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CORRELATION OF HEMOGLOBIN A1C WITH FASTING BLOOD PLASMA GLUCOSE IN PATIENTS WITH DIABETES MELLITUS AND ITS IMPLICATION AS A MARKER OF GLUCOSE CONTROL

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ABSTRACT
Diabetes mellitus (DM) is a chronic disease whose prevalence continues to increase globally. Objective: This study aimed to analyze the correlation between hemoglobin A1c (HbA1c) and fasting blood plasma glucose (GDP) in patients with diabetes mellitus and its implications as a marker of glucose control. Method: A cross-sectional study was conducted using the medical records of 299 patients with diabetes mellitus (170 males and 129 females; age range: 19-90 years) treated at Bali Mandara Hospital from January to December 2022. Data on GDP levels and HbA1c values were collected and classified based on glycemic control. The correlation between GDP and HbA1c levels was tested using Spearman's test. Results: The mean HbA1c value was not significantly different between the sexes and age groups, with higher values found in the 45-59 years age group and in women (7.88 ± 0.20%). The GDP ranged from 72-594 mg/dL, with a mean value of 181.45 ± 4.43 mg/dL. A significant positive correlation was observed between GDP and the HbA1c level ($p<0.05$). Poor glycemic control was found in 54.18% of the patients based on HbA1c and 69.23% based on GDP. Conclusions: Correlation between HbA1c levels and GDP is crucial for determining accurate and effective diabetes management strategies in clinical practice.

Keywords: blood plasma glucose; degenerative disease; diabetes mellitus; glycemic control; HbA1c

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INTRODUCTION

Diabetes mellitus (DM) is a chronic disease whose prevalence continues to increase globally. This disease has already caused mortality in up to 2 million people worldwide (World Health Organization, 2023). To date, the global prevalence of diabetes mellitus increased by 129.7%, from 211.2 million in 1990 to 476.0 million in 2017 (Lin et al., 2020). This increase in cases is also experienced by Indonesia, the country with the fifth highest number of diabetes mellitus cases in the world after China, India, Pakistan and the United States (International Diabetes Federation, 2021). After China, India, Pakistan and the United States, Indonesia ranks fifth in terms of diabetes mellitus cases(International Diabetes Federation, 2021). The prevalence in the age group above 15 years in 2013 was 1.5%, which increased to 2% in 2018 (Kementerian Kesehatan RI., 2020). The prevalence of diabetes mellitus in Bali Province was 1.33%, of which 1.31% were women and 1.35% were men. The greatest percentage of patients were aged 55-64 years, reaching 6.10% (Kemenkes-RI, 2019).

Effective diabetes management requires close monitoring of blood glucose levels to prevent long-term complications. Diabetes mellitus-related examinations can be performed using four

parameters: fasting plasma glucose (126 mg/dL), 2-hour plasma glucose during a 75 g oral glucose tolerance test (200 mg/dL), HbA1c (6.5%), and random glucose (200 mg/dL). Hemoglobin A1c (HbA1c) has long been used as an indicator of long-term glycemic control, while fasting blood plasma (GDP) glucose measurement is often used in daily routine assessments of patients. Postprandial blood plasma glucose levels are more closely related to HbA1c than are fasting blood plasma glucose levels. Postprandial blood plasma glucose levels are better used to predict blood sugar control when HbA1c is not available. However, another study reported that fasting blood plasma glucose is significantly related to HbA1c in patients with type II diabetes (Hutagalung et al., 2019; Tika et al., 2019). Fasting plasma glucose and 2-hour postprandial plasma glucose levels are positively correlated with HbA1c. Thus, there is a mismatch between the glucose management index and HbA1c; therefore, HbA1c screening may not be as accurate as glucose averaging, and the relationship between glucose and HbA1c should be interpreted on an individual basis (Murtiningsih et al., 2021)

Although HbA1c and GDP are often used together, the relationship between them is not fully understood by many healthcare practitioners. This limitation may lead to a lack of accuracy in diabetes monitoring and management. Therefore, there is an urgent need to clarify the correlation between HbA1c and GDP to improve effective diabetes management strategies. In this study, the following questions were raised: what is the correlation between hemoglobin A1c levels and fasting blood plasma glucose in patients with diabetes mellitus? Moreover, is HbA1c more reliable as a reliable marker of glucose control than GDP in the everyday clinical context? needs to be clarified further.

