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RELATIONSHIP BETWEEN MICRONUTRIENT FERRITIN, VITAMIN D, AND CALCIUM WITH THE SEVERITY OF DIABETIC FOOT BASED ON THE WAGNER-MEGGITT CRITERIA.

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ABSTRACT

Background. Diabetic foot is a significant complication for Type 2 Diabetes Mellitus (T2DM) patients. Previous studies have linked diabetic foot to micronutrients such as ferritin, vitamin D, and calcium, but there have been no follow-up studies in Medan. This study aimed to analyze the relationship between levels of ferritin, vitamin D, and calcium with the severity of diabetic foot, as measured by the Wagner-Meggit criteria, in T2DM patients

Methods. A cross-sectional study with 48 T2DM patients at Adam Malik General Hospital from December 2022 to December 2023. Micronutrient levels were measured, and the severity of diabetic foot was assessed using the Wagner-Meggitt classification.

Results, The majority of participants (64.6%) were female. High ferritin levels were observed in 91.6% of patients, while 93.75% had low levels of calcium and vitamin D. Bivariate analysis revealed no significant correlations between ferritin, corrected calcium, or vitamin D levels and Wagner grades 2-5 (p=0.515, p=0.646, p=0.377, respectively). Non-parametric correlation analysis showed significant relationships between corrected calcium (p=0.022) and vitamin D (p=0.027) with Wagner grades.

Discussion. Among the 48 subjects, bivariate testing found that ferritin levels above 150 ng/ml were not linked to diabetic foot severity. Low calcium levels (below 8.5 ng/dl) were significantly associated with increased severity of diabetic foot ($p < 0.03$). 93.75% of participants had low vitamin D levels, which also correlated significantly with foot severity (p=0.027).

Conclusion. The study concluded that calcium and vitamin D levels correlate with the severity of diabetic foot, but not ferritin levels.

Keywords: Diabetic foot, Ferritin, Vitamin D, Calcium, Wagner Meggitt

ABSTRAK

Latar Belakang. *Kaki diabetik adalah komplikasi signifikan bagi pasien Diabetes Melitus Tipe 2 (T2DM). Penelitian sebelumnya telah mengaitkan kaki diabetik dengan mikronutrien seperti ferritin, vitamin D, dan kalsium, tetapi belum ada studi lanjutan di Medan.Tujuan penelitian untuk menganalisis hubungan antara kadar ferritin, vitamin D, dan kalsium dengan tingkat keparahan kaki diabetik, yang diukur menggunakan kriteria Wagner-Meggit, pada pasien T2DM di Rumah Sakit Umum Haji Adam Malik, Medan, Indonesia.*

Metode. *Sebuah studi potong lintang dilakukan dengan 48 pasien T2DM di Rumah Sakit Adam Malik dari Desember 2022 hingga Desember 2023. Kadar mikronutrien diukur, dan tingkat keparahan kaki diabetik dinilai menggunakan klasifikasi Wagner-Meggitt.*

Hasil. *Mayoritas peserta (64,6%) adalah wanita. Kadar ferritin tinggi teramati pada 91,6% pasien, sementara 93,75% memiliki kadar kalsium dan vitamin D*

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yang rendah. Analisis bivariata menunjukkan tidak ada korelasi signifikan antara kadar ferritin, kalsium yang dikoreksi, atau kadar vitamin D dengan grade Wagner 2-5 (p=0,515, p=0,646, p=0,377, masing-masing). Analisis korelasi non-parametrik menunjukkan hubungan signifikan antara kalsium yang dikoreksi (p=0,022) dan vitamin D (p=0,027) dengan grade Wagner.
Diskusi. *Di antara 48 subjek, pengujian bivariata menemukan bahwa kadar ferritin di atas 150 ng/ml tidak terkait dengan keparahan kaki diabetik. Kadar kalsium rendah (di bawah 8,5 ng/dl) secara signifikan terkait dengan peningkatan keparahan kaki diabetik (p < 0,03). Sebanyak 93,75% peserta memiliki kadar vitamin D yang rendah, yang juga berhubungan signifikan dengan keparahan kaki (p=0,027).*
Kesimpulan. *Studi ini menyimpulkan bahwa kadar kalsium dan vitamin D berkorelasi dengan keparahan kaki diabetik, bukan dengan kadar ferritin*

