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Hypoglycemia Incidence Rate in National and Non-National Health Insurance of Type 2 Diabetes Patients in COVID-19 Pandemic at Central Borneo

(Tingkat Kejadian Hipoglikemia pada Pasien Diabetes Melitus Tipe 2 Peserta JKN dan Non-JKN pada Masa Pandemi COVID-19 di Kalimantan Tengah)

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Abstract: Community activity restrictions during the COVID-19 pandemic in Indonesia impact the quantity and quality of health services for type 2 diabetes (T2DM). This limitation could increase the risk of hypoglycemia in type 2 diabetes patients. The study aimed to compare the incidence rate of hypoglycemia between national (NHIP) and non-national health insurance participants (N-NHIP) with T2DM during the COVID-19 pandemic in Indonesia. The study used a cross-sectional design and was conducted at a government hospital in Central Borneo. Data was collected by consecutive sampling from September to November 2021. Sixty-two participants were divided into two groups (NHIP and N-NHIP groups). Each group consisted of 31 participants. They were interviewed regarding their experience with hypoglycemia in the last three months. The incidence rate of hypoglycemia in N-NHIP was higher than in NHIP (93.55% vs. 87.10%; $p>0.05$). Hypoglycemia is mostly presented in patients using a combination of short-acting and long-acting insulin. The incidence rate of hypoglycemia in T2DM during the COVID-19 pandemic in Central Borneo was relatively high. In future studies, it is necessary to analyse the factors that significantly affect the incidence of hypoglycemia in the population of T2DM patients in Indonesia.

Keywords: Hypoglycemia incidence rate, national health insurance, the COVID-19 pandemic, type 2 diabetes.

Abstrak: Penerapan program pembatasan kegiatan masyarakat selama pandemi COVID-19 di Indonesia berdampak pada pelayanan kesehatan diabetes melitus tipe 2 (DMT2). Hal ini meningkatkan risiko hipoglikemia pada pasien DMT2. Penelitian ini bertujuan untuk membandingkan tingkat kejadian hipoglikemia pada pasien DMT2 peserta jaminan kesehatan nasional (JKN) dan non-JKN pada masa pandemi COVID-19 di Kalimantan Tengah. Penelitian ini menggunakan desain cross-sectional yang dilakukan di RSUD X Kalimantan Tengah. Data dikumpulkan secara consecutive sampling dari Bulan September-November 2021. Enam puluh dua (62) peserta dibagi menjadi dua kelompok: kelompok JKN dan non-JKN dengan masing-masing 31 peserta. Pasien diwawancara terkait pengalaman hipoglikemia yang dialami dalam tiga bulan terakhir. Tingkat kejadian hipoglikemia pada kelompok non-JKN lebih tinggi dibandingkan kelompok JKN (93,55% vs 87,10%; $p>0,05$). Hipoglikemia paling banyak dialami oleh pasien DMT2 penggunaan kombinasi insulin kerja pendek dan insulin kerja panjang. Tingkat kejadian hipoglikemia pada pasien DMT2 Peserta JKN dan Non-JKN pada masa pandemi COVID-19 di RSUD X Kalimantan Tengah relatif tinggi. Pada penelitian selanjutnya, perlu dilakukan analisis terhadap faktor-faktor yang mempengaruhi hipoglikemia pada DMT2.

Kata kunci: DMT2, JKN, pandemi COVID-19, tingkat kejadian hipoglikemia.

