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Correlation Between HbA1c Levels and Chronic Complications in Patients with Type 2 Diabetes Mellitus at UNS Hospital

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ABSTRACT

Introduction: Diabetes mellitus has been a burden for global health with 422 million patients. Complication in diabetes patients increase the cost of patient care. This research was conducted to determine the correlation between HbA1c levels and chronic complications of type 2 diabetes mellitus in UNS hospital. Furthermore, the HbA1c predictive threshold and the incidence of chronic problems linked to type 2 diabetes mellitus are also explained in this paper.
Methods: This study used a retrospective cross-sectional design based on 133 inpatient medical records from 2022. Data were collected using a purposive sampling method that adjust the inclusion and exclusion criteria. Data analysis using SPSS 23 software with logistic regression.
Results: (1) There is a significant correlation of HbA1c levels and chronic complication of type 2 diabetes mellitus patients in UNS Hospital. (2) HbA1c score of 6.5% or above is best cutoff to use for determining whether type 2 diabetes mellitus was developing chronic problems. (3) The prevalence of the organ with the most involvement in complication is cardiovascular (51,4%).
Conclusion: There is a significant correlation of HbA1c levels and chronic complication of type 2 diabetes mellitus in UNS Hospital with cardiovascular as the organ with the most involvement.

Keywords: Correlation between type 2 diabetes mellitus; HbA1c; Chronic; Complication; Prevalence

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder with hyperglycemia, a condition where blood glucose levels increase beyond normal conditions. There are four types of diabetes mellitus, namely: type 1 diabetes mellitus, type 2 diabetes mellitus, gestational diabetes, and other types of diabetes[1]. Diabetes mellitus is a global health burden with over 422 million affected individuals. According to an analysis conducted by the International Diabetes Federation in 2021 on 144 countries, there is an estimated increase in the prevalence of diabetes mellitus by 16% in 2045 due to an increase in population, especially in developing countries. Meanwhile, in poor countries, the increase is estimated to reach 94%[2]. Elevated blood sugar levels in T2DM patients heighten the risk of cardiovascular disease and other complications, leading to 2.2 million deaths. The IAF Diabetic Model project forecasts a rise in the rates of vision loss (from 4,267,000 to 6,260,000 cases), kidney complications (from 62,020 to 89,390 cases), and leg amputations (from 53,860 to 67,190 cases). Complications in diabetic patients significantly increase healthcare costs [4,5]. This study is important to be performed in uns hospitals as a

study base on the significance of routine hba1c monitoring in T2DM cases to adjust the treatments and reduce the socioeconomic impact.

The United States has developed a strategy for managing diabetes mellitus until 2030, which includes efforts to raise public awareness and inform policymaking. It is crucial to conduct early screening and education to detect diabetes and prediabetes cases promptly. Early diagnosis can be achieved by identifying classic diabetes symptoms and conducting laboratory tests such as fasting blood glucose, oral glucose tolerance, and HbA1c measurements[1]. Apart from early diagnosis, routine control as a follow-up and control of the patient's condition needs to be carried out routinely to prevent complications, metabolic control can prevent the development of diabetes complications[1]. In addition to early diagnosis, routine follow-up and metabolic control are necessary to prevent the development of diabetes complications[5]. HbA1c, a method for examining hyperglycemia, is associated with complications and case mortality. Conducting studies on the relationship between HbA1c and chronic complications in T2DM is expected to contribute to the clinical assessment and prognosis of the disease.

Prior researches has discussed the correlation between HbA1c and the prevalence of chronic T2DM complications[7] but none has been done in the location of this research. It is necessary to examine the chronic complications of type 2 diabetes mellitus as it increased the mortality rate and patient's expenditure. This retrospective study investigates the relationship between HbA1c levels and the emergence of complications in individuals with diabetes mellitus. Employing a logistic regression analysis, the findings demonstrate the positive predictive value of the data utilized in this research. Additionally, the paper provides a predictive threshold for HbA1c and the occurrence of chronic complications associated with type 2 diabetes mellitus.

