for improving the quality of life for T2DM patients by implementing effective and efficient therapies that align with the actual conditions of patients treated at RSUD Dr. Soetomo. Therefore, it is necessary to conduct research to gather this specific information.

2. Methods

This study is descriptive research conducted in the form of a retrospective study involving a retrograde anamnesis of patients with Type 2 Diabetes Mellitus (T2DM) undergoing sulfonylurea therapy in the outpatient unit of RSUD Dr. Soetomo Surabaya during the period of June to September 2023. The research methodology employed is a cross-sectional study. The sampling technique in this research involves using the total sampling method with the entire population that meets the inclusion criteria, namely patients with T2DM undergoing sulfonylurea therapy during the period of June to September 2023, and excluding patients undergoing insulin therapy. All patients who have agreed to be interviewed have filled out and signed the informed consent form. The tool used for the study was sociodemographic variables and anamnesis questions covering whether there has been a history of hypoglycemia, the type of medication used, the timing of hypoglycemia occurrences, factors causing hypoglycemia, and the results of Fasting Plasma Glucose lab tests. Identification of patient names will only be recorded with initials or specific codes to maintain patient confidentiality. The researcher will ensure the confidentiality of patient data, and all patient information will be used solely for research purposes. The obtained data will be summarized and grouped according to variables. Subsequently, the data will be analyzed descriptively and presented in the form of diagrams and tables using the Microsoft Excel application.

3. Results

3.1 Distribution of sociodemographic variables

In this study, data were obtained from a sample of 50 interviewed patients, and the majority of them were women (58%). Most of the participants belonged to the age group between 56-65 years (38%), based on the categorization done by the health department, which includes the late elderly age group[9]. Regarding their education level, the majority had completed high school or vocational school (40%). A significant portion (60%) of them were unemployed, and 64% hailed from within Surabaya. About 22.22% of the participants had comorbid heart disease.

Table 1. Distribution of sociodemographic variables

Sex	**Frequency**	**Percentage (%)**
Male	21	42%
Female	29	58%
Group of Age		
Adolescence (17-25 tahun)	1	2%
Early Adult (26-35 tahun)	0	0%
Late Adult (36-45 tahun)	4	8%
Early Elderly Age (46-55 tahun)	16	32%
Late Elderly Age (56-65 tahun)	19	38%
Extremely Late Elderly Age (>65 tahun)	10	20%
Education Level		
Illiterate	2	4%

Elementary School	9	18%
Junior High School	10	20%
Senior High School/Vocational School	20	40%
Diploma	3	6%
Bachelor	6	12%
Occupation status		
Employed	20	40%
Unemployed	30	60%
Patient's domicile		
Inside Surabaya	32	64%
Outside Surabaya	16	32%
No data	2	4%
Medical History		
Heart Disease	14	22,22%
Hypertension	13	20,63%
Stroke	5	7,93%
Kidney Disease	4	6,35%
Etc	27	42,86%

3.2 Distribution of sulfonylurea drug usage.

In this study, four types of sulfonylureas used by patients were identified, namely glibenclamide, glimepiride, gliclazide, and gliquidone. Among them, the most commonly used by patients is glimepiride (54%). Additionally, glimepiride with the addition of one oral medication other than sulfonylurea is the most frequently used combination therapy by patients (42%) compared to single or three-drug combination therapies.