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INTRODUCTION

HYPOGLYCEMIA is an acute complication that can be life-threatening in diabetic patient[1,2]. Low blood sugar levels characterise hypoglycemia up to <70 mg/dl[3,4]. Although this condition was often found in patients with type 1 diabetes (T1D), many studies showed that hypoglycemia also occurs in patients with type 2 diabetes (T2D). The prevalence of hypoglycemia in T2D patients was relatively high. Around 30% to more than 90% of T2D patients reported some experiences of hypoglycemia[5–8]. A study in Nigeria showed that 35.2% of T2D outpatients experienced hypoglycemia[5]. Other studies in Brazil and India also showed a similar result, where respectively 61.8% and 96% of T2D patients also experienced hypoglycemia[6,8]. More than 10% of patients have severe hypoglycemia[6–9]. Meanwhile, in Indonesia, the prevalence of hypoglycemia in T2D patients reaches 99.4%. Patients experienced at least one hypoglycemia event in 4 weeks, with a rate of 25.7 per patient-year[7]. A lack of patient knowledge causes most hypoglycemia events in Indonesia. 36.4% of patients do not know about hypoglycemia, and 62.7% have poor awareness of hypoglycemia[7]. Health professionals need to educate T2D patients regarding the prevention of hypoglycemia. However, in this era of the COVID-19 pandemic, health services for T2D patients have decreased. Pharmacists cannot optimally monitor patients' blood glucose and treatment processes. This problem increases the risk of hypoglycemia in T2D patients[10–12]. Another risk factor for hypoglycemia was an anti-diabetic medication[13]. The restrictions on anti-diabetic drugs in the national formulary cause differences in therapeutic patterns in national and non-national health insurance participants with T2D. In national health insurance participants, insulin was the first choice to be combined with metformin for patients with a history of arteriosclerotic cardiovascular disease (ASCVD), chronic kidney disease (CKD), and heart failure (HF). Insulin is known to be safe for patients with cardiovascular disease. It was also relatively cheaper than GLP-1 RA or SGLT-2 inhibitors[14]. In addition, sulfonylureas (SU) use was also high among national health insurance participants with T2D in Indonesia[14]. SU has become the first-choice therapy for patients without a history of ASCVD and CKD, and the cost was a significant issue[3]. These differences can affect the incidence of hypoglycemia in national and non-national health insurance participants. Insulin and SU were strong predictors of hypoglycemia[15–18].

Based on these problems, this study aimed to compare the incidence of hypoglycemia in national health insurance participants (NHIP) and non-national health insurance participants (N-NHIP) with T2D during the COVID-19 pandemic in Indonesia. Although dangerous, proper education can prevent hypoglycemia[19]. Health professionals have an essential role in providing education.

This preliminary study can be used to design an intervention or educational model related to hypoglycemia in T2D patients during and after the COVID-19 pandemic. This study can also be used as a basis for revising the drug use and health services policies for T2D patients in Indonesia.

MATERIALS AND METHODS

MATERIALS. Patients with hypoglycemia in the last three months at a government hospital in Central Borneo from September to November 2021.

METHODS. Study Design. The study used a cross-sectional design and was conducted at a government hospital in Central Borneo. Patients were interviewed regarding their experience with hypoglycemia in the last three months. It was self-reported hypoglycemia. Hypoglycemia events were confirmed by asking the patients whether they had hypoglycemia symptoms. Hypoglycemia symptoms included suddenly feeling hungry, dizzy, weak, shaking, cold, sweating, restlessness, blurred vision, and palpitations. If they experienced any of these symptoms, the patient was further asked whether the symptoms of hypoglycemia had improved after consuming sweet foods and drinks. If the patient's answer was "yes, " the patient was confirmed as a patient with hypoglycemia. Meanwhile, data on clinical characteristics and patient treatment were obtained from medical records. Data collection was carried out for three months, from September to November 2021. In those months, Indonesia had just passed the second wave of COVID-19, but the restrictions on patients visiting hospitals were still applied. At that time, all T2D patients could not see the doctor at any time; the appointment was scheduled for only two days. The first day was for a laboratory examination, while the second was for taking and consulting the medication. Patients usually took regular medication every month but were prescribed for two to three months during the pandemic. This problem caused a limited number of samples to be obtained. This study was approved by the Medical and Health Research Ethics Commission at Universitas Muhammadiyah Prof. Dr. Hamka, No: 03/21.09/01293.

Study Participants. Sixty-two T2D patients were involved in this study. All respondents agreed to be involved in the study by signing informed consent.

Patients had complete medical record data, such as patient characteristics including age, gender, height, body weight, previous medical history, family history, length of time diagnosed with diabetes, and medication used.

Inclusion/Exclusion Criteria. The inclusion criteria were patients with T2D who underwent outpatient therapy, were willing to be respondents, and had complete medical record data. Meanwhile, patients with gestational diabetes were excluded from the study. There was one patient with gestational diabetes, and two patients refused to be respondents because they were in a rush. We used time-limited consecutive sampling (three months), so all patients who met the inclusion and exclusion criteria were included in this study.

Group Characteristics. Sixty-two T2D patients were divided into two groups. The first group was the NHIP (31 patients), and the second group was the N-NHIP (31 patients). Both groups had similar characteristics. Next, both groups were assessed for a history of hypoglycemia experienced in the last 3 months, and then the incidence rates were compared.

Statistical Analysis. The data was tabulated in a table. The distribution of clinical characteristics, treatment, and description of the incidence of hypoglycemia was shown in percentage. Meanwhile, the comparison of the incidence of hypoglycemia in national and non-national health insurance participants with T2D was analysed statistically with a bivariate analysis (chi-square test).