METHOD

This study used a retrospective cross-sectional design based on 133 inpatient medical records from 2022. The inclusion criteria in this study were inpatients with T2DM who experienced chronic and acute complications, has been tested for HbA1c, and the medical records used were from 2022. The exclusion criteria in this study were incomplete medical records, anemic patients, and patients with a history of transfusion in the last 2 - 3 months.

This research data analysis uses logistic regression method to determine the relationship and predict the relationship between HbA1c and the incidence of chronic complications in T2DM patients at UNS Hospital in 2022. The data obtained from the research is in the form of HbA1c data which is a numerical variable as an independent variable and data on chronic complications of T2DM patients at UNS Hospital which is a categorical variable on a nominal scale as the dependent variable. This research was carried out with a written statement of ethical suitability provided by the Research Ethics Committee of RSUD Dr. Moewardi with letter number 923/V/HREC/2023 and a research permit granted by UNS Hospital with letter number 2707/UN27.46/TA.04.19/2023.

RESULT

Characteristic of Research Subjects

The research subjects' characteristics are displayed in Table 1, where 67 individuals (50,4%) were discovered to be female and 66 individuals (49,6%) to be male. After classifying the 133 research participants based on age, it was found that, with 66 people in each group, the age groups with the highest prevalence of diabetes mellitus were over 60 and 30 to 60 years old. This figure is significantly greater than the one person (0.8%) observed in the group under 30. There were 59 patients (44.4%) with risk factors for hypertension, based on the risk factor category. Out of the 133 patients with type 2 diabetes mellitus (T2DM) that were sampled, 89 of them had chronic complications, and the other 44 had various complications, such as acute complications and/or infection.

Table 1. Characteristics of Research Subjects

Characteristics		Frequency (n)	Percentage (%)
Gender	Male	66	49,6
	Female	67	50,4
Age	<30	1	0,8
	30—60	66	49,6
	>60	66	49,6
Risk Factor	Hypertension	59	44,4
	Without hypertension	74	55,6
Chronic complication	Existed	89	66,9
	Not existed	44	33,1

Distribution of HbA1c Levels in Research Subjects

Table 2 shows the majority of individuals diagnosed with type 2 diabetes mellitus, including those with and those without chronic problems, had HbA1c levels above 7.0%. Nonetheless, compared to patients without a chronic complications, those who experienced one showed a higher average of HbA1c level which was 9,78%, against 8,38% in patients without chronic complications.

Table 2. Distribution of HbA1c Levels in Research Subjects

HbA1c levels	Average	<6.5% (%)	6.5%—7.0% (%)	>7.0% (%)
Chronic complication present	9.78	10 (11,2)	12 (13,5)	67 (75,3)
Chronic complication not present	8.38	7 (15,9)	7 (15,9)	30 (68,2)

Correlation Between HbA1c Levels and Chronic Complication of Type 2 Diabetes Mellitus

Logistic regression test in table 3 provides a significance level of 0.021 ($p<0.05$), suggesting a significant correlation between type 2 diabetes mellitus chronic complications and HbA1c levels. The likelihood of developing chronic problems rises by 1.184 times (CI 95% 1.026 — 1,368) for every 1% increase in HbA1c.

Table 3. Relationship between HbA1c levels and complications in diabetes mellitus patients

	Sig	Exp (B)	95% *CI for Exp(B)*	
			Lower	*Upper*
HbA1c	0,021	1,184	1,026	1,368

Predictive HbA1c Levels with the Incidence of Chronic Complication of Type 2 Diabetes Mellitus

Table 4. Predictive HbA1c levels with the incidence of chronic complications of type 2 diabetes mellitus

		Prediction		
		Chronis complication based on HbA1c levels		Percentage Correct (%)
		Present	Not present	
Chronic complication based on data	Present	89	0	0
	Not present	44	0	100
Total percentage				66,9

The logistic regression method classification test in Table 4 showed that 89 of the patients with chronic complications actually had complications, and the remaining 44 were expected to have chronic complications as well. As a result, the positive predictive value of the data in this research is 66,9%. The results indicate that a significant number of patients without a prior diagnosis of chronic complications are either currently experiencing or predicted to develop such complications.