Table 2. Distribution of sulfonylurea drug usage

Variable	Frequency	Percentage (%)
Type of Sulfonyurea		
Glibenclamide	1	2%
Gliclazide	20	40%
Glimepiride	27	54%
Gliquidone	2	4%
Total	**50**	
Distribution of Oral Antidiabetic Drug (OAD) Combination		
Glibenclamide + 2 drugs combination	1	2%
Gliclazide	4	8%
Gliclazide + 1 drug combination	12	24%
Gliclazide + 2 drugs combination	4	8%
Glimepiride	3	6%
Glimepiride + 1 drug combination	21	42%

Glimepiride + 2 drugs combination	3	6%
Gliquidone + 1 drug combination	2	4%
Total	50	

3.3 The occurrence of symptomatic hypoglycemia based on the sociodemographic characteristics of patients.

From the 50 sampled patients who were interviewed, it was found that 31 individuals had experienced symptomatic hypoglycemia, with a prevalence rate of 62.0%. Among the 31 patients with hypoglycemia, 51.61% were female. The majority of those experiencing symptomatic hypoglycemia belonged to the early elderly group (45-54 years) with 11 individuals (35.48%) and the late elderly group (56-65 years) with 10 individuals (32.26%). Most of the patients with hypoglycemia had completed their education up to high school/vocational school, with 14 individuals (45.16%), followed by those with primary education at 22.58%. About 64.52% of those experiencing symptomatic hypoglycemia were unemployed, and in terms of patient domicile, the majority were from within Surabaya at 58.06%.

Table 3. The occurrence of symptomatic hypoglycemia based on the sociodemographic characteristics of patients.

Patient Distribution		
Hypoglycemia	31	
Normal	19	
Symptomatic Hypoglycemia Prevalence	62,0	
Sex	**Hypoglycemia**	**Percentage (%)**
Male	15	48,39%
Female	16	51,61%
Group of Age		
Adolescence (17-25 tahun)	0	0%
Early Adult (26-35 tahun)	0	0%
Late Adult (36-45 tahun)	3	9,68%
Early Elderly Age (46-55 tahun)	11	35,48%
Late Elderly Age (56-65 tahun)	10	32,26%
Extremely Late Elderly Age (>65 tahun)	7	22,58%
Education Level		
Illiterate	0	0%
Elementary School	7	22,58%
Junior High School	5	16,13%
Senior High School/Vocational School	14	45,16%
Diploma	1	3,23%
Bachelor	4	12,90%
Occupation status		

Employed	11	35,48%
Unemployed	20	64,52%
Patient's domicile		
Inside Surabaya	18	58,06%
Outside Surabaya	12	38,71%
No data	1	3,23%
Total sample with Hypoglycemia	**31**	

3.4 The occurrence of symptomatic hypoglycemia based on the medical history of the disease

In this study, the results showed that the highest percentage of symptomatic hypoglycemia occurred in the group of patients with a history of heart disease at 28.21%, followed by hypertension at 20.51%, hepatitis at 5.13%, and other diseases accumulated at 46.15%, with each disease accounting for 1-2 cases.

Table 4. The occurrence of symptomatic hypoglycemia based on the medical history of the disease

Variable	Frequency	Percentage
Medical history	**Hypoglycemia**	**(%)**
Heart disease	11	28,21%
Hypertension	8	20,51%
Hepatitis	2	5,13%
Etc	18	46,15%

3.5 The occurrence of symptomatic hypoglycemia based on Sulfonylurea medication

In this study, the results showed that 64.52% of patients who experienced symptomatic hypoglycemia used Glimepiride, followed by gliclazide at 32.26%. The highest data for the combination of Oral Antidiabetic Drugs (OAD) with Sulfonylurea (SU) was found in the group using the combination of glimepiride + 1 other medication, accounting for 54.84%.

Table 5. The occurrence of symptomatic hypoglycemia based on Sulfonylurea medication

Variable	Frequency	Percentage
Type of Sulfonylurea	**Hypoglycemia**	**(%)**
Glibenclamide	0	0%
Gliclazide	10	32,26%
Glimepiride	20	64,52%
Gliquidone	1	3,22%
Total	**31**	
Distribution of Oral Antidiabetic Drug (OAD) Combination		
Glibenclamide + 2 drugs combination	0	0%
Gliclazide	0	0%
Gliclazide + 1 drug combination	8	25,81%
Gliclazide + 2 drugs combination	2	6,45%
Glimepiride	1	3,22%
Glimepiride + 1 drug combination	17	54,84%
Glimepiride + 2 drugs combination	2	6,45%
Gliquidone + 1 drug combination	1	3,22%
Total	31	