RESULTS AND DISCUSSION

Patient Characteristics at A Government Hospital in Central Borneo-Indonesia. T2D patients at a government hospital in Central Borneo-Indonesia were dominated by patients aged less than 60 years, female, overweight, diagnosed with T2D less than five years, uncontrolled HbA1c, with hypertension, active in physical activity, not consuming alcohol or smoking, and with a family history of diabetes. There was no significant difference in characteristics between the two groups.

Clinical characteristics of patients can be the risk of hypoglycemia. Elderly, uncontrolled HbA1c, newly diagnosed DM, or diagnosed for more than ten years were reported as predictors of hypoglycemia[5,15,16]. The presence of comorbidities also increases the risk of hypoglycemia in T2D. Hypoglycemia-related comorbidities were CKD, CVD, obesity, malignancy, and cognitive dysfunction[15,20–22]. The characteristics of T2D patients in NHIP and N-NHIP with T2D are shown in Table 1.

Anti-diabetic Usage Profile in National and Non-National Health Insurance Participants with T2D. The patients received anti-diabetic therapy to control their blood glucose. There was no difference in the distribution of anti-diabetic use in the NHIP and N-NHIP groups. The combination of short- and long-acting insulin was the most widely prescribed therapy in both groups of patients. Insulin users were more at risk of hypoglycemia than other antidiabetics. Other studies also showed the same result[5,8,15,21,23]. Patients on insulin therapy were recommended to do regular self-monitoring of blood glucose to prevent hypoglycemia[3,24].

The algorithm treatment for T2D patients in Indonesia recommends using insulin for patients with HbA1c > 9% with catabolism symptoms or patients who do not reach the therapeutic target with three combination oral drugs[14]. This treatment differs from the recommendations of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) in 2018, which prefer the use of GLP-1 agonists. Insulin was only given if HbA1c > 11% or there were symptoms of catabolism[3].

For patients with T2D with comorbid ASCVD, HF, and CKD in Indonesia, insulin is the first choice to be combined with metformin [14]. This choice was because insulin has been proven safe for cardiovascular disease, and the price was relatively lower[14]. In contrast, the ADA/EASD recommends using GLP-1 receptor agonists or SGLT-2 inhibitors in combination with metformin[3]. Recent evidence has shown that using GLP-1 or SGLT-2 inhibitors in T2D patients with a history of ASCVD, CHF, and CKD provides more benefits. However, these two drugs were classified as new drugs in Indonesia. They have not been included in the national formulary drug list, so patient or family approval was required to pay for the drugs independently.

From the result, we could see that the N-NHIP also prescribed a similar therapy to NHIP. The use of GLP-1 agonists and SGLT-2 inhibitors in N-NHIP with T2D in Indonesia was still limited. The drug was only used for VIP, middle to upper-class patients because the price was relatively higher. Usually, patients with GLP-1 agonists and SGLT-2 inhibitors were mostly treated in a private hospital. The distribution of anti-diabetic use among national and non-national health insurance participants can be seen in Table 2.

Comparison of Hypoglycemia Incidence in National and Non-National Health Insurance Participants with T2D. This study showed that during the COVID-19 pandemic in Indonesia, the incidence rate of hypoglycemia in N-NHIP with T2D was higher

(93.55%) than in NHIP (87.10%). However, this difference was not statistically significant (p>0.05). The results of this study were different from the survey that was conducted in Argentina. They compared the prevalence of hypoglycemia in T2D patients in public and private sectors (but not in the COVID-19 pandemic era). The results showed that the incidence of hypoglycemia was higher in the public sector than in the private sector. The risk of hypoglycemia was four times higher in the public sector than in the private sector[23]. Patients with no diabetological education were 2.28 times more at risk in for hypoglycemia. Similarly, other factors related to social vulnerability,

Table 1. **Patient characteristics in national and non-national health insurance participants with T2D.**