Kata Kunci: *Kaki diabetik, Ferritin, Vitamin D, Kalsium, Wagner Meggitt*

1. Introduction

Diabetes mellitus (DM) is a group of metabolic diseases marked by elevated blood glucose levels, leading to complications such as diabetic foot. Individuals with DM face a doubled risk of foot problems and peripheral artery disease. The incidence of DM is on the rise globally, with Indonesia expected to experience significant growth in cases. In 2022, many patients at Haji Adam Malik General Hospital were diagnosed with diabetic foot, resulting in numerous amputations [1]-[4].

Diabetic foot ulcers (DFUs) develop due to the interplay of neuropathy, ischemia, and infections, which can be aggravated by factors like anemia and vitamin deficiencies, while anemia is frequently seen in DM patients and can worsen complications. The diagnosis of diabetic foot ulcer involves a comprehensive clinical assessment, beginning with a detailed medical history including diabetes duration, glycemic control, and previous foot ulcers or amputations. Physical examination includes visual inspection for deformities, ulcers, infection signs, and assessment of peripheral pulses. Laboratory tests help evaluate glycemic control and inflammation. Imaging modalities like X-ray or magnetic resonance imaging (MRI) are used to detect complications such as osteomyelitis. Ankle-brachial index (ABI) may be performed to assess peripheral arterial disease. Accurate diagnosis guides appropriate management and helps prevent serious outcomes like amputation [5].

As many as 50% of individuals with DFU also have concurrent peripheral artery disease (PAD), resulting in a markedly elevated risk of adverse limb events and cardiovascular illness. Timely detection of PAD in patients with DFUs is crucial, as PAD correlates with a heightened risk of nonhealing ulcers, infections, major limb amputations, cardiovascular complications, and elevated overall mortality [6]. Management of diabetic foot ulcers (DFU) requires a multidisciplinary approach that includes glycemic control, wound debridement, infection management, vascular assessment, offloading, and nutritional optimization. Micronutrients, including calcium, vitamin D, and ferritin, play significant roles in the pathophysiology and healing of DFUs. Vitamin D contributes to immune modulation and tissue repair; its deficiency is associated with delayed wound healing and increased infection risk. Calcium is vital for cellular signaling and keratinocyte proliferation, and its serum levels have been shown to decline with increasing DFU severity. Ferritin, an acute-phase reactant, is often elevated in chronic inflammation and may reflect iron metabolism disturbances that contribute to impaired healing. Optimizing these micronutrients may support improved outcomes in patients with diabetic foot complications [4]-[8].

This study aimed to investigate the association between serum levels of ferritin, vitamin D, and calcium with the severity of DFUs in patients with T2DM. Given the high prevalence of diabetic foot complications and their substantial impact on morbidity, particularly at Haji Adam Malik General Hospital, understanding the potential role of micronutrient imbalances in ulcer severity could provide

insight into risk stratification and therapeutic strategies. By evaluating these parameters using the Wagner-Meggitt classification system, the study seeks to determine whether alterations in ferritin, vitamin D, and calcium levels correlate with more advanced stages of DFUs.

2. Method

2.1. Study Design and Setting

This study is an observational analytical research with a cross-sectional design, using retrospective data collection with laboratory result documentation instruments from medical records. Cross-sectional research is a study design that examines the dynamics of the association between dependent and independent variables at a single point in time (point time approach). The research was conducted at Haji Adam Malik General Hospital after obtaining approval from the Health Research Ethics Committee of the Faculty of Medicine, USU/Adam Malik Hospital. The study was carried out at one time, and data were collected from December 2022 to December 2023 until the sample size was met.

