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# ASSOCIATION BETWEEN HEMOGLOBIN LEVELS AND SEVERITY OF DIABETIC FOOT ULCERS IN TYPE 2 DIABETES MELLITUS PATIENTS AT RSUP PROF. DR. I.G.N.G NGOERAH DENPASAR

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## ABSTRACT

**Background**: Diabetic Foot Ulcer (DFU) is a condition characterized by loss of skin integrity in the distal foot, involving at least the epidermis and part of the dermis in individuals with a history of Diabetes Mellitus (DM). Anemia which is defined by low hemoglobin levels, may exacerbate DM-related complications. However, the connection between hemoglobin levels and the severity of DFU remains poorly understood. **Methods**: This study aimed to describe the prevalence of anemia and investigate the association between hemoglobin levels and DFU severity among type 2 DM patients at Prof. Dr. I.G.N.G. Ngoerah General Hospital, Denpasar. An analytical observational study with a cross-sectional design was conducted on type 2 DM patients presenting with DFU, who were registered at the hospital from 2022-2023. Consecutive sampling was used to select subjects and secondary data were sourced from medical records. Data analysis included univariate and bivariate Chi-Square tests. **Results**: A total of 74 patients aged 38-77 years were included in the study. Anemia was identified in 64 patients (86.5%) with 15 (20.3%) experiencing mild anemia, 37 (50%) moderate anemia, and 12 (16.2%) severe anemia, while 10 patients had normal hemoglobin levels. A total of 41 patients (55.4%) had severe DFU and 33 patients (44.6%) had mild to moderate DFU. **Conclusion**: Bivariate Chi-Square analysis revealed no significant association between hemoglobin levels and DFU severity ($p = 0.635$).

**Keywords :** anemia, diabetic foot ulcers, hemoglobin levels, type 2 diabetes mellitus.

## INTRODUCTION

Diabetes Mellitus (DM) is a metabolic disorder marked by persistent high blood sugar levels.[1] According to the 10th edition of the International Diabetes Federation (IDF) Atlas, in 2021, approximately 537 million people worldwide were affected by diabetes. Indonesia ranked fifth, with an estimated 19.5 million cases. Approximately 90% of all diabetes cases were caused by Type 2 Diabetes Mellitus (T2DM), establishing it as the most widespread form of the disease.[2–4]

One of the most serious long-term/chronic complications of diabetes is Diabetic Foot Ulcer (DFU). DFU is defined as a full-thickness wound on the skin, that develops in the distal area of lower limbs in individuals with diabetes.[5] The condition was primarily caused by neuropathy, peripheral arterial disease, and inadequate foot care. Ulcers typically develop in areas subjected to repeated trauma or excessive pressure.[6] Approximately 19-34% of patients with DM experienced DFU.[7] Diabetic foot ulcer remains a significant challenge due to its substantial contribution to global morbidity and mortality. The high frequency of recurrent hospitalizations and the increased risk of limb amputation have led to substantial healthcare expenditures. Furthermore, the availability of reliable biomarkers for predicting non-healing ulcers and monitoring therapeutic responses has been limited.[8] Various classification systems exist for grading the severity of DFU, with the Meggit-Wagner classification being among the most commonly used.[9] Anemia defined by reduced hemoglobin (Hb) levels, is another critical concern in diabetic patients.[10] Hemoglobin plays an essential function in transporting oxygen from the lungs to body tissues and adequate oxygen supply is necessary for wound healing and tissue regeneration.[11–13] In DM, chronic hyperglycemia and persistent inflammation often result in reduced Hb levels. Anemia in diabetic patients often goes unrecognized, not realizing its symptoms. It is considered a key contributor to impaired microcirculation and is commonly recognized as an important contributor to delayed wound healing, wound infection, higher amputation rates, and increased mortality.[14,15]

Several studies have looked at the association between anemia and outcomes in DFU. According to Li et al., it was discovered that 53% of T2DM patients with DFU had anemia, significantly higher than the 13% observed in T2DM patients without DFU.[14] Kumar et al. found that more than three-quarters of T2DM patients with DFU complications presented with moderate to severe anemia, and Hb levels continued to decline during hospitalization despite clinical improvement in foot infections.[16] However, a study conducted at Bone Regency

stated different results, reporting a weak negative correlation between anemia and DFU severity, which was not statistically significant.[17] In Bali, no similar study has been conducted to date.