Patient's Characteristics	NHIP (n = 31)	N-NHIP (n = 31)	p-value*
Age (mean ± SD)	57.45 ± 5.81	56.65 ± 5.73	0.788
< 60 y.o (n=41)	21 (67.74%)	20 (64.52%)	
≥ 60 y.o (n=21)	10 (32.26%)	11 (35.48%)	
Gender			0.610
Male (n=28)	15 (48.39%)	13 (41.94%)	
Female (n=34)	16 (51.61%)	18 (58.06%)	
T2D Diagnosed (mean ± SD)	2.42 ± 0.89	2.07 ± 0.58	
< 5 years (n=62)	31 (50%)	31 (50%)	
HbA1c (mean ± SD)	9.20 ± 1.36	8.84 ± 1.24	0.062
< 7%	0 (0%)	0 (0%)	
7% - 9% (n=25)	10 (43.48%)	15 (71.43%)	
> 9% (n=19)	13 (56.52%)	6 (28.57%)	
BMI (mean ± SD)	24.56 ± 3.27	25.15 ± 2.37	0.200
18, 5 – 24, 9 (n=27)	16 (51.61%)	11 (35.48%)	
25-29, 9 (n=35)	15 (48.39%)	20 (64.52%)	
Comorbidities			
Hypertension	19 (61.30%)	13 (41.90%)	
Dyslipidemia	5 (16.10%)	6 (19.40%)	
Congestive heart failure	3 (9.70%)	2 (6.50%)	
Cardiovascular disease	1 (3.20%)	1 (3.20%)	
Chronic kidney disease	1 (3.20%)	0 (0.00%)	
Stroke	1 (3.20%)	0 (0.00%)	
Neuropathy	6 (19.40%)	3 (9.70%)	
Without comorbidities	4 (12.90%)	11 (35.50%)	
Physical Activity			0.386
Less active (n=6)	4 (12.90%)	2 (6.45%)	
Active (n=42)	22 (70.97%)	20 (64.52%)	
Very active (n=14)	5 (16.13%)	9 (29.03%)	
Smoking			1
Yes (n=12)	6 (19.35%)	6 (19.35%)	
No (n=50)	25 (80.65%)	25 (80.65%)	
Alcohol Consumption			0.119
Yes (n=13)	9 (29.03%)	4 (12.90%)	
No (n=49)	22 (70.97%)	27 (87.10%)	
Family History with DM			0.602
Yes (n=24)	13 (41.94%)	11 (35.48%)	
No (n=38)	18 (58.06%)	20 (64.52%)	

NHIP = National Health Insurance Participants; N-NHIP = Non-National Health Insurance Participants; *Chi-square test.

Table 2. Anti-diabetic usage profile in national and non-national health insurance participants with T2D.

Anti-diabetic Usage Profile	NHIP (n = 31)	N-NHIP (n = 31)
Acarbose + short-acting insulin + long-acting insulin	0 (0.00%)	4 (12.90%)
Metformin + short-acting insulin + long-acting insulin	2 (6.45%)	0 (0.00%)
Short-acting insulin + long-acting insulin	27 (87.10%)	25 (80.65%)
Metformin + long-acting insulin	1 (3.23%)	1 (3.23%)
Short-acting insulin	0 (0.00%)	1 (3.23%)
Long-acting insulin	1 (3.23%)	0 (0.00%)

NHIP=National Health Insurance Participants; N-NHIP=Non-National Health Insurance Participants; *Chi-square test

such as unemployment (OR 5.04 95% CI 2.69-9.46) and marginal socioeconomic level (OR 60.79 95% CI 14.89-248.13) also showed a significant increase in the hypoglycemia risk [23].

More than 90% of patients from the NHIP and N-NHIP groups have experienced at least one symptom of hypoglycemia in the last three months. 16.1% of N-NHIP with T2D experienced symptoms of hypoglycemia at least once in 1 month. Hypoglycemia was more common during the day in both groups of patients. Most of the patients were still at their productive age and actively working during the day. High physical activity at work without adequate calorie intake can reduce blood glucose[13]. Most patients had hypoglycemia symptoms such as shaking, sweating, restlessness, dizziness, headaches, and blurred vision. Besides increasing the calorie intake when experiencing hypoglycemia symptoms, the NHIP also asked for help from the nearest health care centre (6.45%). But only a few patients did the self-monitoring blood glucose (6.45%) in the NHIP group and none in N-NHIP. A comparison of the incidence of hypoglycemia in national and non-national health insurance participants with T2D patients is shown in Table 3.

Patient knowledge was one of the predictors of hypoglycemia in T2D. Lack of knowledge about the disease and the drugs used can affect patient behaviour in treatment[25–27]. Patients with poor medication behaviour risk developing hypoglycemia[28]. A study in Ethiopia in 2021 showed that insufficient knowledge and negative attitudes towards treatment led to inappropriate use of insulin in type 2 DM patients[29]. Hypoglycemia could also worsen in patients who were not aware of self-management of hypoglycemia. Only some patients (65.7%) know what to do when experiencing symptoms of hypoglycemia[6].