2.2. Population, Sample, and Variables

The target population of the study is patients or individuals with type 2 diabetes mellitus, while the accessible population consists of type 2 diabetes mellitus patients who are hospitalized due to diabetic foot ulcers at Adam Malik Hospital. The research sample consists of the accessible population that meets the inclusion criteria and does not meet the exclusion criteria. The sampling technique was conducted using non-probability sampling, specifically through consecutive sampling. Based on the sample size calculation for this study, a minimum of 47 individuals is required. The inclusion criteria for this study include patients diagnosed with type 2 diabetes mellitus with diabetic foot complications classified as Wagner-Meggit grades 1-5 who are hospitalized. The exclusion criteria for this study are a) patients who have undergone surgical procedures related to diabetic foot; b) patients with hematologic malignancies such as thalassemia; c) patients with conditions causing hypocalcemia or hypercalcemia, d) patients experiencing iron deficiency anemia; and, c) patients are currently taking medications that may affect vitamin D, calcium, and ferritin levels in the body. The dependent variable in this study is the severity of diabetic foot, assessed using the Wagner-Meggitt classification. The independent variables are the levels of micronutrients in the blood, such as calcium, ferritin, and vitamin D.

2.3. Data Collection and Management

The data collection process includes all research data such as age, gender, occupation, history of diabetes mellitus, body mass index, severity of diabetic foot based on the Wagner-Meigge classification, and levels of micronutrients such as vitamin D, calcium, and ferritin. The process involves transferring data from the collection site into a computer. Data entry is conducted on a Data View sheet, where each row represents one respondent and each column represents one variable. The program used is SPSS version 26. Data cleaning involves checking the data entry by identifying missing data—i.e., checking if there are any unfilled entries—and assessing data variability by generating frequency distributions, as well as minimum and maximum values for each variable.

2.4. Statistical Analysis

Data is presented descriptively in terms of count (n) and percentage (%) for various variables such as age, gender, and laboratory results in patients. To determine the relationship between the severity of diabetic foot and serum levels of ferritin, vitamin D, and calcium, a Chi-Square test will be conducted if the data is normally distributed, or a Kolmogorov-Smirnov test if the data is not normally

distributed. The significance level used is 5%. The differences in mean serum levels of ferritin, vitamin D, and calcium between subgroups will be tested using the chi-squared test. Analysis will be performed using statistical software (Statistical Product and Service Solutions), with a confidence interval of 95%, where a p-value < 0.05 is considered statistically significant.

3. Results

A total of 48 subjects were included in this study, with the majority being female (64.6%) and most subjects being under 60 years old (56.25%), with an average age of 57.1 ± 1.6. The subjects underwent tests for ferritin, calcium, vitamin D, albumin, and HbA1c, and were classified using the Wagner classification. About 37.5% of the subjects had diabetic foot classified as Wagner grade 4, and 95.8% had HbA1c levels > 6.4%. The majority of subjects had ferritin levels > 150 (91.6%), serum calcium < 8.5 (93.75%), and albumin < 3.4 (97.9%). The corrected calcium calculation showed that 97.9% of subjects had corrected calcium levels < 10.2. Additionally, 93.75% of patients had vitamin D levels < 20. The basic characteristic data of the study can be seen in Table 1. The Shapiro-Wilk test was conducted to assess the normality of the distribution in this study. The normality test results indicated that age and albumin data were normally distributed (albumin p = 0.599 and age p = 0.546), while ferritin, corrected calcium, vitamin D, and Wagner classification data showed a non-normal distribution (ferritin p < 0.001, corrected calcium p < 0.041, vitamin D p < 0.024, Wagner p < 0.001).

Table 1 Baseline characteristics

Variable	**n=48 (%)**
Gender	
Male	17 (35,4%)
Female	31 (64,6%)
Age (year)	
< 60	27 (56.25%)
≥ 60	21 (43.75%)
Ferritin (ng/mL)	
<150	4 (8.3%)
≥150	44 (91.6%)
Calcium (mg/dL)	
< 8.5	45 (93.75%)
≥8.5	3 (6.25%)
Albumin (g/dL)	
<3.4	47 (97.9%)
≥ 3.4	1 (2.08%)
Calcium corrected	
< 10.2	47 (97.9%)
≥ 10.2	1 (2.08%)
Vitamin D (ng/mL)	
< 20	45 (93.75%)
≥ 20	3 (6.25%)
HbA1c (%)	
< 6.4	2 (4.16%)
≥ 6.4	46 (95.8%)
Wagner	
1	-
2	4 (8.3%)
3	14 (29.1%)
4	18 (37.5%)
5	12 (25%)