In summary, although previous research has suggested that anemia may exacerbate mortality risk in diabetic patients, the occurrence and prognosis of anemia in DFU patients are still not well understood. Clarifying whether anemia serves as a prognostic factor for poor outcomes in DFU is crucial. Knowledge regarding the association between hemoglobin levels or the intensity of anemia and the extent of DFU severity will provide valuable insights for optimizing therapeutic strategies. Therefore, this study seeks to explore the prevalence of anemia and the association between hemoglobin levels and DFU severity among type 2 DM patients at Prof. Dr. I.G.N.G. Ngoerah General Hospital, Denpasar who were treated between 2022 and 2023.

## LITERATURE REVIEW

### Type 2 Diabetes Mellitus

Diabetes mellitus (DM) is a metabolic disorder primarily characterized by persistent hyperglycemia. The typical symptoms of diabetes, known as the diabetic triad, include polyuria, polydipsia, and polyphagia. Additional symptoms often reported are fatigue, blurred vision, delayed wound healing, paresthesia, pruritus, and sexual dysfunction.[3]

Diabetes mellitus (DM) is classified into several types, with type 2 DM being the most prevalent. Type 2 Diabetes Mellitus (T2DM) is caused by a combination of pancreatic β-cell dysfunction and increased insulin resistance.[4] The peripheral insulin resistance, combined with an inadequate insulin secretory response, results in elevated blood glucose levels. The lipotoxicity, glucotoxicity, and glucolipotoxicity contribute to metabolic and oxidative stress, impairing the integrity of islet cells and causing β-cell dysfunction. This was supported by findings of low-grade inflammation markers such as Tumor Necrosis Factor (TNF)-α, Interleukin (IL)-6, C-Reactive Protein (CRP), and IL-1 in patients with DM.[18]

A high-calorie diet rich in fats and carbohydrates has been linked to increased production of Reactive Oxygen Species (ROS), further aggravating oxidative stress. These pathological changes disrupt the regulation of insulin and glucagon worsening hyperglycemia.[18] As a result, complications of DM and broadly categorized into acute and chronic. One of the serious chronic complications which involves both microvascular and macrovascular dysfunction, is the development of DFU. The increased oxidative stress plays a crucial role in accelerating these complications, ultimately leading to the formation of diabetic foot ulcers.[1]

### Diabetic Foot Ulcer

According to the International Working Group on the Diabetic Foot (IWGDF), a disturbance in the skin integrity of the foot's skin is known as a diabetic foot ulcer, involving at least the epidermal layer and part of the dermal layer, in patients with a history of DM. Diabetic Foot Ulcers (DFUs) are frequently associated with peripheral neuropathy and/or Peripheral Artery Disease (PAD). The pathophysiology of DFU commonly involves three key components known as the 'triad': neuropathy, vascular insufficiency, and trauma, often followed by secondary infection due to foot injuries. Motor-sensory neuropathy contributes to uneven pressure distribution on the plantar surfaces, altered gait, and reduced pain sensitivity, which increases the risk of ulcer formation. Autonomic neuropathy results in dry skin due to diminished secretion from sebaceous and sweat glands, making the skin more prone to cracking. This compromise in skin barrier integrity allows for easier microbial invasion when trauma or an ulcer is present. Vascular insufficiency in diabetic patients also leads to arterial narrowing, resulting in ischemia of the foot.

The diagnosis of DFU includes a thorough medical history, followed by a physical examination that assesses dermatological, vascular, neurological, and musculoskeletal aspects, as well as signs of infection. Common clinical findings include neurological symptoms like burning sensations or numbness and vascular symptoms such as intermittent claudication, rest pain, and non-healing ulcers. After the diagnosis, the classification of DFUs by severity is performed. The Wagner classification system is widely used due to its simplicity and its superior predictive capacity for assessing the risk of amputation.