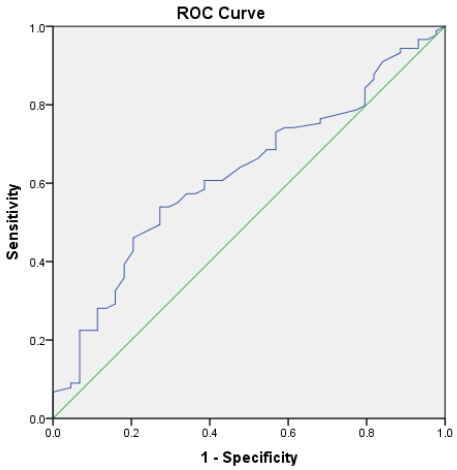

Image 1. ROC Curve of HbA1c Levels with Chronic Complications of Type 2 Diabetes Mellitus

According to the ROC curve study, predicting the development of chronic complications in individuals with a HbA1c level of 6.5% has an 86.5% sensitivity and an 81.8% specificity (AUC=0.622). HbA1c levels of 6.5% or higher were found to be the optimal threshold for predicting chronic complications.

Table 5. Sensitivity and Specificity of HbA1c Levels with the Incidence of Chronic Complications of Type 2 Diabetes Mellitus

HbA1c (%)	Sensitivity	Specificity
6,5	86,5%	81,8%
6,6	84,3%	79,5%
6,7	79,8%	79,5%
6,8	78,7%	77,3%
6,9	77,5%	72,7%
7,0	76,4%	68,2%

Prevalence of Diagnosis of Chronic Complications of Type 2 Diabetes Mellitus Based on Organ

Based on the recorded cases cardiovascular complications were the most prevalent (51.4%). On the other hand, complication involving the peripheral nervous system and eyes were less prevalent, with only 1 case reported for each (0,6%). While heart-related damage exhibited the highest rate, the most frequent observed complication diagnose was kidney failure, occurring in 30 cases (19,4%). Comprehensive data on the prevalence of diagnosed chronic complications of Type 2 Diabetes Mellitus, categorized by affected organ, can be found in Table 6.

DISCUSSION

Diabetes mellitus type 2 rates increased equally in both men and women. Men are often diagnosed with diabetes mellitus at a younger age and with a lower BMI[8]. In contrast to men, women have a greater risk of developing obesity which is a risk factor for diabetes mellitus and experiencing changes in the estrogen hormone, such as menopause at an advanced age[8,9].

Apart from gender, age also influences the incidence of type 2 diabetes mellitus. The majority in the 30-60 year age group and above 60 year age group are 66 people (49.6%). Type 2 diabetes mellitus is low in the age group under 30, but increases drastically in the age group over 60 years due to the increased risk of metabolic syndrome, chronic inflammation that causes insulin resistance, lack of physical activity, and eating disorders experienced by the elderly[10–12].

Hypertension is a risk factor for insulin resistance which causes hyperglycemia[13], however in this study it was found that there were more T2DM subjects without hypertension, namely 66.2%. Similar data was also found in research conducted at Soetomo Hospital, Surabaya, that there were 686 diabetes mellitus patients without hypertension (77.8%)[14] and research in Palestine which showed that the percentage of diabetes patients without diabetes was 77%[15]. Even if an individual doesn't have hypertension, there are still many risk factors for T2DM that can be considered, such as age, genetics, physical activity, living habits, and BMI[10].