The bivariate analysis results between the independent and dependent variables showed no relationship between ferritin, corrected calcium, and vitamin D with Wagner grades 2-5 (p = 0.515, p = 0.646, and p = 0.377, respectively) (Table 2). Similar results were obtained in the bivariate analysis between ferritin and corrected calcium, where no statistically significant relationship was found with the less severe Wagner groups (grades 1-2) and the more severe groups (grades 3-5), with p-values of 1.0, 1.0, and 1.0, respectively (Table 3).

Table 2 The correlation between ferritin, corrected calcium, vitamin D, and the Wagner classification

	Wagner				
	2	**3**	**4**	**5**	**P**
Ferritin (ng/mL)					
< 150	0	2	2	0	0.515
≥ 150	4	12	16	12	
Calcium corrected					
<10.2	4	14	17	12	0.646
>10.2	0	0	1	0	
Vitamin D (ng/mL)					
< 20	4	12	18	11	0.377
≥ 21	0	2	0	1	

Table 3 The correlation between ferritin, corrected calcium, vitamin D, and the Wagner classification for less severe and more severe cases

	Wagner			
	Less Severe	**More Severe**	**P**	**OR (95% CI)**
Ferritin (ng/mL)				
< 150	0	4	1.000	1.1 (1.002 – 1.208)
≥ 150	4	40		
Calcium corrected				
<10.2	4	43	1.000	0.915 (0.838 – 0.998)
≥10.2	0	1		
Vitamin D (ng/mL)				
<20	4	41	1.000	0.911 (0.832 – 0.998)
≥20	0	3		

The albumin variable was normally distributed, and the results of the parametric correlation test did not show a significant correlation between albumin and the Wagner classification (p = 0.124) (Table 4). Meanwhile, for the ferritin and corrected calcium variables, which were not normally distributed, the non-parametric Spearman test indicated a statistically significant correlation between corrected calcium and Wagner grades (p = 0.022), as well as between vitamin D and Wagner grades (p = 0.027) (Tabel 5).

Table 4 Parametric correlation

	Age	**Ferritin**	**Kalsium**	**Albumin**	**Ca Cor**	**Vit D**	**HbA1c**	**Wagner**
Usia		0.027	0.761	0.033	0.472	0.121	0.973	0.409
Ferritin	0.027		0.495	0.102	0.839	0.432	0.080	0.191
Calcium	0.761	0.495		0.719	< 0.001	0.683	0.881	0.069
Albumin	0.033	0.102	0.719		0.002	<0.001	0.069	0.124
Calcium corrected	0.472	0.839	< 0.001	0.002		0.295	0.448	**0.017**
Vitamin D	0.121	0.432	0.683	<0.001	0.295		0.835	**0.040**
HbA1C	0.973	0.080	0.881	0.069	0.448	0.835		0.342
Wagner	0.409	0.191	0.069	0.124	**0.017**	**0.040**	0.342	

Table 5 Non-parametric correlation (Spearman)

	Age	**Ferritin**	**Kalsium**	**Albumin**	**Ca Cor**	**Vit D**	**HbA1c**	**Wagner**
Age		0.038	0.351	0.070	0.737	0.112	0.779	0.617
Ferritin	0.038		0.690	0.220	0.623	0.423	0.037	0.203
Calcium	0.351	0.690		0.793	< 0.001	0.432	0.970	**0.030**
Albumin	0.070	0.220	0.793		< 0.001	0.001	0.371	0.220
Calcium corrected	0.737	0.623	< 0.001	<0.001		0.150	0.816	**0.022**
Vitamin D	0.112	0.423	0.432	0.001	0.150		0.985	**0.027**
HbA1C	0.779	0.037	0.970	0.371	0.816	0.985		0.308
Wagner	0.617	0.203	**0.030**	0.220	**0.022**	**0.027**	0.308	

