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ASSOCIATION OF GLYCOSYLLATED HEMOGLOBIN (HbA1C) LEVELS TO THE SEVERITY OF DIABETIC FOOT ULCER IN TYPE 2 DIABETES MELLITUS PATIENTS IN RSUP. H. ADAM MALIK MEDAN

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Abstract. Introduction: Diabetic ulcers with neuropathy require amputation or time to fully heal. The worse blood sugar control, it will worsen the condition of complications such as diabetic ulcers, diabetic neuropathy, and other complications. Wound healing in diabetic ulcers is influenced by controlled HbA1c levels. Methods: This study is an observational analytic study with a retrospective design used in this study with secondary data. This study is analytical because it aims to obtain the correlation of HbA1c with the severity of diabetic ulcers in patients with diabetes mellitus at H. Adam Malik Hospital. Results: The average age of the patients was 62 with the majority of respondents being male. The dominance of respondents came with Grade IV as many as 17 people, with uncontrolled HbA1c levels as many as 39 people. Using Spearman Corelation test, the value of r = 0.735, 0.736, and 0.785, respecttively for the corelation between HbA1c, Hb and ESR levels with the severity of diabettic foot ulcers ,with a value (p = 0.0001). Conclusion: We found a strong correlation and a significant relationship between HbA1c, Hb, and ESR levels with the severity of diabetic foot ulcers.

1   Introduction

Diabetes mellitus (DM) is one of the most common diseases in the world. Approximately 170 million people worldwide suffer from diabetes, including about 23.6 million people in the United States (7.8% of the total population of the United States) (Cowie CC, 2009). This figure increases over time, where in 2018 there were 34.2 million people with Diabetes Mellitus in the United States or about 10.7% of the total population. In Indonesia alone, in 2019 there were 10.7 million

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people suffering from diabetes mellitus. In people who have diabetes mellitus, about 28.5% have diabetic neuropathy (Sudoyo AW, 2009).

Poor blood sugar control is associated with the onset of neuropathy and the risk of developing ulcers and requiring amputation. Ulcers on the feet are often found in people with diabetes mellitus, with an incidence of about 1-2%. Approximately 15% of people with diabetes mellitus in the United States will experience diabetic foot ulcers at some point in their lives (Al-Rubean K, 2015).

Expenditures needed for foot ulcers in diabetes mellitus include interventions to prevent wounds, treatment to heal wounds, and treatment and care for surgery and disability (Zubair M, 2015). In 2001, expenditure on diabetic ulcers reached 10.9 billion dollars. Whereas in 2014, the expenditure figure for diabetic ulcers reached 13 billion dollars. This figure is predicted to increase in tandem with the predicted increase in the prevalence of people with diabetes mellitus (Lauterbach S, 2013).

Given the heavy expense of treating diabetic ulcers, it is important to identify modifiable factors that can benefit healing and help optimize ulcer care (Assaad-Khalil SH, 2015). Previous studies in a population of diabetes mellitus patients identified prognostic factors in wound healing, but most of these studies have focused on non-modifiable factors such as the basis of the wound area, duration of injury, age, and gender (Abolfotouh M. A, 2011). .

These studies have clearly demonstrated that diabetic ulcers with neuropathy require amputation or time to fully heal. Few of these studies have addressed cure rates. In the literature it is still unclear whether Hemoglobin A1c (HbA1c), a standard blood sugar test every 2-3 months, is associated with the rate of wound healing (Zubir M, 2015). Casadei, G. found in his research that the poorer blood sugar control, the worse the condition of complications such as diabetic ulcers, diabetic neuropathy, and other complications. (Casadei G, 2021).

In Xiang's research, J. et al. It was found that wound healing in diabetic ulcers was influenced by controlled HbA1c levels. (Xiang, J. et al. 2019). However, this study did not determine how large the correlation (r value) was, and was based on the high number of DM patients with the risk of diabetic foot in patients with uncontrolled blood glucose. (Suastidewi, P. et al. 2020). Therefore, researchers are interested in conducting research on how big the relationship between HbA1c and the severity of diabetic foot is.