This study aimed to analyze the correlation between hemoglobin A1c and fasting blood plasma glucose in patients with diabetes mellitus and its implications as a marker of glucose control. Understanding the correlation between HbA1c and GDP is crucial in the clinical context, as it can help determine more accurate and effective diabetes management strategies. This study not only provides insight into the effectiveness of using HbA1c as a marker of long-term glucose control but also may influence clinical guidelines for monitoring and managing patients with diabetes mellitus. With this information, health care practitioners can improve the quality of care and long-term health outcomes of patients with diabetes.

METHOD

Analytic observational research using a cross-sectional approach was conducted in this study (Darwin et al., 2021). The study data were obtained from the medical records of patients with diabetes mellitus at RSUD Bali Mandara who underwent intensive care between January and December 2022. The collected data included fasting plasma glucose and HbA1c values. The research samples selected were those that met the inclusion criteria, including having been treated for three months or more and having complete data on fasting blood glucose and HbA1c. The exclusion criteria in this study were diabetes mellitus patients who were not intensively treated, had controlled blood sugar levels, and had diseases other than diabetes mellitus. All research data were collected on the author's data recording sheet, and permission was obtained from the Research Section of Bali Mandara Hospital. Ethical permission was obtained from the Health Research Ethics Committee of RSUD Bali Mandara (permit number: 026/EA/KEPK/RSBM.DISKES/2023).

HbA1c values >6,5% were classified as poor glycemic control, 5,7-64% as moderate glycemic control, and HbA1c values <5,7% as good glycemic control. Moreover, a GDP >126 mg/dL was classified as poor glycemic control, 100-125 mg/dL as moderate glycemic control, and <99 mg/dL as good glycemic control.(PERKENI, 2021) All the data were

tabulated in Microsoft Excel®, Inc., version 2019, and then statistically analyzed using SPSS, Inc., USA, version 25.0. All the data were tested for normality using the Kolmogorov–Smirnov test. The correlation between fasting blood sugar and HbA1c levels was tested using the Spearman test because the data obtained were not normally distributed (Paulus et al., 2023). Differences between the two groups were tested using the Mann–Whitney test with a probability of 95% ($p<0.05$). All the data are presented in tables, figures, and narratives.

RESULTS

Characteristics of respondents based on age and gender

A total of 299 patients (170 men and 129 women; age range, 19–90 years) with diabetes mellitus who were treated at Bali Mandara Hospital were included in this study; the ages of the patients ranged from 19–90 years. HbA1c values ranged from 4.6% to 16.2%. The mean HbA1c value was not different ($p>0.05$; Mann–Whitney test) between sex and age; however, higher values were found in 45–59-year-olds, as well as in women, namely, 7.88 ± 0.20%. The characteristics of the respondents by age and sex are presented in Table 1.

Table 1.
Characteristics of diabetes mellitus patients by age group and gender

Age	Characteristics				Total		Age			Gender		
	Male		Female				Mean ± SE	Min	Max	Rerata± SE	Min	Max
	f	%	f	%	f	%	(%)	(%)	(%)	(%)	(%)	(%)
19-44	23	7,7	13	4,3	36	12	7,77 ± 0,41	5,0	13,4	7,79 ± 0,18	4,8	16,2
45-59	58	19,4	48	16,1	106	35,5	8,12 ± 0,23	4,7	15,6	7,88 ± 0,20	4,6	14,2
≥60	89	29,8	68	22,7	157	52,5	7,66 ± 0,18	4,6	16,2	7,83 ± 0,13	4,6	16,2

Remaks: Mann–Whitney test (p>0,05); Min: Minimum, Max: Maximum; SE: Standard error

Characteristics of glycemia control based on HbA1c value, age and sex

Based on the characteristics of glycemic control based on HbA1c values, most diabetes mellitus patients had poor glycemic control; namely, 198 people had an average HbA1c value of 8.91 ± 0.15%. Furthermore, in terms of sex, poor glycemic control was mostly male, namely, 114 people had an average HbA1c value of 83 ± 2.12%. Based on age, poor glycemic control is mostly observed at the age of > 60 years. The characteristics of glycemic control based on HbA1c values, age, and sex are presented in Tables 2, 3, and 4.