### Anemia

Anemia is identified by decreased hemoglobin (Hb), hematocrit (HCT), or erythrocyte counts.[10] Hemoglobin is a vital protein in erythrocytes that serves as the primary transporter of oxygen in the human body, with approximately 98% of blood oxygen bound to hemoglobin. Each heme group in hemoglobin contains an iron molecule capable of binding and releasing oxygen, thereby enabling efficient oxygen delivery throughout the body. Oxygen is crucial for Adenosine Triphosphate (ATP) production via oxidative phosphorylation, which underscores the importance of maintaining adequate oxygen distribution to all metabolically active cells.[12,13]

Chronic conditions, especially those characterized by inflammation such as DM, frequently result in anemia of chronic disease (ACD) or inflammatory anemia. This type of anemia typically progresses slowly and may present without symptoms. Several mechanisms are involved including the link between diabetic nephropathy and decreased erythropoiesis, which is marked by reduced erythropoietin (EPO) production. This decline is closely associated with diabetic microvascular complications and autonomic neuropathy. Elevated pro-inflammatory cytokines, including TNF-α and IL-1, have been implicated in the pathogenesis of ACD, as they contribute to increased erythrocyte destruction via macrophage activation. Inflammatory cytokines disrupt erythropoiesis and increase erythrocyte turnover. Hematological changes characteristic of ACD include normochromic and normocytic anemia, which is marked by a shorter lifespan of erythrocytes and a reduction in erythropoiesis.[19]

**Association between Hemoglobin Levels and Severity Of Diabetic Foot Ulcers in Type 2 Diabetes Mellitus Patients**

The connection between anemia and the complications of DFU can be attributed to the role of hemoglobin in oxygen transport. Hemoglobin in erythrocytes carries most of the oxygen delivered to tissues, thus, anemia reduces the oxygen supply to the ulcer site, delaying wound healing and hindering infection control.[14] Adequate blood flow is vital for wound healing because it delivers essential oxygen and nutrients needed for tissue repair.[11,20] Oxygen supports the regeneration of damaged tissue and is necessary for oxidative metabolism, which produces ATP, primary energy source required for the wound healing process. The ATP generated provides the energy needed for tissue repair and activates wound healing mechanisms.[21] So, anemia in DFU patients may exacerbate ischemia of the lower extremities, increase the risk of infection, and delay healing, thereby worsening the severity of DFUs.

## MATERIAL AND METHODS

This study was conducted over 8 months from February 2024 to September 2024. Ethical clearance was obtained from the Research Ethics Committee of the Faculty of Medicine, Udayana University (Ethical Clearance No. 2729/UN14.2.2.VII.14/LT/2023). This study employed a cross-sectional, observational, descriptive-analytic (non-experimental) design. Type 2 Diabetes Mellitus (T2DM) patients who developed DFU and received treatment at RSUP Prof. Dr. I.G.N.G Ngoerah Denpasar in 2022-2023 were included in the sample. Study participants were chosen based on specific inclusion and exclusion criteria.

Inclusion criteria: The study included both female and female patients aged 18-80 years who were diagnosed with T2DM and had DFU classified according to the Meggit-Wagner grading system (Grade I-V). All participants were registered at RSUP Prof. Dr. I.G.N.G. Ngoerah Denpasar during 2022-2023. Exclusion criteria: The study excluded patients with any diabetes diagnosis other than T2DM, pregnant women with T2DM, patients with a record of hematologic disorders, and those diagnosed with Chronic Kidney Disease (CKD) presenting with a Glomerular Filtration Rate (GFR) below 15 mL/min. Additionally, patients lacking complete medical records were not included in the analysis.