Methods

This study was an observational analytic study with the design used in this study is retrospective. The data taken was secondary. This study is analytical because it aims to obtain the correlation of HbA1c with the severity of diabetic ulcers in patients with diabetes mellitus at H. Adam Malik Hospital. The study was conducted at the Medical Record Section of the Haji Adam Malik General Hospital, Medan. Data collection began when the research proposal was approved by the ethics committee. The population in this study were DM patients with a diagnosis of diabetic foot at H. Adam Malik Hospital, Medan, starting from 2019 - 2021.

The study sample was DM patients with a diabetic foot diagnosis who had been treated at H. Adam Malik Hospital Medan starting from January 2019 until November 2021. The sampling technique is non-probability sampling, namely the consecutive sampling technique, where each subject that meets the selection criteria is sequentially included in the study until it meets the required number of samples.

Inclusion criteria in this study were patients diagnosed with diabetes mellitus, patients diagnosed with diabetic ulcers and aged > 40 years. The exclusion criteria in this study were patients with a history of trauma and patients diagnosed with Covid-19 in the last 3 months. Researchers collected medical records of patients with diabetes mellitus with diabetic ulcers, collected HbA1c laboratory data and collected patient identities (age, gender).

The collected data will be analyzed descriptively, which is recorded as mean ¬± standard deviation, median, and range for numerical scale data and percentages for categorical scale data. To analyze the correlation of HbA1c with the severity of diabetic ulcers, the Spearman test was used if the data were not normally distributed. P value <0.05 is said to be statistically significant.

Results

This study was followed by 83 research subjects, but 54 people entered according to the inclusion criteria and exclusion criteria. The purpose of this study was to determine the relationship between glycosylated hemoglobin levels (HbA1c) and the severity of diabetic foot ulcers in patients with type 2 diabetes mellitus at the RSUP. H. Adam Malik Medan, presented in table 1. The majority of respondents are 62 years old on average, with the youngest age being 49 years old and the oldest being 89 years old.

Table 1. Characteristics of Research Subjects Based on Age

Characteristics   n=54

Age (years)

Mean   63

Median (Min-Max)   62 (49-89)

Based on gender in this study, Table 2, from 54 subjects, the majority of respondents were Men as many as 30 people and women as many as 24 people

Table 2. Characteristics of Research Subjects Based on Gender

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Female	24	44.4	44.4	44.4
	Male	30	55.6	55.6	100.0
	Total	54	100.0	100.0	

Based on the Diabetic Ulcer Grade in this study, Table 3, from 54 subjects the majority of respondents had a diabetic ulcer grade with Grade IV as many as 17 people, followed by grade III as many as 16 people, followed by grade II as many as 9 people, followed by grade V as many as 8 people. and the last grade I as many as 4 people.

Table 3. Characteristics of Research Subjects Based on Diabetic Ulcer Grade

Frequency	Percent	Valid Percent	Cumulative

Percent

Valid	Grade I 4	7.4	7.4	7.4	
	Grade II	9	16.7	16.7	24.1
	Grade III	16	29.6	29.6	53.7
	Grade IV	17	31.5	31.5	85.2
	Grade V	8	14.8	14.8	100.0
	Total	54	100.0	100.0	

Based on the HbA1C examination in this study (Table 4), the majority of the 54 subjects with uncontrolled HbA1C were 39 people, followed by 15 controlled HbA1C. And said with controlled HbA1C below equal to 7 and uncontrolled above with 7. With the lowest HbA1C value 6.1 and the highest 11.9.

Table 4. Characteristics of Research Subjects Based on HbA1C

Frequency

Percent

Valid Percent   Cumulative

Percent

Valid	Controlled	15	27.8	27.8	27.8
	Not controlled	39	72.2	72.2	100.0
	Total	54	100.0	100.0	

Based on the Hb examination in this study (Table 5), out of 54 research subjects, with below 12 were said to be anemic and above 12 were said to be not anemic, the majority of respondents with anemia were 37 people, and with no anemia as many as 17 people.