3.6 Distribution of Causes, Symptoms, and Timing of Hypoglycemia Occurrence.

In Table 6, data on the causes of symptomatic hypoglycemia according to patient opinions are presented. A total of 48.39% of the occurrences of symptomatic hypoglycemia in patients were attributed to forgetting to eat. In addition to the causes, data on the timing of symptomatic hypoglycemia according to patients are also presented, with 45.16% occurring at uncertain times.

Table 6. Distribution of Causes, Symptoms, and Timing of Hypoglycemia Occurrence.

Variable	**Frequency**	**Percentage**
Causes of Hypoglycemia Symptoms	**Hypoglycemia**	**(%)**
Due to fasting	1	3,22%
Insufficient food intake	6	19,35%
Fatigue after activity	2	6,45%
Skip meals	15	48,39%
Reduced appetite	1	3,22%
Not sure	6	19,35%
Timing of Hypoglycemia Symptoms		
Morning	5	16,13%
Noon	10	32,26%
Evening	1	3,22%
Uncertain times	14	45,16%
Before breaking the fast	1	3,22%
Total	**31**	

3.7 The blood sugar profile of the patients

We have also inquired about the patients' routine of checking blood sugar every month and asking about the results. The data on the patients' blood sugar profile are as follows: 48 individuals (96%) consistently check their blood sugar every month, while 2 individuals (4%) do not check it regularly each month. Additionally, data on fasting Plasma Glucose (FPG) were obtained from all sampled patients, totaling 45 individuals (5 individuals had incomplete data). The FPG values ranged from a minimum of 70 mg/dl to a maximum of 238 mg/dl, with an average of 130.44 mg/dl. In the group of patients using a single Sulfonylurea, the FPG values were a minimum of 89 mg/dl, a maximum of 215 mg/dl, with an average of 125.50 mg/dl. For the group of patients using Sulfonylurea with one additional drug combination, the FPG values were a minimum of 70 mg/dl, a maximum of 238 mg/dl, with an average of 134.54 mg/dl. In the group of patients using Sulfonylurea with two drug combinations, the FPG values were a minimum of 97 mg/dl, a maximum of 170 mg/dl, with an average of 127.86 mg/dl.

Table 7. The blood sugar profile of the patients.

Regular Blood Sugar Monitoring (/Month)	**Frequency**	**Percentage (%)**
No	2	4.0%
Yes	48	96.0%
Total	**50**	

Variable	**FPG (mg/dl)**		
	Min	Max	Mean
All sample	70	238	130.44

Sulfonylurea alone	89	215	125,50
SU + 1 drug	70	238	134,54
SU + 2 drugs	97	170	127,86