Data were collected on variables including HbA1c levels, age, Body Mass Index (BMI), sex, Hb levels, and the severity of DFU which was assessed using the Wagner classification. Having a hemoglobin concentration below 12 g/dL in women and less than 13 g/dL in men is considered anemia based on World Health Organization (WHO) criteria. Anemia was further divided into three subgroups: mild anemia (males Hb 11-12.9 g/dL, females: Hb 11-11.9 g/dL), moderate anemia (Hb 8-10.9 g/dL), and severe anemia (Hb <8 g/dL). The severity of DFU was determined using the Meggit-Wagner classification system, which was grouped into two categories for analysis purposes. Group 1 comprised Grades I–III, which were categorized as mild to moderate severity, and Group 2 included Grades IV–V, which were classified as severe severity.

For data analysis, Statistical Program for Social Science (SPSS) software version 26.0 for Windows was used. Univariate analysis was conducted to describe the patient characteristics including age, sex, BMI, and HbA1c levels, as well as to evaluate the prevalence of anemia status in T2DM patients with DFU. Bivariate analysis was conducted using a chi-square test to assess the relationship between the independent variable (hemoglobin levels) and the dependent variable (severity of DFU).

## RESULTS

### Characteristics of Research Subjects

A total of 74 research subjects aged 38 to 77 years were part of this study, with the majority being over 40 years old (94.5%), as shown in Table 1. The sample consisted of 36 males and 38 females. BMI distribution revealed that although most subjects had a normal weight (36.5%), malnutrition was prevalent (63.5%), including underweight (9.5%), overweight (18.9%), obesity class I (16.2%), and obesity class II (18.9%). The majority of subjects (68.9%) also had uncontrolled HbA1c levels.

**Table 1.** Distribution of Research Subjects Based on Age, Sex, BMI, and HbA1c Levels

| Characteristics | Frequency (n = 74) | | Median (Minimum-maximum) |
|---|---|---|---|
| | f | % | |
| Age | | | 60 (38-77) |
| 18-40 | 4 | 5.4 | |
| 41-60 | 34 | 45.9 | |
| 61-80 | 36 | 48.6 | |
| Sex | | | |
| Male | 36 | 48.6 | |
| Female | 38 | 51.4 | |
| Body Mass Index (BMI) (kg/m$^2$) | | | 23.44 (17-44) |
| Underweight (<18.5) | 7 | 9.5 | |
| Normal (18.5-22.9) | 27 | 36.5 | |
| Overweight (23-24.9) | 14 | 18.9 | |
| Obesity class I (25-29.9) | 12 | 16.2 | |
| Obesity class II (≥30) | 14 | 18.9 | |
| HbA1c Levels (%) | | | 8.45 (4.9-14) |
| Good glycemic control (<7) | 23 | 31.1 | |
| Poor glycemic control (≥7) | 51 | 68.9 | |

According to row percentages in Table 2, all subjects aged 18-40 years presented with mild to moderate DFUs. In the 41-60 age group, the proportion of severe DFUs was higher (55.9%) than mild to moderate ulcers (44.1%). This pattern was consistent in the 61-80 age group where severe DFUs were more frequent (61.1%). Regarding sex differences, males experienced a higher rate of severe ulcers (66.7%), whereas females had a higher incidence of mild to moderate DFUs (55.3%). Based on row percentage of BMI data, underweight subjects showed a higher incidence of severe DFUs (57.1%) compared to mild-moderate ulcers (42.9%). Among subjects with normal BMI, severe DFUs were dominant (74.1%). In overweight subjects, there was an equal distribution of mild to moderate and severe ulcers (50%). Conversely, mild to moderate DFUs were more prevalent in those with obesity class I (83.3%), while subjects with obesity class II had a higher incidence of severe DFUs (57.1%). Subjects with poor glycemic control were more frequently observed in both the mild-to-moderate DFU group (56.5%) and the severe DFU group (54.9%). These results indicate that poor glycemic control was associated with increased severity of DFUs.