Table 5. Characteristics of research subjects with Hb

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Anemia	37	68.5	68.5	68.5
	Not anemia	17	31.5	31.5	100.0
	Total	54	100.0	100.0	

Based on the examination of Current Blood Sugar Levels in this study (Table 6), of the 54 research subjects with normal values < 200 mg/dL and abnormal values > 200 mg/dL, the majority of respondents with abnormal blood sugar levels were 7 people, followed by with normal blood sugar levels as many as 47 people.

Tabel 6. Karateristik Subjek Penelitian Berdasarkan KGD Sewaktu

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Normal	7	13.0	13.0	13.0

Abnormal	47	87.0	87.0	100.0
Total	54	100.0	100.0	

Based on the erythrocyte sedimentation rate examination in this study (Table 4.7), from 54 subjects the majority of respondents had an abnormal erythrocyte sedimentation rate value of 49 people, followed by a normal erythrocyte sedimentation rate value of 5 people.

Table 7. Characteristics of Research Subjects Based on Sedimentation Rate

Frequency

Percent

Valid Percent   Cumulative

Percent

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Normal	5	9.3	9.3	9.3
	Abnormal	49	90.7	90.7	100.0
	Total	54	100.0	100.0	

Based on this study (Table 4.8), analyzed using SPSS Version 26 with the Spearman test because the data were not normally distributed, the results were found with a value ($r = 0.735$), and a value ($p = 0.0001$) meaning that there was a strong correlation and a significant relationship between HbA1c levels. with the degree of diabetic foot ulcers.

Table 8. Relationship between HbA1c levels and the degree of diabetic foot ulcers

HbA1C GradeUlkusKaki Diabetik

			HbA1C	GradeUlkusKaki Diabetik
Spearman's rho	HbA1C	Correlation Coefficient	1.000	.735**
		Sig. (2-tailed)	.	.000
		N	54	54
	Grade	Correlation Coefficient	.735**	1.000
		Sig. (2-tailed)	.000	.
		N	54	54

**. Correlation is significant at the 0.01 level (2-tailed).

Distribution of HbA1c data on the degree of diabetic foot ulcers

		Grade					Total
		Grade I	Grade II	Grade III	Grade IV	Grade V	
HbA1Ckategory	Controlled	3	6	2	3	1	15
	Not controlled	1	3	14	14	7	39
Total		4	9	16	17	8	54

Based on this study (Table 4.9), analyzed using SPSS Version 26 with the Spearman test because the data were not normally distributed, the results were found with a value (r = 0.736), and a value (p = 0.0001) meaning that there was a strong correlation and a significant relationship between Hb levels. with the Degree of Diabetic Foot Ulcers.

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Table 9. Relationship of Hb Levels with the Degree of Diabetic Foot Ulcers

HB   GradeUlkusKaki Diabetik

Spearman's rho HB   Correlation Coefficient 1.000   .736**

                        Sig. (2-tailed)   .   .000

                        N   54   54

            Grade   Correlation Coefficient .736** 1.000

                        Sig. (2-tailed)   .000   .

                        N   54   54

**. Correlation is significant at the 0.01 level (2-tailed).

Based on this study (Table 10), analyzed using SPSS Version 26 with Spearman's test because the data were not normally distributed, the results were found with a value (r = 0.785), and a value (p = 0.0001) which means that there is a strong correlation and a significant relationship between levels of Blood sediment with the degree of diabetic foot ulcers.

Table 10. Correlation between erythrocyte sedimentation rate and the degree of diabetic foot ulcers

Discussion

This research is an observational analytic study with the design used in this study is retrospective. The data taken is secondary. This study is analytical because it aims to obtain the correlation of HbA1c with the severity of diabetic ulcers in patients with diabetes mellitus at H. Adam Malik Hospital. The majority of respondents are 62 years old on average, with the youngest age being 49 years old and the oldest being 89 years old.