4. Discussion

Epidemiological data show that 0.2-11% of diabetes patients experience foot ulcer complications each year. This incidence is higher compared to the general population, where foot ulcers are found in 0.1-8% of the population annually. Globally, diabetic foot is more common in type 2 diabetes compared to type 1 diabetes. This study does not compare the prevalence of foot ulcers in diabetic and non-diabetic patients, nor does it compare the prevalence of diabetic foot in type 1 and type 2 diabetes. The study involved 48 subjects with type 2 diabetes who had diabetic foot. Among all subjects, there were 4 subjects (8.3%) with Wagner grade 2, 14 (29.1%) with Wagner grade 3, 18 (37.5%) with Wagner grade 4, and 12 (25%) with Wagner grade 5.

The risk of diabetic foot increases with age, duration of diabetes, and the effects of hyperglycemia, as well as the rising prevalence of micro- and macrovascular complications in older individuals. However, younger and middle-aged diabetes patients often have more severe degrees of diabetic foot and more frequent complications, requiring hospitalization and experiencing recurrent ulcers more often than older patients. Younger diabetic foot patients generally indicate poorly managed diabetes mellitus and require special attention for glycemic control and lifestyle modifications in this population [2].

The majority of subjects in this study were female (64.6%). This figure differs from previous research, which indicated that the incidence of diabetic ulcers was one and a half times higher in males than in females [1]. Males tend to develop diabetic feet at a younger age and are more frequently affected than females (1.4-3.5 times) [1]-[2]. Females generally have better adherence to therapy, self-care abilities, and foot examination compliance compared to males. Additionally, males are more likely to have risk factors such as smoking and more frequently experience complications like peripheral neuropathy, peripheral artery disease, and cardiovascular disease, which are risk factors for diabetic foot [1]. Another study by Vanherwegen et al. also reported similar findings, with 72% of subjects being male. The severity of ulcers in males was greater, with more instances of bone involvement and severe infections that spread throughout the body (systemic infections). Males have a higher prevalence of requiring lower extremity revascularization, while females have a 26% higher likelihood of healing ulcers without requiring amputation during the first occurrence [3].

In this study, 95.8% of subjects with diabetic foot had HbA1c levels > 6.4%, which is consistent with previous theories and research. Hemoglobin A1c (HbA1c) is the standard laboratory test for assessing glycemic control in patients with Diabetes Mellitus (DM). Hemoglobin A1c is formed from a permanent bond between glucose and hemoglobin in the beta chains of red blood cells, reflecting the average blood sugar levels over the past 8-12 weeks. Research shows that high HbA1c levels (>6.5%) are associated with an increased risk of diabetes complications, such as nerve damage and peripheral blood flow issues, which can lead to diabetic foot ulcers. Therefore, achieving optimal glycemic and HbA1c targets is a primary goal in managing diabetic foot patients.

A study conducted by Akyuz et al. found that an HbA1c value ≥10.1% in a population with type 2 DM is strongly correlated with Wagner Type 4 and PEDIS Stage 3, indicating a high degree of severity for diabetic foot. This research also showed that higher HbA1c levels are associated with an increased rate of amputations that threaten patients' functional health [4] Another study by Sachar et al. found that HbA1c levels are significantly related to infections in diabetic feet (p=0.04). Hemoglobin A1c is linearly associated with the severity of diabetic foot (Wagner classification) and can be used to predict the occurrence of diabetic foot and its complications [7].

Ferritin is an acute-phase protein that increases in response to tissue damage and inflammation. Elevated ferritin levels are associated with diabetes mellitus (DM), obesity, metabolic syndrome, and atherosclerosis [8]. Research by Kumar et al. indicated a significant relationship between ferritin levels and the severity of diabetic foot (p<0.0001) [9]. In this study, 91.6% of subjects had ferritin levels greater than 150 ng/ml. Unlike the study by Kumar et al., our bivariate and correlation tests did not show any relationship between ferritin levels and the severity of diabetic foot. A study conducted by Pena et al. also found lower ferritin levels in 5.9% of diabetic foot patients, and similar to our findings, this study did not demonstrate a relationship between ferritin levels and the severity of diabetic foot [10].

