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The Relationship between HbA1c, GDP and Disease Duration on the Occurrence of Diabetic Neuropathy at Ibnu Sina Hospital

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ABSTRACT
Diabetes Mellitus (DM) affects over 693 million adults globally by 2045, with complications like neuropathy underscoring the need for effective monitoring. This observational case-control study at Ibnu Sina Hospital, Makassar, explores the relationship between HbA1c levels, fasting blood sugar (GDP), disease duration, and diabetic neuropathy. Analyzing 77 medical records, the study found that most participants were aged 56-65 years, predominantly male, with high rates of uncontrolled HbA1c (80.5%) and GDP (67.5%). Diabetic neuropathy prevalence was 61.0%. Statistical analysis revealed significant correlations between neuropathy and HbA1c levels (p=0.000), GDP (p=0.002), and disease duration (p=0.041). These findings highlight the impact of glycemic control and disease duration on neuropathy in DM patients.

INTRODUCTION

Diabetes Mellitus (DM) is a disease of the endocrine system diagnosed by very high blood glucose levels. DM is one of the most common and fastest growing diseases throughout the world, estimated to affect 693 million adults in 2045, an increase of >50% from 2017 (Cole & Florez, 2020). Diabetes mellitus is also a chronic disease that occurs in millions of people in the world, where this disease is caused by a lack of insulin production in the pancreas or the insulin produced cannot be used effectively by the body (Nurjana & Veridiana, 2019). This disease is also caused by metabolic disorders with the characteristics of hyperglycemia which is caused by abnormalities in insulin due to impaired insulin work or secretion (Hapsari Hidayati & Putri Indarwati Abdullah, 2020).

Based on data from the International Diabetes Federation, it shows a prevalence of 425 million people worldwide in 2017, increasing to 628 million in 2045. According to 2018 Basic Health Research Data (Riskesdas), it shows that the prevalence of DM in Indonesia is based on blood tests at ages ≥15 years in In 2013 there was 6.9% then increased in 2018 to 8.5% (Hasnita et al., n.d.). Meanwhile, South Sulawesi is one of the provinces in Indonesia with a fairly high prevalence of DM. Based on the 2013 Riskesdas results, the prevalence of DM diagnosed by doctors was 1.6% and the highest was in Pinrang Regency, reaching 2.8%. This was followed by Makassar City as the capital of South Sulawesi Province, which reached 2.5%. The high prevalence rate of DM in Makassar City can also be seen in the increase in the number of stroke patients visiting Bhayangkara Hospital cases that occurred at the Labuang Baji Makassar Regional General Hospital and the Pelamonia Makassar Level II Hospital where the results of the study concluded that poor glucose management was considered to be the cause of diabetes mellitus patients (Suryanti, 2021).

In patients who suffer from diabetes for a long time and are uncontrolled, the possibility of damage to micro and macro blood vessels increases (SK Rachman et al., 2021). Many factors influence the occurrence of diabetic peripheral neuropathy, such as glycemic status, lipid profile, hypertension, smoking, obesity, long duration of diabetes, and history of ulcers on the lower extremities (A. Rachman & Dwipayana, 2021). In the United States, 6-70% of DM patients suffer from complications of diabetic neuropathy. In Indonesia, 60% of diabetic neuropathy is found. Diabetic neuropathy is more common in older adults (>50 years), as it takes time for nerve damage and pain to develop (Zakin et al., 2019). Neuropathy complications will affect the quality of life of patients with diabetes mellitus. Diabetic neuropathy, if not treated properly, will cause peripheral somatosensory disorders or neuropathic pain (Pebrianti et al., 2020).