The results of this study are in line with previous studies that examined 270 patients and found an average age of 60.7 years being diagnosed with diabetic foot ulcers between 2012 and 2017 (Fesseha et al, 2018). Another study also found the mean age of patients with a diagnosis of diabetic foot ulcer was 61 years out of 183 patients from Johns Hopkins Wound Center between 2004 - 2010 (Christman et al, 2011). A study conducted at the Diabetic Clinic, King Fahad specialist diabetes center, Buriadah, Qasim, Kingdom of Saudi Arabia revealed that in his

research the average age of patients with diabetic foot ulcers was 56 years, which was taken from February 2014 to February 2015 (AlGoblan et al, 2016).

The mean age of presentation of diabetic foot ulcers in studies in India in 2015 to 2017 was 54 years with a sample of 280 people, of which 45% of patients had diabetes for 10 years, 36.8% for 10-20 years, and 16.4% for 20 years (Cheng, et al, 2011). Research conducted at H. Adam Malik Hospital Medan also found that out of 70 patients, the average age of patients was 55.65 years (Silalahi, 2017).

In this study, from 54 research subjects, the majority of respondents were male as many as 30 people (55.6%) and 24 women (44.4%), this study is also in line with research in India from 2015 to 2017 with a sample of 280 people, of which men amounted to as many as 196 people (70%), and women as many as 84 people (30%) (Cheng et al, 2011). Another study also stated that from a sample of 298 patients with diabetic foot ulcers, 69.5% of patients were men, namely 207 patients, and the rest were women as many as 91 people (30.5%) (Xiang et al, 2018). Another study also suggested that of the 88 patient samples studied, 45 people (51.13%) were men, and 43 women (48.86%) (Farooque et al, 2020). The research that America studied also showed that out of 270 people, there were 59.3% men and 40.7% women (Fesseha et al, 2018). Another study also suggested from King Abdullah University Hospital Review Boar with 225 patients taken from January 2014 to December 2015 found 153 men and 72 women (Shatnawi et al, 2018). This is based on why women have a lower risk than men for diabetic foot ulcers because in men it is more severe if affected by neuropathy, due to increased joint mobility, and higher pressure on the feet, which leads to work (Dihn et al, 2008).

Based on the Diabetic Ulcer Grade in this study, table 3, from 54 subjects the majority of respondents had a diabetic ulcer grade with Grade IV as many as 17 people, followed by grade III as many as 16 people, followed by grade II as many as 9 people, followed by grade V as many as 8 people. and the last grade I as many as 4 people. This study is in line with that conducted at the Major Hospital in Shaheed Benazrabad in 88 patients found that the grades of diabetic foot ulcers were: Grade IV as many as 32 people (36.36%), followed by Grade III as many as 29 people (32.95%), followed by Grade V as many as 20 people (22.72%), followed by Grade 2 as many as 6 people (6.81%), and followed by Grade 1 as many as 1 person (1.13%) (Farooque et al, 2020).

A study conducted at the Suburban Teaching Hospital showed that in the results of the study 50 subjects were found to be mostly in Grade II diabetic foot ulcers as many as 21 people (42%), followed by 17 people (34%) with Grade III, followed by Grade IV as many as 6 people (12%), Grade I as many as 4 people and Grade V as many as 2 people (Shah et al, 2022). Another study

conducted in China showed that of 298 patients suffering from diabetic foot ulcers, the most were Grade IV as many as 166 people (55.7%), followed by Grade III as many as 96 people (32.2%), and followed by Grade II as many as 36 people (12.1%), while Grade I and Grade V were not found in this study (Xiang et al, 2018). Another study also stated that from the King Abdullah University Hospital Review Board with 225 patients taken from January 2014 to December 2015, the highest grade of diabetic foot ulcers was found in Grade III with 68 people, followed by Grade 4+5 with 54 people, followed by Grade II with 41 people, and 36 people who are not classified (Shatnawi et al, 2018).