In this study, 93.75% of subjects had calcium levels < 8.5 mg/dL. Bivariate tests did not reveal a relationship between calcium levels and the severity of diabetic foot. However, correlation tests indicated a significant relationship between calcium levels and the severity of diabetic foot (p < 0.03). A meta-analysis conducted by Kurian et al. found a significant relationship between calcium and diabetic foot (p < 0.00001, CI 95% 8.71-9.49) [11]. Research by Xu et al. also showed a relationship between low serum calcium levels and the prognosis of diabetic foot (p = 0.022), including the risk of amputation, although further research is needed to explore the underlying mechanisms [12].

In our study, 93.75% of subjects had low vitamin D levels. Correlation tests showed a significant relationship between vitamin D levels and the severity of diabetic foot (p = 0.027). A study by Tang et al. found that 71.8% of diabetic foot patients experienced vitamin D deficiency, with the prevalence of deficiency increasing in the diabetic foot population with osteomyelitis (82.1%). The study reported that 100% of diabetic patients with Wagner Type 4 had vitamin D deficiency [13].

These findings are supported by a meta-analysis conducted by Kurian et al., which analyzed 13 studies and found that low vitamin D levels were present in diabetic foot patients (p < 0.001, 95% CI -8.06 to -2.76) [11]. Vitamin D deficiency in diabetic patients is associated with the occurrence of diabetic foot and foot infections. It is linked to the progression of diabetes and both micro- and macrovascular complications. The risk of developing diabetic foot increases 3.2 times in patients with vitamin D deficiency.

Vitamin D plays a role in wound healing, including the healing process of diabetic foot. It acts as an immunomodulator that facilitates the activation of T and B cells by macrophages. Vitamin D3 supplementation in vitro enhances macrophage phagocytosis under diabetic foot conditions. It inhibits pro-inflammatory T-helper 1 (Th1) cells and stimulates T-helper 2 (Th2) cells that assist in wound healing. Additionally, vitamin D induces the transcription of cathelicidin and defensins, which aid in phagocytosis and activate the antimicrobial effects of the nonspecific immune system [11] [13].

In several studies, including this one, no significant relationship was found between the occurrence of diabetic foot and micronutrient deficiencies. Several factors may explain the absence of a relationship in these findings. According to Pena et al., compensatory mechanisms in the body could be one of the factors [14]. Diabetic patients often take supplements or receive dietary counseling as part of their management plan. These interventions may reduce the effects of micronutrient deficiencies, thereby decreasing the likelihood of observing a direct relationship between

micronutrient levels and the occurrence of diabetic foot. Additionally, other physiological compensatory mechanisms that protect against the development of diabetic foot, despite micronutrient deficiencies, should not be overlooked.

Diabetic foot is a multifactorial condition influenced by various factors, including vascular, neurological, immunological, and metabolic parameters, in addition to body compensation as noted by Pena et al [14]. Micronutrient deficiency is just one potential risk factor among many others. The lack of a significant relationship in this study may suggest that other factors, such as glycemic control, blood pressure, lipid levels, and genetic predisposition, play a more dominant role in the development of diabetic foot. Therefore, focusing solely on micronutrient status may not capture the complex interactions of the factors contributing to diabetic foot.

Kurian et al. also noted in their findings that confounding factors can obscure the relationship between micronutrient deficiencies and diabetic foot [15]. Variables, such as eating habits, socioeconomic status, access to healthcare, and adherence to diabetes management regimens, can influence both micronutrient status and the risk of diabetic foot. If these confounding factors are not well-controlled, they can mask or mimic relationships, leading to incorrect conclusions.

In addition to confounding factors, Kurian et al [15] pointed out that the temporal relationship between micronutrient deficiencies and the development of diabetic foot complications is another influencing factor. Micronutrient deficiencies may need to persist for an extended period before contributing to the development of diabetic foot. If the study period is too short to capture this temporal aspect, the relationship may not be apparent.