**Table 2.** Distribution of Research Subjects Based on Age, Sex, BMI, and HbA1c Levels, Presented with Row Percentages

| Characteristics | Mild-moderate Ulcer f (%) | Severe Ulcer f (%) |
|---|---|---|
| Age | | |
| 18-40 | 4 (100) | 0 (0) |
| 41-60 | 15 (44.1) | 19 (55.9) |
| 61-80 | 14 (38.9) | 22 (61.1) |
| Sex | | |
| Male | 12 (33.3) | 24 (66.7) |
| Female | 21 (55.3) | 17 (44.7) |
| Body Mass Index (BMI) (kg/m$^2$) | | |
| Underweight (<18.5) | 3 (42.9) | 4 (57.1) |
| Normal (18.5-22.9) | 7 (25.9) | 20 (74.1) |
| Overweight (23-24.9) | 7 (50) | 7 (50) |
| Obesity class I (25-29.9) | 10 (83.3) | 2 (16.7) |
| Obesity class II (≥30) | 6 (42.9) | 8 (57.1) |
| HbA1c Levels (%) | | |
| Good glycemic control (<7) | 10 (43.5) | 13 (56.5) |
| Poor glycemic control (≥7) | 23 (45.1) | 28 (54.9) |

**Prevalence and Characteristics of Anemia in Type 2 Diabetes Mellitus Patients with Diabetic Foot Ulcers at Prof. Dr. I.G.N.G. Ngoerah General Hospital Denpasar during 2022-2023**

As shown in Table 3, the median Hb level of 74 patients with DFUs was 10 g/dL, with 5.2 g/dL as the lowest value and 14.4 g/dL as the highest. Most patients (86.5%) had anemia categorized as mild in 20.3% of cases, moderate in 50%, and severe in 16.2%.

**Table 3.** Hemoglobin Levels in Diabetic Foot Ulcers Patients

| Hemoglobin Levels (g/dL) | Frequency (n = 74) | | Median (minimum-maximum) |
|---|---|---|---|
| | f | % | |
| Normal (Male ≥13; Female ≥12) | 10 | 13.5 | 10 (5.2 -14.4) |
| Mild anemia (Male 11-12.9; Female 11-11.9) | 15 | 20.3 | |
| Moderate anemia (8-10.9) | 37 | 50 | |
| Severe anemia (<8) | 12 | 16.2 | |

According to row percentages in Table 4, when analyzed based on age group, patients aged 18-40 years had a threefold higher proportion (75%) of individuals without anemia compared to those with anemia (25%). In the 41-60 years age group, 94.1% of patients had anemia, while in the 61-80 years age group, 86.1% experienced anemia. Regarding gender differences, compared to men (77.8%), women (94.7%) had a higher prevalence of anemia.

**Table 4.** Hemoglobin Levels in Diabetic Foot Ulcers Patients**,** Presented with Row Percentages Based on Age and Sex

| Characteristics | Nonanemia f (%) | Anemia f (%) |
|---|---|---|
| Age | | |
| 18-40 | 3 (75) | 1 (25) |
| 41-60 | 2 (5.9) | 32 (94.1) |
| 61-80 | 5 (13.9) | 31 (86.1) |
| Sex | | |
| Male | 8 (22.2) | 28 (77.8) |
| Female | 2 (5.3) | 36 (94.7) |

**Characteristics of Diabetic Foot Ulcer Severity in Type 2 Diabetes Mellitus Patients at Prof. Dr. I.G.N.G. Ngoerah General Hospital Denpasar during 2022-2023**

Among the 74 patients included in the study, 5 had Wagner I ulcers, 14 had grade II, 14 had grade III, 31 had grade IV, and 10 had grade V. The majority of patients (55.4%) presented with severe DFUs, classified as Wagner grades IV-V. The detailed percentage distribution of each grade is shown in Table 5.