Based on the HbA1C examination in this study, table 4, the majority of 54 research subjects with uncontrolled HbA1C were 39 people followed by controlled HbA1C as many as 15 people. And said with controlled HbA1C below equal to 7 and uncontrolled above with 7. With the lowest HbA1C value 6.1 and the highest 11.9. in another study also showed that from 298 patients with HbA1c below 7 there were 51 people, in the range between 7.1-8.0 there were 81 people, in the range between 8.1-9.0 there were 54 people, and above 9.0 there were 72 people, this study was conducted in China in 2013 to 2016 (Xiang et al, 2018).

Another study also showed in a study at Johns Hopkins Multidisciplinary Diabetic Foot of 270 patients with HbA1C < 6.5% as many as 149 people, followed by 6.5-8.0% as many as 162 people, and the most >8% as many as 298 people. (Fesseha et al, 2018). This study is also in line with research conducted at Nigerians Hospital with a total of 336 subjects, 124 patients with Grade IV were found, followed by Grade III as many as 88 people, followed by Grade II as many as 57 people, followed by Grade V as many as 54 people, and at least Grade 1 with 13 people (Gezewa et al, 2019).

Based on the Hb examination in this study, table 5, from 54 research subjects, with below 12 were said to be anemic and above 12 were said to be not anemic, the majority of respondents with anemia were 37 people, and those without anemia were 17 people. The study conducted by Chuan et al reported that from 353 patients, 236 patients had anemia and the rest did not have anemia (Yammine et al, 2021). In a study in China at the First Affiliated Hospital of Chongqing Medical University, Chongq, it showed that from 353 research subjects, 236 patients with anemia were found and 117 people were not anemic. (Chuan et al, 2016).

In a study conducted at Nigerians Hospital as many as 336 subjects, it was found in this study with 180 subjects experiencing anemia while 156 subjects did not experience anemia. (Gezewa et al, 2019). Many studies report low Hb caused by reduced tissue perfusion in patients with compromised peripheral vascular status. Low hemoglobin levels are thought to exacerbate lower limb ischemia due to reduced blood oxygen. Anemia can also cause thrombus generation by

inducing a hyperkinetic circulatory state (Yammine et al, 2019). Causes of anemia were reported by two studies, the first of which Wrigt et al reported the incidence of anemia caused by iron deficiency. And in Evran Olgun et al divided the causes of anemia, which are mostly caused by iron deficiency, folic acid deficiency, and chronic disease (Yammine et al, 2019).

Based on the ESR in this study table 7, from 54 subjects the majority of respondents had an abnormal erythrocyte sedimentation rate value of 49 people, followed by a normal erythrocyte sedimentation rate value of 5 people. In a study conducted at H. Adam Malik Hospital, Medan, from 20 research subjects who experienced diabetic foot, it was found that there was an increase in ESR in every person (Sitepu, 2018). This is based on the fact that ESR represents a response to trauma, inflammation or pregnancy due to an increase in globulin and fibrinogen levels. An increase in ESR accompanies acute and chronic inflammation, and can indicate a process of extensive tissue damage, for example in people with diabetes mellitus (Jou et al, 2011).

Based on this study, table 2, analyzed using SPSS Version 26 with the Spearman test because the data were not normally distributed, the results were found with a value ($r = 0.735$), and a value ($p = 0.0001$) meaning that there was a strong correlation and a significant relationship between HbA1c levels and degrees. Diabetic Foot Ulcers. This is also in line with a study conducted at the Major Hospital in Shaheed Benazirabad on 88 patients with the results found a significant relationship between HbA1c and Wagner's classification with p Value ($p < 0.00001$). This study describes a linear relationship between HbA1c levels and Grade from Wagner's classification. Patients who have grades 0-2 in the Wagner classification have a slight increase in HbA1c levels, while patients who have grades 3-5 in the Wagner classification have very high increases in HbA1c levels which are often found in non-complicated patients. HbA1c levels can be used as a screening tool in the above-mentioned high-risk diabetic patients for diabetic foot to predict its occurrence, because HbA1c has a linear relationship with the value of the Wagner classification of diabetic foot (Farooque et al, 2020).