4. Discussion

The samples for this study were taken from interviews with patients at the Endocrine Clinic of Dr. Soetomo Hospital in Surabaya within the timeframe of June-September 2023. The results were obtained from 50 T2DM patients undergoing sulfonylurea therapy, with a breakdown of 42% males and 58% females. These findings align with another similar study conducted by Lopes A, et al, where, in their research with a total of 420 randomly selected samples, data showed a higher percentage of women than men, specifically 51.4% women [10]. Distribution of age among T2DM patients at Dr. Soetomo Hospital during the period of June-September 2023 reveals that the majority fall within the Late Elderly group (56-65 years) at 38%, followed by the Early Elderly group (46-55 years) at 32%, and the Elderly (>65 years) at 20%. The results are consistent with other existing research, although with a different range of data. For example, in a study conducted by Zihui Yan et al in Shanghai, China, data on the prevalence of people with diabetes mellitus was found to be 11.1% for the age range of 40-49 years, while for the age group of 60-69 years, it was 23.9% [11]. This can be explained by the fact that the elderly age group has a higher risk of diabetes compared to younger age groups due to hormonal changes and a less active lifestyle, making the elderly more susceptible to obesity and insulin resistance [11]. The distribution of education levels among patients in this study reveals that the highest data comes from the high school/vocational school education group, accounting for 40%, while the lowest is 4% for those without formal education. This result differs significantly from the study conducted by Thenmozhi P., where the highest percentage was in the primary education (SD) group at 50%, and the lowest was for education above high school at only 3.33% [12]. This difference can be attributed to the variation in the regions used for the research. The aforementioned study was conducted in a rural area, where respondents with lower education levels predominated. In contrast, this current study was conducted in a metropolitan area, resulting in an opposite distribution. The distribution of patients' employment status in this study shows that 20 individuals are employed (40%), while 30 individuals are unemployed (60%). These results indicate that occupation may influence the risk of developing diabetes mellitus. In a study, it was explained that blood glucose levels can be controlled through physical activity during work [13]. The variety of occupations undoubtedly determines an individual's level of physical activity, so the above results are also influenced by the physical activity of each patient within and outside of their work. The distribution of patients' domiciles in this study reveals that 32 individuals (64%) are from within Surabaya, 16 individuals (32%) are from outside Surabaya, and data for 2 individuals (4%) are unavailable. These results are consistent with a study conducted in Myanmar, where the prevalence of diabetes mellitus is higher in urban areas (12.1%) compared to rural areas (7.1%) [14]. In this study, patient medical history data revealed the highest prevalence of heart disease in 14 individuals, followed by hypertension in 13 individuals. These results differ slightly from a study conducted in Turkey, where the most common comorbidities were hypertension (84.9%) and hyperlipidemia (65.6%), with coronary heart disease at 22.8%. Another study found that chronic kidney disease was the most prevalent comorbidity in the UAE and Kuwait at 44.3% [15], [16]. According to the author's assumption, comorbidities in patients with type 2 diabetes may vary significantly in each region, based on other research journals showing diverse results. However, all these studies align in indicating a strong association between T2DM and cardiovascular diseases. In this study, the dominant use of the sulfonylurea (SU) glimepiride was found in 27 individuals (54%), followed by gliclazide at 40%. These results align well with a study conducted by Annisa, et al., at the Regional General Hospital of West Nusa Tenggara Province, where glimepiride was the most frequently used at 25.13%, followed by gliclazide and gliquidone at 1.54% each [17]. Additionally, in this study, it was found that the combination therapy of glimepiride with one other oral antidiabetic drug (OAD) dominated with a percentage of 42%, followed by gliclazide with one OAD combination at 24%. This aligns with findings from research conducted in Gorontalo, where 47% of patients received glimepiride therapy in combination with metformin [18]. Although this study did not explicitly mention metformin, raw field data indicates a concordance that metformin is the most common combination, even with each type of SU.

In this study, the prevalence of symptomatic hypoglycemia events in patients with T2DM using sulfonylurea therapy was found to be 62.0%. This result is relatively high when compared to other research. According to Edridge C, et al, in a systematic review and meta-analysis of 46 studies, data for treatment regimens using sulfonylurea showed a prevalence of mild/moderate hypoglycemia at 30%, while severe hypoglycemia was 5% [19]. The results also showed the dominance of the female group at 51.61% having experienced symptomatic hypoglycemia. Using different methods, the findings of this research align with a study conducted by Kajiwara A, et al, where the multivariable logistic regression analysis indicated a significant association between the female gender and hypoglycemia symptoms with a p-value of 0.007 [20]. However, it is still not precisely explained why this happens. According to Kajiwara et al., there is a tendency for