Table 6. Prevalence of Diagnosis of Chronic Complications of Type 2 Diabetes Mellitus Based on Organ

Chronic complication based on organs	Frequency (n)	Percentage (%)
CNS	39	25,1
Cerebral infract	26	16,8
Plegia	12	7,7
Stroke	1	0,6
Cardiovascular	80	51,4
Valve disorder	20	12,9
Congestive heart failure	17	11
Myocard infarct	14	9
Heart failure	12	7,7
Ischemic	7	4,5
Cardiac arrest	5	3,2
Pulmonary heart disease	2	1,3
Cardiogenic shock	1	0,6
Atherosclerosis	1	0,6
Heart attack	1	0,6
Kidney	30	19,4
Kidney failure	30	19,4
PNS	5	3,2
Neuropathy	5	3,2
Eyes	1	0,6
Cataract	1	0,6
Total	155	100

There is a significant relationship between HbA1c levels and chronic complications in T2DM patients (p=0.021) with every 1% increase in HbA1c levels increasing the likelihood of complications by 1.184 times (CI 95% 1.026—1.368). This is in line with previous research that high HbA1c levels influence the incidence of chronic complications in 63.4% of patients with uncontrolled HbA1c levels. HbA1c is a good method for measuring chronic hyperglycemia and its complications[17]. Uncontrolled hyperglycemia in type 2 diabetes mellitus patients can cause complications and reduce the patient's quality of life[4]. High levels of HbA1c are associated with atherosclerosis, retinopathy and nephropathy which lead to complications[18].

Based on the results of the logistic regression classification test in table 2, it was found that 44 subjects without chronic complications were predicted to experience complications and 89 subjects with chronic complications indeed experienced complications, so the percentage of subjects with chronic complications from the data should be 100%. Table 2 shows the distribution of HbA1c of research subjects showing a high percentage of HbA1c levels of 6.5%—7.0% and >7.0%, both in subjects with complications and in subjects without complications. Previous research shows that chronic complications tend to occur in patients with uncontrolled HbA1c levels (>7.0%), but in this study it was still found that patients with HbA1c levels <7.0% experienced complications and were predicted to experience complications.

ROC curve analysis of the data shows that HbA1c levels >7.0% have a sensitivity of 76.4% and specificity of 68.2%, while sensitivity and specificity show higher numbers at 6.5% with sensitivity of 86.5% and specificity of 81,8%. This finding is similar to previous research. ROC curve analysis in diabetes mellitus patients with the incidence of diabetic neuropathy with HbA1c levels >6.5% showed a sensitivity of 80.6% and a specificity of 86.9%. This makes an HbA1c level >6.5% the cut off for diagnosing complications of diabetic neuropathy in diabetes mellitus patients[19]. Type 2 diabetes mellitus patients with HbA1c levels >6.5% have shown a decrease in cardiac perfusion and ejection function resulting in an increased incidence of hypertension, complications of heart failure, and CAD[20]. Type 2 diabetes mellitus patients with HbA1c levels >6.7% show a higher risk of small artery occlusion causing stroke[21]. Large artery occlusion patients with HbA1c >6.5% showed a significant increase in the decline in functional independence and the incidence of mortality[22]. The explanation above shows that an HbA1c level >6.5% is more suitable as a cut off for the incidence of chronic complications in type 2 diabetes mellitus patients. However, the HbA1c level cannot be the sole parameter for diagnosing complications in diabetes mellitus patients because of the many factors involved in pathogenesis of chronic complications of diabetes, such as age, genetics, living habits, and comorbidities[10,11,23].

Calculation of the prevalence of diagnosed complications in this study showed data of 155 data which exceeded the number of research subjects. This occurred because there were patients who experienced diagnosed complications in more than one organ. Research conducted in China showed similar results in that more than half of the study subjects experienced at least one chronic complication and almost a quarter of the study subjects experienced two or more complications.