Based on research conducted at the surgical department, akash institute of medical sciences and research center, Devanahalli showed that HbA1c levels were strongly related to the process and duration of diabetic foot ulcer healing. An increase in HbA1c is also associated with a poorer prognosis and an increase in Wagner's classification of diabetic foot ulcers (Manjunath et al 2018), which is in line with the current study. Based on research conducted at H. Adam Malik General Hospital Medan with 70 subjects, the results of the analysis obtained were $p = 0.0001$ ($p < 0.05$), this means that there is a significant relationship between HbA1c levels and diabetic foot. In addition, the OR = 3.1 (CI = 95%, $p<0.05$). Patients with HbA1c levels >7 mg/dL are three to five times more likely to develop diabetic foot, as shown in the table below. In accordance with research conducted by Hasan et al, it was found that uncontrolled HbA1c levels are a strong

indicator of uncontrolled blood sugar levels (Silalahi, 2017). Uncontrolled HbA1c levels in diabetic patients result in metabolic disorders which ultimately lead to disturbances in protein and fat metabolism. Disorders of protein and fat metabolism result in disturbances in the wound granulation process (Silalahi, 2017).

Based on research conducted in Saudi Arabia with a sample of 140 patients with diabetic foot ulcers, it was found that there was a relationship between BMI and HbA1c levels on the duration of wound healing from diabetic feet and the degree of Wagner classification (AlGoblan et al, 2016). This study is not in line with research conducted at Sangalah Hospital in 2015-2016 with a sample of 62 samples with the results of the study that there was no significant relationship between HbA1c levels and the degree of diabetic foot in diabetic foot patients at Sangalah Hospital (P value 0.290; P> 0.05). These results can be influenced by confounding variables in patients. Confounding variables in the form of body mass index, cholesterol, triglycerides, HDL, fasting blood sugar, and blood sugar 2 hours postprandial are factors that influence the incidence of diabetic foot (Suastidewi et al, 2020).

Based on this study, table 3, analyzed using SPSS Version 26 with Spearman's test because the data is not normally distributed, the results are found with a value (r = 0.736), and a value (p = 0.0001) which means that there is a strong correlation and a significant relationship between HbA levels and degrees. Diabetic Foot Ulcers. This is in line with the research conducted by Yammine et al which suggested that there was a relationship between low Hb levels (anemia) and diabetic foot ulcers: three times the reported incidence in patients with anemia and diabetic foot ulcers. This study also demonstrated a clear relationship with the severity of anemia and the severity of Wagner's calcification in diabetic foot ulcer patients. And there is some evidence showing anemia as a predictor of amputation and mortality; low Hb levels are associated with poor patient outcomes (Yammine et al, 2019).

Conclusion

The results showed that there was a strong correlation and significant relationship between the levels of HbA1c, Hb, and ESR with the severity of diabetic foot ulcers with the Spearman test results, respectively, r = 0.735, 0.736, and 0.785 with a value (p = 0.0001). This study aims to determine the relationship between HbA1c levels and the severity of diabetic foot based on the Wagner classification, from 54 research subjects found the average age of the patient was 62 years with the youngest age 49 years and the oldest age being 89 years old, in this study also found the majority of respondents male sex as many as 30 people and women as many as 24 people.

Characteristics of research subjects based on the grade of diabetic ulcers found that from 54 subjects the majority came with Grade IV as many as 17 people, followed by grade III as many as 16 people, followed by grade II as many as 9 people, followed by grade V as many as 8 people and the last grade I as many as 4 people. Based on HbA1c levels, the majority of 54 people with uncontrolled HbA1c levels were 39 people, the remaining 15 people with controlled HbA1c levels. In the examination of Hb levels, it was found that from 54 subjects the majority of respondents were anemic as many as 37 people and not anemic as many as 17 people.

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