Hemoglobin A1c (HbA1c) is hemoglobin used to monitor the status of glucose levels in the previous 2 or 3 months. Recommendations from the American Diabetes Association (ADA), HbA1c levels should be maintained at 7% in all DM patients. If the HbA1c level exceeds 7% it will increase the risk of complications, especially microvascular complications (Hunaifi et al., 2021). Apart from HbA1c in Indonesia, the diagnosis is made if the fasting blood sugar (GDP) level is ≥ 126 mg/dl; or random blood sugar (GDS) ≥ 200 mg/dl with symptoms of frequent hunger, frequent thirst, frequent urination and large

amounts and weight loss. Intensive blood sugar control can significantly reduce the risk of microvascular complications in type 2 DM patients. Therefore, average GDP data is very important for controlling blood sugar (Hasanah & Ikawati, Apt., 2021). However, several studies that focused on the relationship between HbA1c levels and the occurrence of diabetic neuropathy complications still obtained varying results. In research conducted (Oktavia Viona et al., 2021), it showed that there was no significant relationship between HbA1c levels and neuropathy in people with type 2 diabetes mellitus.

Research conducted by (Liu et al., 2023) through systematic review obtained the final model included data from 95,604 patients with Type 2 Diabetes Mellitus (T2DM) across 18 cohorts. The factors considered in the analysis were age, smoking status, body mass index, duration of diabetes, hemoglobin A1c levels, low HDL cholesterol, high triglycerides, hypertension, as well as the presence of diabetic retinopathy, diabetic kidney disease, and cardiovascular disease. Based on the description above, the researcher was interested in conducting research at a hospital in Makassar namely Ibnu Sina Hospital with the title "The relationship between HbA1c, GDP and disease duration on the occurrence of neuropathy in DM patients at Ibnu Sina Hospital".

METHODOLOGY

Tools and Materials

In this study, we did not use tools and materials to obtain research results, but used secondary data contained in medical record data containing data on DM patients at Ibnu Sina University Hospital, Makassar.

Design

This research is an observational analytical study with a case control approach, namely looking for the relationship between HbA1c, GDP and disease duration as independent variables with neuropathy complications as the dependent variable, which occur in the research object. The sampling technique used in this research is purposive sampling, which is included in the category of non-probability sampling techniques. Inclusion criteria for this study included diabetes mellitus (DM) patients who were treated at Ibnu Sina Hospital, both outpatient and inpatient, and had complete medical records. On the other hand, the exclusion criteria include DM patients who do not have HbA1c and GDP results in the medical record.

Data Analysis

Statistical analysis in this research is divided into two main stages: univariate analysis and bivariate analysis. Univariate analysis to describe the frequency distribution of each variable used in the research, with the results presented in the form of a frequency distribution table. Meanwhile, bivariate analysis was carried out using the Chi Square test to evaluate the significant relationship between the independent variables and the dependent variable. The basis for decision making in this research is based on the level of significance (p value), where if the p value < 0.05, the research hypothesis is accepted, whereas if the p value > 0.05, the research hypothesis is rejected.

RESULTS

Distribution of DM Patient Characteristics

Table 1. Characteristics of DM Patients

Variable	DM Neuropathy (n=47)		Non-neuropathic DM (n=30)		Total	
Age	n	%	n	%	n	%
26 - 35 years old	1	2.1	0	0.0	1	1.3
36 - 45 years old	6	12.8	9	30.0	15	19.5
46 - 55 years old	8	17.0	8	26.7	16	20.8
56 - 65 years old	19	40.4	11	36.7	30	38.9
> 65 years	13	27.6	2	6.6	15	19.5
Gender						
Man	24	51.1	22	73.3	46	59.7
Woman	23	48.9	8	26.7	31	40.3
Drug Class						
Sulfonylurea	12	25.6	9	30.0	21	27.3
Biguanine	8	17.0	7	23.4	15	19.5
Dipeptidyl Peptidase-4 (DPP-4) Inhibitors	1	2.1	0	0.0	1	1.3
Calcium-channel blockers	3	6.4	0	0.0	3	3.9
Insulin	23	48.9	14	46.6	37	48.0
Long time DM						
< 5 years	15	31.9	23	76.6	38	49.4
> 5 years	32	68.1	7	23.4	39	50.6
HbA1C levels						
≤ 7%	3	6.4	14	46.6	17	22.0
>7%	44	93.6	16	53.4	60	78.0
GDP levels						
< 130	14	29.8	19	63.3	33	42.85
≥ 130	33	70.2	11	36.7	44	57.15
Total	47	100	30	100	77	100

Table 1. shows the distribution of sample age characteristics based on the Indonesian Ministry of Health where the majority of the sample is aged 56-65 years (late elderly) as many as 30 patients (38.9%) with male gender as many as 46 patients (759.7%). The majority of the sample was given insulin class drugs, namely 37 people (48%), the majority of the sample, 39 people (50.6%) had suffered from DM for more than 5 years. Then, most of the samples experienced complications of diabetic neuropathy, namely 47 people (61.0%) with HbA1c levels >7% (78%) and GDP ≥ 130 (57.15%) uncontrolled.