Table 2.
Glycemia control of patients with diabetes mellitus based on HbA1c values

Glycemia Control	f	HbA1c		
		Mean ± SE (%)	Min (%)	Max (%)
Poor	197	8,93 ± 0,15	6.5	16.2
Medium	57	6,04 ± 0,03	5.7	6.4
Good	45	5,30 ± 0,04	4.6	5.6

Table 3.
Glycemia control of patients with diabetes mellitus stratified by sex

Gender	Glycemia Control	Mean ± SD (%)	N
Male	Poor	8,83 ± 2,12	114
	Medium	6,04 ± 0,25	30
	Good	5,27 ± 0,26	26
	Total	7,79 ± 2,30	170
Female	Poor	9,06 ± 2,09	83
	Medium	6,05 ± 0,24	27
	Good	5,35 ± 0,32	19

Table 4.
Age-based glycemic control in patients with diabetes mellitus

Age (Year)	Glycemia Control	Mean ± SD (%)	f
19-44 Years	Poor	9,18 ± 2,13	22
	Medium	6.00 ± 0,22	4
	Good	5.37 ± 0,24	10
	Total	7.77 ± 2,45	36
45-59 Years	Poor	9,32 ± 1,96	70
	Medium	6,02 ± 0,26	23
	Good	5,16 ± 0,27	12
	Total	8,12 ± 2,35	105
>60 Years	Poor	8,61 ± 2,16	105
	Medium	6,07 ± 0,23	30
	Good	5,35 ± 0,29	23
	Total	7,66 ± 2,23	158

Remarks: SD: Standard deviation

Correlation of HbA1c with fasting blood plasma glucose in diabetes mellitus patients

The results of the identification of the mean fasting blood plasma glucose (GDP) levels were not significantly different (P>0.05; Mann–Whitney test) between the characteristics of sex and age; however, higher values were found at the age of 45–59 years, which amounted to 171.15 ± 6.40 mg/dL, and in women, which amounted to 165.87 ± 6.75 mg/dL. The correlation between HbA1c and fasting blood plasma glucose in patients with diabetes mellitus is presented in Tables 5 and 6.

Table 7.
Mean fasting blood plasma glucose levels by group

Age (Years)	f	Mean±SE (mg/dL)	Min (mg/dL)	Max (mg/dL)
19-44	36	164,39 ± 12.00	85	371
45-59	105	171,15 ± 6,40	89	392
>60	158	161,64 ± 5,89	33	455
Total	299	165,31 ± 4,10	33	455

Remaks: P>0,05; Mann–Whitney test

Table 8.
Mean fasting blood plasma glucose levels by sex

Gender	f	Mean±SE) (mg/dL)	Min (mg/dL)	Max (mg/dL)
Male	170	164,89±5,09	33	381
Female	129	165,87±6,75	78	455
Total	299	165,31±4,10	33	455

Remaks: P>0,05; Mann–Whitney test

Based on fasting blood sugar levels, most patients with diabetes mellitus had poor glycemic control (194 people with an average GDP of 198.91 ± 4.76 mg/dL), which was dominated by male patients (117 people with an average GDP of 193.01 ± 60.93 mg/dL). This condition was dominated by male patients, namely, 117 people with an average GDP of 193.01 ± 60.93 mg/dL, and there were 99 people over the age of 60 years with an average GDP of 196.84 ± 72.40 mg/dL. The results of glycemia control based on GDP levels, sex, and age are presented in Tables 9, 10, and 11. Correlation analysis revealed a significant correlation ($p < 0.05$) between the HbA1c level and the fasting blood plasma glucose level in patients with diabetes mellitus, with a correlation coefficient of 0.584 (58.40%), while the other factors were not examined in this study (Figure 1).