Educating T2D patients about hypoglycemia during the pandemic was quite a challenge. The pandemic causes limited health services, so the provision of counseling to T2D patients to increase patient knowledge and medication compliance was lacking[30]. Health workers have a strategic role in preventing hypoglycemia during the COVID-19 pandemic. The health worker factor was related to safety culture, which includes care and health workers' awareness about patient safety, leadership, teamwork and communication, and a supportive environment[31–33]. The intervention of health workers was proven to prevent

Table 3. Comparison of hypoglycemia incidence in national and non-national health insurance participants with T2D.

Hypoglycemia	NHIP (n = 31)	N-NHIP (n = 31)	p-value*
Incidence rate	27 (87.10%)	29 (93.55%)	0.390
Frequency			
Never	4 (12.90%)	2 (6.45%)	
Once a month	2 (6.45%)	5 (16.13%)	
Twice a month	2 (6.45%)	3 (9.68%)	
Three times a month	1 (3.23%)	2 (6.45%)	
Four times a month	2 (6.45%)	2 (6.45%)	
> Four times a month	0 (0.00%)	1 (3.23%)	
One to two times in the last three months	20 (64.52%)	16 (51.61%)	
Time of Occurrence			
Morning	5 (16.13%)	9 (29.03%)	
Midday	12 (38.71%)	13 (41.94%)	
Evening	5 (16.13%)	6 (19.35%)	
After taking medicine	6 (19.35%)	3 (9.68%)	
Other time	5 (16.13%)	4 (12.90%)	
Symptoms			
Suddenly feeling hungry	5 (16.13%)	12 (38.71%)	
Shaking	13 (41.94%)	16 (51.61%)	
Cold and sweating	19 (61.30%)	19 (61.30%)	
Restlessness	12 (38.71%)	9 (29.03%)	
Throws-up	6 (19.35%)	2 (6.45%)	
Dizziness	7 (22.58%)	7 (22.58%)	
Headache	7 (22.58%)	14 (45.16%)	
Palpitations	5 (16.13%)	9 (29.03%)	
Blurred vision	13 (41.94%)	8 (25.81%)	
Management of Hypoglycemia			
Increasing calorie intake	31 (100%)	31 (100%)	
Ask for help from the nearest health center	2 (6.45%)	0 (0%)	
Self-Monitoring Blood Glucose	2 (6.45%)	0 (0%)	

NHIP = National Health Insurance Participants; N-NHIP = Non-National Health Insurance Participants; *Chi-square test

the incidence of hypoglycemia in T2D patients. Interventions can include collaboration between health workers (doctors, nurses, pharmacists, dietitians, and diabetes educators), telehealth programmes, and home visits[33–36]. These interventions were aligned with the ADA/EASD recommendation, where T2D patients were encouraged to participate in the Diabetes Self-Management Education and Support (DSME/S) programme. The DSME/S program involves face-to-face meetings in groups or individual sessions with trained educators to increase patient knowledge, glycemic control, compliance with medication, a healthy lifestyle, and increased self-efficacy. DSMES has also been shown to reduce hospitalisation rates and the risk of death in T2D patients[3].

Using technology in health facilities during a pandemic can support the success of therapy and prevent hypoglycemia in patients. In China, using technologies such as mobile-enabled apps has been shown to reduce the incidence of hypoglycemia and improve glycemic control in T2D patients[37].

This study has several limitations. This study was a self-reported type of survey, which could be biased. Besides that, due to the implementation of the patient's visit restrictions policy during the COVID-19 pandemic, we could only find a limited number of samples. The unavailability of another predictor of hypoglycemia (such as GFR) can also affect the result. However, the author has made various efforts to minimise biassed impacts, such as confirming the symptoms of hypoglycemia experienced by patients, whether they improve after consuming sweet foods or drinks, and seeking the number of samples to meet the minimum testing requirements statistically.

In future studies, it was necessary to conduct a similar study with a larger sample size and represent the population of T2D patients in areas throughout Indonesia to generalise the results. In addition, it was also necessary to survey the factors that significantly affect the incidence of hypoglycemia in the population of type 2 DM patients in Indonesia.

CONCLUSION

The incidence of hypoglycemia in T2D patients during the COVID-19 pandemic in Indonesia was relatively high. The incidence of hypoglycemia in N-NHIP was higher than in NHIP during the COVID-19 pandemic in Indonesia, but it was not statistically significant. Hypoglycemia was more common in patients taking insulin. The provision of education related to preventing hypoglycemia, especially for insulin users, needs to be increased. The implementation of DSME/S can be further developed to be widely applied in Indonesia.

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