**Table 5.** Severity of Diabetic Foot Ulcers

| Severity of Diabetic Foot Ulcers | Frequency (n = 74) | |
|---|---|---|
| | f | % |
| Mild to moderate ulcers | | |
| *Wagner* I | 5 | 6.8 |
| *Wagner* II | 14 | 18.9 |
| *Wagner* III | 14 | 18.9 |
| Severe ulcers | | |
| *Wagner* IV | 31 | 41.9 |
| *Wagner* V | 10 | 13.5 |

**Association between Hemoglobin Levels and Severity Of Diabetic Foot Ulcers in Type 2 Diabetes Mellitus Patients at Prof. Dr. I.G.N.G. Ngoerah General Hospital Denpasar during 2022-2023**

As illustrated in Table 6, among the study participants, 10 patients had normal Hb levels. Of these, 6 presented with mild to moderate DFUs, while 4 had severe DFUs. The severity of DFUs among patients with mild anemia was relatively balanced, with 7 patients experiencing mild to moderate ulcers and 8 patients having severe ulcers. Patients with moderate anemia showed a higher percentage of severe ulcers, with 21 patients affected by severe DFUs, compared to 16 patients who

had mild to moderate DFUs. Among the 12 patients with severe anemia, 8 experienced severe DFUs and 4 had mild to moderate DFUs. Overall, the data indicate that lower Hb levels were related to a higher probability of severe DFUs. Nevertheless, the chi-square test bivariate analysis produced a p-value of 0.653, indicating that hemoglobin levels and ulcer severity did not statistically significantly correlate ($p > 0.05$).

**Table 6.** Association between Hemoglobin Levels and Severity of Diabetic Foot Ulcers in Research Subjects

| | | Severity of DFU f (%) | | *p* value |
|---|---|---|---|---|
| | | Mild-Moderate Ulcers | Severe Ulcers | |
| Hb Levels | Normal | 6 (8.1) | 4 (5.4) | 0.653 |
| | Mild Anemia | 7 (9.5) | 8 (10.8) | |
| | Moderate Anemia | 16 (21.6) | 21 (28.4) | |
| | Severe Anemia | 4 (5.4) | 8 (10.8) | |

## DISCUSSIONS

Based on the age distribution of research subjects, most participants (94.5%) were within the 41-80 years range. This finding indicates that the incidence of DFU tends to increase with age, which could be attributed to reduced insulin secretion, suboptimal glucose control, prolonged duration of diabetes, the cumulative impact of hyperglycemia, and the high incidence of microvascular and macrovascular complications. Aging also affects insulin secretion and leads to insulin resistance, contributing to angiopathy, particularly in the lower extremities, thereby increasing the risk of DFU.[7,17]

The study findings showed a greater prevalence of DFU in women than in men. These findings aligned with the study by Hadi et al., which reported that 56.7% of DFU patients were female, likely due to unhealthy lifestyle factors. However, this study also found that men were more frequently found to have severe DFU, while women tended to present with mild to moderate ulcers.[22] This discrepancy might be related to the higher prevalence of complications such as peripheral neuropathy and PAD in men, along with lower adherence to self-care and therapy. Male patients also exhibited additional risk factors including smoking, hypercholesterolemia, and obesity, while female patients showed better adherence to self-care and therapy.[23] This finding aligns with data indicating that the occurrence of DFU was 1.5 times greater in men, with a greater likelihood of amputation compared to women.[7]

Based on BMI data, the majority of the subjects were malnourished, either underweight, overweight, or obese. This observation was in line with the findings of Yin et al., who stated that overweight and obesity are risk factors that can exacerbate diabetes complications. Excess adiposity impairs insulin function and increases blood glucose levels, thereby influencing DFU severity.[23] Consequently, individuals with poor nutritional status may experience more severe complications, highlighting the importance of managing weight and insulin sensitivity in preventing or mitigating diabetic foot ulcers.

In this study, most subjects had uncontrolled HbA1c levels, which is a key risk factor for delayed wound healing and higher amputation rates in DFU patients.[7,23] Elevated HbA1c levels were associated with impaired oxygen delivery due to alteration in RBCs, leading to tissue hypoxia. These conditions disrupted blood flow, delayed wound healing, and increased the risk of tissue necrosis and ulcer formation.[9] Thus, poor glycemic control significantly impacts the severity of DFUs.