Relationship between HbA1C Levels and Neuropathy

Table 2. Relationship between HbA1C levels and neuropathy

	Variable	Diabetic Neuropathy						*P*	*OR CI 95% (low-up)*
		Yes		No		Total			
		n	%	n	%	n	%		
HbA1C	≤ 7%	3	6.4%	14	46.6%	17	22.1%	0,000	0.086 (0.017-0.423)
	>7%	44	93.6%	16	53.4%	60	77.9%		
	Total	47	100%	30	100%	77	100%		

Table 2. shows that there is a significant relationship between HbA1C levels and the occurrence of DM and neuropathy (p-value 0.000 <0.05).

Relationship between GDP Levels and Neuropathy

Table 3. Relationship between GDP levels and neuropathy

	Variable	Diabetic Neuropathy						*P*	*OR CI 95% (low-up)*
		Yes		No		Total			
		n	%	n	%	n	%		
GDP	<130	14	29.8%	19	63.3%	33	42.8%	0.004	0.575 (0.177-1.866)
	≥130	33	70.2%	11	36.7%	44	57.2%		
	Total	47	100%	30	100%	77	100%		

Table 3. shows that there is a significant relationship between GDP levels and the occurrence of DM and neuropathy (p-value 0.004 <0.05).

Long-term Relationship between DM and Neuropathy

Table 4. Relationship between GDP levels and neuropathy

	Variable	Diabetic Neuropathy						*P*	*OR CI 95% (low-up)*
		Yes		No		Total			
		n	%	n	%	n	%		
Long time DM	<5 years	24	51.1%	23	76.6%	38	49.3%	0.021	0.248 (0.072-0.860)
	>5 years	23	48.9%	7	23.4%	39	50.7%		
	Total	47	100%	30	100%	77	100%		

Table 4. shows that there is a significant relationship between the duration of DM and the occurrence of DM and neuropathy (p-value 0.021 <0.05).

DISCUSSION

Characteristics of Diabetes Mellitus Patients

Most of the samples were aged 56 - 65 years as many as 30 patients (38.9%) with male gender as many as 46 patients (59.7). These results are in line with research from (Ferlitasari et al., 2022) regarding "Characteristics of Type 2 Diabetes Mellitus Patients Inpatients at Pertamina Cirebon Hospital in 2019" found that 94.6% of the sample was over 50 years old with male gender of 54 .1%. The distribution of samples suffering from DM where the majority of samples have had DM for more than 5 years, namely 50.6%. This research is in line with (Schoon et al., 2023) regarding "The Relationship between the Duration of Diagnosed Type 2 Diabetes Mellitus and HbA1C Levels with the Degree of Diabetic Retinopathy in Patients Taking Part in the Chronic Disease Management Program at the Kedaton Bandar Lampung Community Health Center" obtained as a sample of 50 respondents using consecutive sampling and data analyzed by Mann Whitney and Kruskal Wallis tests. As many as 46% of respondents had a duration of diabetes mellitus of 5-15 years, 44% < 5 years, 10% > 15 years.

Sex differences in diabetes prevalence change according to reproductive life stage, with more men suffering from DM before puberty, while more women suffering from DM after reaching menopause and at later ages. Boys show more impaired glucose tolerance after eating in adolescence. One factor is the influence of sex hormone-binding globulin (SHBG), a protein produced in the liver and capable of binding testosterone, dihydrotestosterone and estradiol (estrogen), and transporting them in an inactive form into the bloodstream. High levels of SHBG may indicate a risk of diabetes that may be related to SHBG gene polymorphisms. In general, women tend to have higher SHBG levels than men (Ciarambino et al., 2022).