women to have lower fasting blood glucose levels and lower gluconeogenesis rates during exercise or fasting [20]. This study revealed that the age group with the highest percentage experiencing symptomatic hypoglycemia was the Early Elderly group (46-55 years) at 35.48%, followed by the Late Elderly group (56-65 years) at 32.26%, and the Elderly (>65 years) at 22.58%. These findings differ slightly from another study conducted by Richard Silbert, et al, which showed that as patients age, incidents of hypoglycemia become more frequent. Data from that study indicated that patients aged ≥75 years experienced 2.3 events/100 person-years, compared to 1.3 events/100 person-years in patients aged 65-74 years, and 0.9 events/100 person-years in patients aged 45-64 years and 18-44 years [21]. However, in another study conducted at Mayo Hospital, data showed that the age group 40-60 years is more vulnerable to hypoglycemia, with a prevalence of 55.56%, while the older age group has a prevalence of 27.78% [22]. These results align with the findings of this study. The explanation regarding the influence of age on the occurrence of hypoglycemia may be due to the fact that most elderly individuals experience a decline in function, resulting in a slower response to hypoglycemic events [23]. Additionally, advancing age may also lead to a decrease in the patients' level of knowledge [24]. Regarding their education level, patients with a high school/vocational school education level constitute the group that most frequently experiences symptoms of hypoglycemia, at 45.16%, followed by elementary school (SD) at 22.58%. The relationship between the patients' education level should ideally align with their knowledge about self-care, as explained by Thenmozi P., who noted that public knowledge is still very limited. Many of them have experienced symptoms of hypoglycemia, but they may not be aware of why it occurs. Moreover, many of them also lack knowledge about the first aid measures to address hypoglycemia [12]. However, from this explanation, it can be concluded that what is closely related to the occurrence of hypoglycemia is the level of patients' knowledge. Therefore, it can be inferred that there is no significant correlation between the level of education and the occurrence of hypoglycemia. This is supported by other research stating that there is no significant relationship between the level of education and an individual's ability to detect the occurrence of hypoglycemia [25]. This study also revealed that the group with the highest percentage experiencing symptomatic hypoglycemia is the unemployed group at 64.52%. Employment status is closely related to the financial level of patients, and economic factors play a crucial role in individual health. Economic decisions, such as food prices and income, influence the food options chosen by individuals. Additionally, the cost of food poses a challenge for families with limited income to opt for healthier food choices [26]. In a study conducted by Madani et al., data showed that the majority of respondents with low financial status tended to have poor knowledge. However, in their research, no significance was found between knowledge of hypoglycemia and the financial status of respondents, with a p-value of 0.354 [27]. Among the patients included in the study, those residing in Surabaya exhibited the highest percentage of symptomatic hypoglycemia, accounting for 58.06% of cases. This result is quite different when compared to two different studies, one conducted in a rural area with a prevalence of hypoglycemia at 57.44% [28], and another in an urban area, specifically at Mayo Hospital endocrine, with a prevalence of hypoglycemia in patients with Oral Antidiabetic Drugs (OAD) therapy at 26.39% [22]. According to the author's assumption, this disparity could be due to differences in sample size, where the study conducted at Mayo Hospital involved 360 individuals, allowing for a better distribution of data. Additionally, these differences may also be influenced by varying characteristics of the samples across countries. This study result indicates that the group of patients with a history of heart disease had the highest percentage of symptomatic hypoglycemia, standing at 28.21%, with those having a history of hypertension following at 20.51%. This result can be explained by other research indicating that acute hypoglycemia in patients can lead to cardiovascular complications due to reduced blood supply to the heart and electrical disturbances causing arrhythmias and prolonged QT intervals [29]. In a study by Tran et al. (2015), it was found that the prevalence of hypoglycemia in T2DM patients with hypertension (4.87%) was higher than those without hypertension (3.87%), and they were 1.12 times more likely to experience hypoglycemia than those without hypertension [30]. Among the 31 patients included in this study who experienced symptomatic hypoglycemia, the majority, accounting for 64.52%, were found to be using glimepiride, followed by 32.26% who were using gliclazide. This result aligns with research by Schernthaner G, et al., which found that the use of gliclazide MR significantly less frequently led to hypoglycemia (3.7%) compared to glimepiride (8.9% of patients) (p=0.003) [31]. This is reinforced by another study by Scheen, explaining that a meta-analysis showed a lower risk of confirmed hypoglycemia with gliclazide, also confirmed by the results of the GUIDE head-to-head trial [32]. However, different results were shown by Algendy in their research, where they found an increased frequency of severe hypoglycemia with the use of gliclazide MR compared to glimepiride in elderly adults who came to the emergency department. However, for the overall occurrence of hypoglycemia, gliclazide MR was insignificantly higher than glimepiride with p=0.444. The increased risk of using gliclazide in Algendy's study was associated with moderate to high doses and could also be due to the pharmacokinetic modifications that prolong half-life and duration of action [33]. In this study, the majority of patients experiencing symptomatic hypoglycemia used Glimepiride + 1 Combination of oral drugs, amounting to 54.84%. This result, when discussed in comparison with the types of sulfonylureas mentioned earlier, particularly glimepiride, indicates that there is no direct research explaining the risk of hypoglycemia between 2 combinations of oral drugs and 3 combinations of oral drugs. In a study conducted by Min Kyong Moon, data showed that thiazolidinedione as an additional therapy to SU + metformin was associated with a significantly higher rate of hypoglycemia. However, no statistically significant data were found showing differences in the risk of hypoglycemia among the other triple therapies, such as DPP4i and acarbose as additions to SU + metformin [34].