Table 9.
Glycemia control based on GDP levels

GDP	f	Mean ± SE (mg/dL)	Min (mg/dL)	Max (mg/dL)
Poor	194	198,91 ± 4,76	126	455
Medium	68	111,93 ± 0,95	100	125
Good	37	87,24 ± 2,23	33	99
Total	299	165,31 ± 4,10	33	455

Table 10.
Glycemia control by sex

Gender	Glycemia Control	Mean±SD (mg/dL)	f
Male	Poor	193,01 ± 60,93	117
	Medium	111,78 ± 8,26	36
	Good	83,82 ± 18,42	17
	Total	164,89 ± 66,36	170
Female	Poor	207,88 ± 73,05	77
	Medium	112,09 ± 7,48	32
	Good	90,15 ± 6,64	20
	Total	165,87± 76,61	129

Table 11.
Glycemia control by age

Age (year)	Glycemia control	Mean ±SD (mg/dL)	f
19-44 Tahun	Poor	204,05 ± 65,68	22
	Medium	109,62 ± 9,27	8
	Good	92,00 ± 6,07	6
	Total	164,39 ± 71,99	36
45-59 Tahun	Poor	200,18 ± 57,86	73
	Medium	111,19 ± 8,29	21
	Good	93,00 ± 3,07	11
	Total	171,15 ± 65,54	105
>60 Tahun	Poor	196,84 ± 72,40	99
	Medium	112,79 ± 7,37	39
	Good	82,65 ± 16,91	20
	Total	161,64 ± 74,08	158

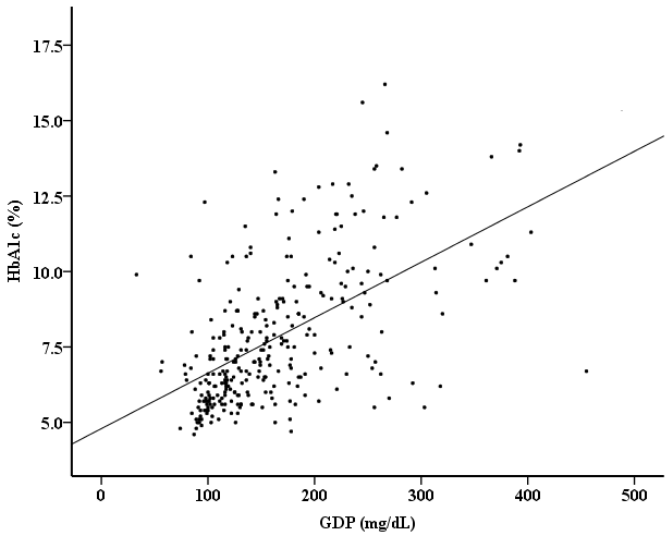

Figure 1. Correlation of fasting blood plasma glucose levels with HbA1c values

DISCUSSION

Correlation of HbA1c with fasting blood plasma glucose in diabetes mellitus patients

The HbA1c and GDP did not differ according to sex or age; however, most diabetes mellitus patients aged > 60 years had poor glycemic control. Generally, with increasing age, the body's immune system decreases, leading to various degenerative diseases. One study revealed associations between age, obesity, lack of physical activity, hypertension, low education, unemployment, and urban residence and prediabetes (Greiner, 2020). The disparities that occur due to a lack of access to health services, as well as the high costs that must be borne, are also factors that hinder diabetes control (Albanese-O'neill, 2022). In adults over 45 years of age, diabetes and prediabetes are also common due to low awareness, treatment and control of diabetes mellitus (Bai et al., 2021). However, younger individuals are also at risk of developing degenerative diseases such as hypertension, heart disease, cholesterol, and diabetes mellitus (Novita & Efrarianti, 2023). Patients with poor glycemic control were predominantly male. However, there is no association between sex and the incidence of type 2 diabetes mellitus (Susilawati and Rahmawati, 2021). Many factors are believed to trigger the emergence of diabetes mellitus, such as age, body mass index, and optimization of energy expenditure, in both men and women (Choi & Shi, 2001). Reduced physical activity and increased obesity may be factors that trigger an increase in the prevalence of diabetes (Nanayakkara et al., 2018).

There was a significant relationship between HbA1c and GDP in patients with diabetes mellitus. This indicates that as HbA1c levels increased, GDP levels also increased. Similar studies have also shown a correlation between fasting plasma glucose and HbA1c (Hasanah & Ikawati, 2021; Supono & Yasa, 2021). Glucose molecules attached to hemoglobin form glycated hemoglobin. Glycated hemoglobin will remain alive in erythrocytes for 120 days (Wang, 2021). Therefore, glycated hemoglobin indicates the average blood glucose level over that time frame and can act as a surrogate marker of glucose concentrations over the previous 8-12 weeks (Hovestadt, 2022). However, because erythrocyte turnover occurs continuously, it is estimated that only 50% of the HbA1c value is glycated with glucose during the previous 30 days, 40% during the previous 31-90 days, and 10% during the previous 91-120 days (Wang, 2021).