In this study, 86.5% of the subjects were anemic, with varying severity including 16.2% had severe anemia, 50% had moderate anemia, and 20.3% had mild anemia. These results were consistent with previous studies that reported high anemia prevalence in DFU patients. Kumar et al. found a 94.3% prevalence of anemia in DFU patients, predominantly with moderate anemia (55.7%).[16] Similarly, Li et al. reported a 53% anemia prevalence in DFU patients, significantly higher than 13% in the non-DFU group, while Gezawa et al. noted anemia in 53.6% of DFU cases, with nearly half requiring blood transfusions due to extremely low Hb levels.[11,14] A study conducted by Mas'ud and Najman also highlighted that 21 out of 30 research subjects had low Hb levels, with the majority of those experiencing anemia being women.[17]

In this study, the association between Hb levels and DFU severity was examined using a bivariate analysis and the chi-square test. The analysis found a p-value of 0.653, indicating no statistically significant association between hemoglobin levels and DFU severity among the subjects ($p > 0.05$). This led to the rejection of the alternative hypothesis and the acceptance of the null hypothesis ($H_0$). These findings are consistent with Mas'ud and Najman, who also found no significant relationship between hemoglobin levels and DFU severity.[17] However, this contradicts other studies that identified a significant association between hemoglobin levels and DFU severity.[11,14–16,20]

Anemia is considered a strong risk factor for delayed wound healing, increased infection rates, higher amputation risk, and mortality in DFU patients. The main cause of anemia in this context is anemia of chronic disease. Anemia reduces oxygen delivery to the ulcer site, impairing wound healing and infection control. Adequate blood flow is essential for wound healing because it supplies oxygen and nutrients critical for tissue regeneration. The oxidative metabolism required for ATP production, which fuels tissue repair, depends on oxygen availability. Thus severe anemia exacerbates ischemia, impedes wound healing, and worsens DFU severity.[11,14,20,21,24]

Differences between the current study and previous research might be explained by methodological variation and the inclusion and exclusion criteria. There are different definitions of anemia and grading/severity of DFU. Variations in defining these variables can impact subject classification and study outcomes. This study also has a number of drawbacks, including a relatively small sample size and data collected from a single site. The cross-sectional design also only allowed observation at a single time point, restricting the ability to evaluate causal relationships between variables. Furthermore, no detailed multivariate analysis was conducted to adjust for confounding variables, such as glycemic control, blood pressure, kidney function (GFR and serum creatinine),

inflammatory markers (CRP), blood biochemistry (cholesterol, triglycerides, High Density Lipoprotein (HDL), High Density Lipoprotein (LDL)), and comorbidities like neuropathy and PAD. Additionally, this study did not provide detailed information on anemia types and contributing factors such as nutritional status, systemic inflammation, and medication. This study used hospital-based and secondary data was obtained from medical records, which often incomplete, reducing the number of eligible subjects. Simplifying the dependent variable into anemia and non-anemia groups might have increased the detection of a significant relationship between anemia and DFU severity, particularly in severe anemia cases. The impact of severe anemia on tissue perfusion and ischemia risk would be more evident, given that low Hb levels drastically impaired tissue oxygenation and delayed wound healing.

Regardless of these limitations, the study provides valuable insights into the prevalence of anemia among DFU patients and its association with ulcer severity. Although hemoglobin levels were not found to be a dominant factor, managing anemia remains crucial in clinical practice to enhance overall health outcomes in diabetic patients.

## CONCLUSION AND RECOMMENDATION

According to the findings from this study, 86.5% of patients with diabetic foot ulcers who had T2DM also had anemia in one of the following forms: mild anemia (20.3%), moderate anemia (50%), and severe anemia (16.2%). However, the chi-squared test bivariate analysis revealed no statistically significant correlation ($p = 0.653$) between hemoglobin levels and the severity of diabetic foot ulcers indicating the lack of a significant association.

Further research is warranted with a larger and more representative sample size, as well as a longitudinal study design such as a cohort study, to evaluate patient outcomes over time. Future studies should also consider incorporating more comprehensive multivariate analyses to explore other potential risk factors associated with the severity of diabetic foot ulcers.

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