Among the patients surveyed in this study, the leading cause reported for symptomatic hypoglycemia was forgetting to eat, constituting 48.39% of the cases. This result aligns with other research studies conducted by Samya et al. (2019) and Shabbir et al. (2022), both indicating that the most common cause of hypoglycemia is forgetting to eat, with a percentage of 89.3% [22], [28]. According to patients, most symptomatic hypoglycemic events occurred at unpredictable times (45.16%), followed by daytime (32.26%), and morning (16.13%). This result is consistent with another study that found the high-risk periods for hypoglycemia were in the time ranges of 00:00-2:00, 22:00-24:00, 2:00-4:00, 8:00-10:00, and 10:00-12:00. Additionally, data on hypoglycemia occurrences before and after meals showed high-risk times as nighttime (23:00) (1.80%), after breakfast (9:00) (1.39%), and before lunch (11:00) (1.29%) [35]. The author assumes that these results may also be influenced by inaccurate patient memory.

Among the sampled patients, a noteworthy 96% were found to consistently perform monthly blood sugar checks, as revealed by this study. The average Fasting Plasma Glucose (FPG) level from 45 available FPG data samples was 130.44. This result is slightly lower than the data obtained by Gonzalez in their research, where the average FPG was 155.4 [36]. When comparing FPG levels with SU therapy, the study found a lower average FPG level in patients using single SU therapy (125.50) compared to SU + 1 OAD therapy (134.54) and SU + 2 OAD therapy (127.86). This result aligns with Gonzalez's study, which found a lower average FPG in patients with single SU therapy (138.7) compared to those with SU + metformin therapy (158.3) [36].

5. Conclusion

In conclusion, this study establishes that the prevalence of symptomatic hypoglycemia in patients with T2DM using sulfonylurea therapy is 62.0%. The demographic profile of those experiencing symptomatic hypoglycemia reveals a predominance of women, particularly in the early elderly age group (46-55 years), individuals with a high school education, the unemployed, and residents of Surabaya. Additionally, the majority of these patients have a history of heart disease. Notably, glimepiride therapy and the combination of glimepiride with another oral diabetes drug are commonly associated with symptomatic hypoglycemia. The primary causes identified for symptomatic hypoglycemia include forgetting to eat, and these episodes often occur at unpredictable times. Furthermore, patients with single Sulfonylurea therapy exhibit a lower average fasting plasma glucose (FPG) compared to those undergoing combination therapy.

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