Central Nerve System

There were 39 diagnoses (25.1%) of central nervous system organ complications that occurred in research subjects. The prevalence of cerebral infarction was 26 cases (16.8%), plegia was 12 cases (7.7%), then stroke was 1 case (0.6%). Previous research stated that there was a significant relationship between diabetes mellitus and central nervous system complications of 0.023 (<0.05)[24]. Type 2 diabetes mellitus causes intracranial plaque which can cause infarction of brain tissue. Due to abnormal metabolism of glucose, plaque formation occurs which then causes thrombosis, rupture, and disruption of the blood vessel endothelium. Apart from that, hyperglycemia also causes an increase in ROS which increases the production of inflammatory mediators which causes the formation of atherosclerosis in blood vessels in the central nervous system which ends in brain tissue ischemia[25].

Cardiovascular System

Cardiovascular complications were the most frequent complications experienced by research subjects with a total of 80 cases (51.4%). The three diagnoses of heart complications with the highest prevalence were heart valve disorders with an incidence of 20 cases (12.9%), congestive heart failure with 17 cases (11%), and heart failure with 12 cases (7.7%). Research conducted in China also showed similar results that cardiovascular disease was a complication with the highest prevalence, namely 30.1%. Heart disease and T2DM have similar risk factors, such as obesity, hypertension, and dyslipidemia, so diabetes mellitus can increase the risk of heart disease[26]. Insulin resistance and hyperglycemia are associated with inflammation and chronic increases in oxidative stress that trigger endothelial dysfunction and cause atherogenesis[27].

Kidney

Although cardiac involvement overall had the highest prevalence, kidney failure was the most frequent complication found in study subjects, namely 30% (19.4%). The prevalence of kidney disease in this study was higher than in previous studies conducted in China, namely 10.7%16. Hyperglycemia conditions in type 2 diabetes mellitus patients cause dysregulation of intercellular metabolism,

inflammation, increased apoptosis, and tissue fibrosis which causes damage to the renal glomerulus which will progressively reduce its function and cause kidney disease[28,29].

Peripheral Nerve System

Previous research stated that diabetic neuropathy was related to the duration of diagnosis of T2DM, a neuropathy prevalence of 8% was found in newly diagnosed diabetes mellitus patients and 50% was found in old patients[30]. All central nervous system complications found in this research were neuropathy, namely 5 diagnoses (3.2%) without considering the duration of diabetes mellitus due to limited research data. In the peripheral nervous system, increasing blood glucose levels will increase ROS production which will then cause endothelial damage and reduce neuronal vasodilation, thereby increasing the progression of neuropathy in diabetes mellitus patients[31]. Every 1% increase in HbA1c will increase the risk of neuropathy by 10-15%[32].

Eyes

One diagnosis (0.6%) of eye complications was found, namely cataracts. The findings of cataract prevalence in this study were lower than previous research which found that cataract prevalence reached 8.6% in the study population. Hyperglycemia and fluctuations in glucose levels experienced by diabetes patients cause stress on the endoplasmic reticulum, thereby increasing ROS levels and causing oxidative stress which causes damage to the lens fibers of the eye. In addition, increased glucose levels in the aqueous humor can cause glycation of proteins in the lens[33].

Research has been carried out as much as possible to achieve research objectives. However, there are several limitations that affect the research results, including population limitations, researchers have not reviewed the patient's family history, lifestyle and BMI due to limited data, researchers have not reviewed the duration of illness suffered by research subjects, and researchers have not reviewed complications other than chronic complications.

From this research, several suggestions can be drawn for various parties, such as clinicians and medical record officials who are expected to include information regarding BMI, family history, lifestyle and duration of the patient's illness in the patient's medical record. Future research is expected to be able to carry out research with a larger population. varied, and with more complete medical data.

CONCLUSION

HbA1c levels are significantly correlated with chronic complications in type 2 diabetes mellitus, with cardiovascular complications being the most prevalent. BbA1c examination in T2DM patients is necessary to prevent its complications.

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CONFLICT OF INTEREST

The author declare that they have no conflict of interest.

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