The duration of diabetes is a triggering factor for DM complications consisting of macrovascular and microvascular complications. Diabetic neuropathy can appear in people with type 2 diabetes mellitus after 10 years, but the duration of diabetes is difficult to determine in DM patients. DM is known as a silent disease and has an asymptomatic phase, namely the phase between the actual onset of diabetes hyperglycemia and the clinical diagnosis of diabetes mellitus. Clinical diagnosis of DM is usually made after 5-10 years of patient suffering or after the asymptomatic phase (Flaxel et al., 2020).

The research results also showed that the distribution of samples had Hb1AC levels where the majority of samples had uncontrolled levels, namely 78%. This research is in line with the results of research by (Zulkarnaini & Triulandari Kusnadi, 2021) regarding "HbA1C Levels in Type 2 Diabetes Mellitus Patients with Complications of Diabetic Neuropathy at RSI Siti Rahmah Padang in 2019-2020" it was found that the highest HbA1c levels were in the uncontrolled category with 23 patients (73, 3%).

The highest HbA1C level was uncontrolled, 62 people (80.5%). Neuropathy is a progressive disease. Good control of blood glucose levels will reduce the progression of neuropathy. In hyperglycemic conditions, there is an increase in glycolysis which will result in excessive mitochondrial electron transport and the formation of ROS (Reactive Oxygen Species) which will damage peripheral nerves. In addition, hyperglycemia conditions can increase the polyol pathway, which is the conversion of glucose into sorbitol by the aldose reductase enzyme which is then converted into fructose by the sorbitol dehydrogenase enzyme, causing increased ROS production which in turn will cause endothelial damage and a decrease in neuronal vasodilation (Hanifah et al., 2021).

The results of the research data also show that the distribution of samples has GDP levels where the majority of samples have uncontrolled levels, namely 57.15%. In a study by (Tsalissavrina et al., 2018) "The Relationship between Time of Being Diagnosed with Diabetes and Blood Glucose Levels with the Cognitive Function of Type 2 Diabetes Patients in East Java" found that 119 samples out of 160 samples were uncontrolled/poor (74.4%).

Measuring fasting blood glucose levels (GDP) is one of the parameters of the fasting blood glucose test which is used to evaluate the effectiveness of medication or the impact of food on individuals who have been diagnosed as diabetics. The PERKENI consensus indicates that GDP levels in diabetes patients

are considered under control if they are in the range of 80-126 mg/dL. In this study, the majority of research subjects showed fasting blood glucose levels that were in the poor or uncontrolled category (> 126 mg/dL) as many as 52 people (67.5%). Controlling diabetes mellitus (DM) through regular monitoring of blood glucose levels is very important to improve the quality of life of sufferers and prevent potential complications in the future. Health evaluation involving checking fasting blood glucose levels, blood glucose levels 2 hours after eating, and checking HbA1c are relevant steps in controlling DM (Agus Kirwanto, 2014).

Relationship between HbA1C Levels and Diagnosis of Diabetes Mellitus

From the research results, it was found that there was a significant relationship between HbA1C levels and the diagnosis of Diabetes Mellitus in the sample with a p value of 0.000. This research is in line with the results of research by (Ilsa Hunafi et al., 2021) regarding "The Correlation Between HbA1c and Neuropathy Disability Score in Type 2 Diabetes" which found 56 research subjects. The mean age was 59.55 (SB 9.48) with 57.1% being female, the median duration of suffering from DM was 5.5 years. The median NDS score is 7.5 and the median HbA1c value is 8.65. Spearman correlation analysis shows a correlation coefficient of 0.487 with a p value = 0.000.

High levels of HbA1c will further accelerate and worsen neuropathy complications. Controlling glucose levels is very important to prevent and reduce complications from DM. High HbA1c levels are associated with higher levels of microvascular complications in people with DM. The limitations of this study are that HbA1c was only evaluated once and electrodiagnostic examination was not performed as the gold standard for determining the severity of neuropathy (Stem et al., 2016). The average HbA1c level obtained by respondents had high HbA1c levels. This is likely influenced by other factors. In some circumstances, HbA1c cannot reflect blood glucose control. This is important to know because it can cause under or over treatment. What can increase HbA1c levels from the actual value are iron deficiency anemia, age, polycythemia rubra vera, second trimester pregnancy, high blood urea levels, HbF or HbG, severe hypertriglyceridemia, hyperbilirubinemia, excessive alcohol consumption, splenectomy, aplastic anemia, use of high doses of salicylates. high in the long term (Beata et al., 2018).