HbA1c is a hemoglobin (Hb) molecule that binds to glucose. HbA1c has been used as a marker of glycemic control in the last three months in patients with diabetes mellitus (Wang, 2021; Koga et al., 2020). Lower HbA1c levels are associated with better metabolic control (Loocke, 2021). This is useful for the further diagnosis and treatment of patients with diabetes. The advantage of the HbA1c test is that patients do not need to fast overnight (Gonzalez et al., 2020). In the fasting blood plasma glucose test, patients are recommended to fast beforehand. HbA1c and fasting blood plasma glucose are effective tests for detecting type 2 diabetes mellitus. The cutoff value of HbA1c is above 6.1%; however, there are differences regarding this cutoff based on ethnic group, age, sex and the prevalence of diabetes in a population (Bennett et al., 2007).

Measuring HbA1c can help patients control their diabetes, motivate behavioral changes, and reinforce healthy lifestyle choices (Hirst et al., 2020). Measuring HbA1c levels is also an acceptable method because it is convenient and useful for diabetes control (Arnold, 2020). In addition, the use of HbA1c as a diabetes control measure is also closely related to cost savings for overall diabetes care (Lage & Boye, 2020). The prevention of diabetes mellitus complications can be minimized by healthy living behavior to improve foot health (Safitri et al., 2022). Awareness can be achieved by controlling this disease to increase life expectancy

and increasing physical activity, and consuming healthy foods can control HbA1c and GDP levels and prevent diabetes mellitus (Murtiningsih et al., 2021).

Implications of HbA1c as a glucose control measure

Based on these findings, the theoretical implications of this study strengthen the validity of HbA1c as a marker for long-term glucose control in patients with diabetes mellitus. The significant correlation between HbA1c and fasting blood plasma glucose (GDP) confirms that HbA1c can be used as a key indicator for evaluating patients' glycemic control (Ojo et al., 2023; Sherwani et al., 2016). The results of this study provide insight into the relationship between these two important parameters in diabetes management (Camargo-Plazas et al., 2023). This helps in understanding how plasma glucose fluctuations affect HbA1c levels, providing a basis for further studies on the molecular and physiological mechanisms underlying glucose control. This research paves the way for more specific follow-up studies, such as longitudinal studies to evaluate changes in HbA1c and GDP over time or intervention studies to examine the impact of new treatments on these two parameters (Anggraini et al., 2020; Gathu et al., 2018; Zhang et al., 2019).

Furthermore, this study has practical implications in that by understanding the strong correlation between HbA1c and GDP, clinicians can confidently use HbA1c as the primary parameter for monitoring glycemic control (Jarvis et al., 2023). This approach facilitates the identification of patients with poor glucose control and allows for faster intervention. Considering that most patients over 60 years of age have poor glycemic control, clinicians need to be more vigilant toward this age group. Diabetes education and management programs specifically designed for elderly people can improve glucose control. The fact that HbA1c and GDP did not differ significantly between sexes or ages means that treatment approaches can be more standardized but still need to be tailored based on age and patient-specific clinical conditions (Dubowitz et al., 2014).

The results of this study can be used in patient education, emphasizing the importance of maintaining glucose control through both GDP and HbA1c monitoring. This education can increase patient awareness of the importance of long-term control and medication adherence (Chen et al., 2023). With evidence that HbA1c is a reliable marker for glucose control, hospitals and clinics can develop clearer clinical protocols for the testing and follow-up of diabetic patients. This includes the frequency of HbA1c testing and actions taken based on the results. Overall, this study confirms the importance of HbA1c as a diagnostic and monitoring tool in diabetes management and encourages improved patient management strategies, especially in the elderly population.

CONCLUSION

A significant positive correlation was observed between GDP and the HbA1c level ($p<0.05$). Poor glycemic control was found in 54.18% of the patients based on HbA1c and 69.23% based on GDP. The discrepancy between HbA1c and GDP in assessing glycemic control highlights the need for individual interpretation of the relationship between these markers. Understanding the correlation between HbA1c levels and GDP is crucial for determining accurate and effective diabetes management strategies in clinical practice. Further research is needed to identify the mechanism by which long-term HbA1c is a marker of glycemic control in patients with diabetes mellitus.

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