In this study, no significant relationship was found between ferritin levels and the Wagner classification. This is supported by several previous similar studies. In addition to its role in acute inflammation, ferritin levels also increase in chronic disease conditions. Diabetic patients often experience low-grade chronic inflammation, which may contribute to elevated ferritin levels regardless of acute ulceration. Therefore, the relationship between ferritin and the Wagner classification may also reflect the underlying chronic inflammatory state in diabetic patients. This is supported by research conducted by Gezawa et al., which included 336 respondents and found that even in the absence of acute infection, diabetic patients with more advanced Wagner stages had higher baseline ferritin levels [16].

Dysregulation of iron metabolism is a common issue in diabetic patients and can contribute to increased ferritin levels and heightened susceptibility to infections. Diabetic foot ulcers, especially at higher Wagner stages, are often associated with poor wound healing and recurrent infections—conditions that can exacerbate iron metabolism dysregulation. This dysregulation may lead to elevated ferritin levels as a protective mechanism against the harmful effects of free iron. Research by Shareef et al. involving 161 respondents found that diabetic patients with higher Wagner stages often exhibited markers of iron metabolism dysregulation, including increased ferritin levels [17].

Understanding the relationship between ferritin levels and the Wagner classification has significant clinical implications. Elevated ferritin levels in patients with diabetic foot ulcers may serve as a marker for more aggressive or advanced disease, potentially guiding more intensive monitoring and treatment strategies. Additionally, monitoring ferritin levels can help assess the effectiveness of treatments aimed at reducing inflammation and controlling infections. As suggested by Wang et al. in a literature review published in 2022, integrating ferritin-level assessment into routine care for patients with diabetic foot ulcers could enhance clinical decision-making and patient outcomes [18].

Based on the correlation between calcium levels and the occurrence of diabetic foot in this study, a significant relationship was found through non-parametric correlation analysis. These findings are supported by several previous studies. According to Fu et al., patients with diabetic foot ulcers often

have lower serum calcium levels compared to those without such complications [19]. In their study involving 3,386 respondents, Fu et al. found a significant correlation between low calcium levels and the severity of diabetic foot ulcers, indicating that calcium deficiency may exacerbate the condition. Xu et al. also supported these findings. They suggested that serum calcium could serve as an inflammatory marker in diabetic foot patients, with levels increasing as systemic inflammation worsens. Therefore, the lower the serum calcium levels in diabetic foot patients, the more severe the degree of diabetic foot they experience, leading to accelerated disease progression towards a worse state [12]. Additionally, a 2023 study by Tsitsou et al. reported that patients with DFUs had significantly lower mean serum calcium levels (9.3 ± 0.5 mg/dL) compared to diabetic patients without ulcers (9.7 ± 0.3 mg/dL), with a p-value of 0.032, indicating a statistically significant difference. These findings suggest that monitoring and correcting calcium deficiencies may be crucial in improving DFU outcomes [20].

This study is the first to report the relationship between micronutrient levels of ferritin, vitamin D, and calcium with the severity of diabetic foot in type 2 DM patients at Adam Malik Hospital and even in North Sumatra. Micronutrient levels can be used as an initial management strategy or preventive measure in dietary control of hyperglycemia due to type 2 DM, helping to prevent the worsening of vascular complications, including diabetic foot.

The limitations of this study include the use of retrospective data from medical records, which results in a lack of in-depth assessment of nutritional status and BMI before patient admission, as well as other underlying infection factors that may increase the risk of bias in elevated ferritin levels due to inflammation. Additionally, the variability in the timing of micronutrient data collection poses a risk of bias in the results obtained.

5. Conclusion.

This study demonstrated a significant correlation between serum levels of calcium and vitamin D with the severity of diabetic foot ulcers in patients with T2DM, as classified by the Wagner-Meggitt system. Lower levels of calcium and vitamin D were associated with more advanced stages of ulceration, suggesting their potential role in the pathophysiology and progression of diabetic foot complications. In contrast, no significant association was observed between ferritin levels and ulcer severity. These findings highlight the importance of assessing and potentially correcting calcium and vitamin D deficiencies in the clinical management of diabetic foot ulcers to support better outcomes and prevent progression. Further prospective studies are warranted to explore the mechanistic pathways and therapeutic implications of micronutrient optimization in diabetic foot care.

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Conflict of interest

The authors declare no conflict of interest.

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