Correlation of GDP Levels with Diabetes Mellitus Diagnosis

From the research results, it was found that there was a significant relationship between GDP levels and the diagnosis of Diabetes Mellitus in the sample with a p value of 0.004. This research is in line with the study by (Sari & Taufiqurrahman, 2021) regarding "Correlation of Long Suffering from Diabetes Mellitus (DM) Type 2 with the Occurrence of DM Neuropathy in Prolanis Patients in Ngemplak, Sleman" it was found that the results of bivariate analysis between diabetic neuropathy and the independent variable showed significance in duration with The OR value was 0.14 (95% CI 0.02-0.99; p=0.020) and the GDP level had an OR value of 0.25 (95% CI 0.06-1.01; p=0.024).

GDP is more reliable as a diagnostic test to determine whether glucose levels are normal or not, in the sense that the patient is compliant with taking

medication and living a correct lifestyle. Self-monitoring of diabetes mellitus sufferers through fasting blood glucose levels and diagnosed with type 2 diabetes based on HBA1c results was recommended by the British National Health Service in 2018 to immediately carry out self-monitoring procedures. Treatment for various cardiovascular risk factors, neurological disorders, hypertension, high cholesterol, and microalbuminuria with normal GDP will improve a person's life expectancy (Anggraini et al., 2020).

Relationship between Duration of DM and Diagnosis of Diabetes Mellitus

From the research results, it was found that there was a significant relationship between the duration of DM and the diagnosis of Diabetes Mellitus in the sample with a p value of 0.021. This research is in line with (Sri Rahmi et al., 2022) regarding "Relationship between long-term suffering from type 2 diabetes and the incidence of diabetic neuropathy" showing that the total number of respondents in this study was 44 people based on inclusion and exclusion criteria. The majority of T2DM patients who suffer from diabetic neuropathy suffer from DM for an average of ≥ 5 years (92.1%).

Research shows that there is a relationship between long suffering and the risk of peripheral neuropathy in type 2 DM patients. The longer a person suffers from DM, the greater the risk of developing neuropathy, where long suffering from DM with high blood glucose levels can weaken and damage the walls of the capillaries that vascularize the nerves so that Nerve damage occurs, namely neuropathy. The process of neuropathy is usually progressive. High blood sugar levels for a long time cause the accumulation of sorbitol which increases the activity of the polyol pathway and results in changes in nervous tissue. This change has an impact on disrupting signal transduction in the nerves which causes type II DM sufferers to experience decreased sensitivity in the feet (Sari & Taufiqurrahman, 2021).

CONCLUSION AND RECOMMENDATION

The results of the study showed that the characteristics of Diabetes Mellitus (DM) patients at Ibnu Sina Hospital were the majority aged 56-65 years, male, and had a history of suffering from DM for more than five years. In addition, the incidence of DM with neuropathy complications is more common than DM without neuropathy complications. The majority of DM patients in this hospital also have uncontrolled HbA1c and GDP levels. This finding is supported by the significant relationship between HbA1c and GDP levels and the occurrence of diabetic neuropathy at Ibnu Sina Hospital. In addition, disease duration was also significantly associated with the occurrence of diabetic neuropathy. This highlights the importance of blood glucose control and DM disease management in an effort to prevent serious neuropathy complications in patients.

FURTHER STUDY

The study's limitations include its small, single-center sample, which may limit generalizability, and its cross-sectional nature, which does not establish

causation. Future research should expand sample size, incorporate diverse settings, and address additional factors like lifestyle and comorbidities.

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To address the study's findings, it is recommended to improve glycemic control through better monitoring and management of HbA1c and fasting blood sugar levels. Implementing comprehensive patient education on diabetes management and neuropathy prevention is essential. Routine neuropathy screening for patients with long-term diabetes or poor glycemic control should be adopted, alongside regular follow-up.

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