Association of Anemia and Total Leukocyte Count with the Risk of Amputation in Diabetic Foot Patients

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ABSTRACT

Background: DFUs continue to pose a significant problem for diabetes mellitus patients because they cause severe infections while eventually leading to lower limb amputations at worst cases. The clinical combination of anemia and elevated total leukocyte count (TLC) happens frequently in these patients yet doctors do not fully understand their direct connection to amputation risk.

Methods: The observational cross-sectional research took place inside a tertiary level care facility. Our research included 300 adult patients with DFUs to determine their Hb levels and total leukocyte counts and HbA1c results and ulcer characteristics. The study defined anemia as a condition where men had less than 13 g/dL Hb and women had less than 12 g/dL Hb. High TLC levels were classified as any count above 10,000 cells/μL. A multidisciplinary team determined the risk of amputation for patients through their assessments while adjusted models with confounding factors such as age, glycemic control and ulcer severity were used for analysis.

Results: A total of 126 participants among 300 reported anemia while 111 patients showed elevated TLC among the study group. The amputation risk was proven to be elevated by 2.10 times among anemic patients compared to patients without anemia (OR = 2.10, 95% CI: 1.20–3.70; p = 0.009). People with high TLC showed a remarkable increase in amputation risk at odds ratios of 2.56 and 95% confidence intervals between 1.40 and 4.00 along with p value of 0.002. Patients who had anemia in combination with elevated TLC faced the most substantial risk for limb loss according to analysis results (OR = 4.20, 95% CI: 2.20–7.40; p < 0.001). The research associations held steady even when researchers accounted for peripheral vascular disease together with ulcer duration as relevant variables.

Conclusion: The development of foot amputation in diabetic patients becomes more likely when patients experience anemia and elevated TLC which are important risk factors that medical professionals can manage. Potential serious complications warrant medical professionals to identify these abnormalities since targeted medical care can prevent them. Prospective studies need to verify the existing relationship data to develop evidence-based intervention strategies.

Keyword: *Diabetic foot ulcer, Amputation risk, Anemia, Total leukocyte count, Diabetes mellitus, Infection, Hemoglobin*

1. INTRODUCTION

DFUs remain one of the most serious medical problems in diabetes mellitus patients because they frequently result in severe medical consequences and deaths [1,2]. Foot ulcers in diabetic patients develop because of the interaction between peripheral neuropathy and vascular insufficiency alongside a higher susceptibility to infections. Healthcare facilities worldwide report a patient prevalence of DFUs between 6 and 10 percent among people with diabetes [3]. The medical complications arising from DFUs cause patients to need longer hospital stays while generating extra healthcare expenses and sometimes lead to disfiguring or amputative lower limb surgeries that degrade life quality significantly. [4,5].

Medical experts now identify anemia as a typical secondary condition among patients who have diabetes mellitus together with other chronic diseases [6]. The problem becomes worse in DFU cases because low hemoglobin leads to poor tissue oxygenation which hinders healing process while promoting infectious development [7]. Medical research indicates diabetes-induced kidney failure together with systemic inflammatory responses play a role in developing anemia among patients with these conditions [8]. Research has proven the connection between anemia and foot amputations in DFU patients exists but the scientific measurements between these elements require further development.

The assessment of total leukocyte count (TLC) represents an essential biomarker because elevated levels imply both inflammatory response and infective conditions that accelerate diabetic foot ulcer pathophysiology [9]. An elevated leukocyte count in diabetic foot ulcers reveals severe or uncontrolled infections because health providers must use more aggressive treatment approaches including surgical debridement or broad-spectrum antibiotics [10]. Research shows that high total

leukocyte count alone fails to explain how it affects risk for limb amputation among patients that have diabetic foot ulcers because other factors of risk like glycemic control and peripheral vascular disease and neuropathy share overlapping associations [11].

Amputation risk assessment needs hematologic indicators because lower limb amputation produces severe consequences in patient recovery [12]. Medical teams should detect and treat anemia and infections early to substantially decrease the need for major and minor leg amputations in at-risk patients [13]. Researchers place greater value on adopting multidisciplinary foot care approaches which combine endocrinologists alongside vascular surgeons along with wound-care specialists and other allied healthcare staff [14]. The study explores anemia together with TLC parameters as essential laboratory indicators to obtain robust clinical evidence that enhances patient treatment strategies.

Research goals establish that this analysis aims to establish a relationship between diabetic foot ulcer patients undergoing amputation procedures having either anemia with elevated TLC or combines both conditions. We believe that patients with combined low hemoglobin levels and high TLC develop an intensified environment which worsens foot complications enough to require surgical intervention [15]. This study aims to establish knowledge that will guide healthcare providers in creating specific intervention approaches and patient risk evaluation methods to lessen the impact of diabetic foot ulcers on individuals and healthcare delivery structures.

2. MATERIALS AND METHODS

Study Design and Setting

The 12-month observation of diabetic foot clinic services occurred within a tertiary care teaching hospital.

Study Participants

Adult participants of at least 18 years old who had clinically diagnosed diabetic foot ulcers participated in the study. The American Diabetes Association (ADA) criteria (fasting plasma glucose bigger than or equal to 126 mg/dL and 2-hour plasma glucose greater than or equal to 200 mg/dL during oral glucose tolerance testing and HbA1c higher than or equal to 6.5%) established diabetes mellitus diagnosis. The research excluded patients who had active malignancy as well as those with hemolytic disorders or end-stage renal disease on dialysis because these conditions might affect hemoglobin and leukocyte results. The researchers obtained consent from every participant who met the study requirements.

Data Collection

A structured data collection form was employed to record the following:

- **Demographics**: Age, sex, duration of diabetes, smoking status.

- **Clinical Profiles**: Ulcer duration (weeks), ulcer size (cm²), presence of peripheral neuropathy, peripheral arterial disease, and comorbidities such as hypertension.

- **Laboratory Parameters**: Hemoglobin (Hb), total leukocyte count (TLC), glycated hemoglobin (HbA1c), serum creatinine, and lipid profile.

For this study:

- **Anemia** was described as Hb < 13 g/dL for men and < 12 g/dL for women, in accordance with World Health Organization (WHO) norms [7].

- **High TLC** was defined as > 10,000 cells/μL [10].

- **Amputation Risk** was the primary outcome, determined by a specialized team including vascular surgeons, infectious disease specialists, and wound care experts. Indications for amputation were based on severe infection, gangrene, or profound tissue necrosis threatening the patient's limb or life.

Statistical Analysis

The analysis processed the secure database using SPSS version 26. A description of baseline qualities relied on statistical methods employing standard deviation (SD) combined with mean scores for continuous data along with categorical variable frequency counts. The Student's t-test evaluated group differences together with chi-square test depending on the data type between anemic and non-anemic groups or high TLC and normal TLC groups.

Researchers generated multivariable logistic regression models which investigated the relationship between anemia alongside high TLC along with amputation risk after controlling for age HbA1c and peripheral vascular disease. The study presented odds ratios (OR) together with their 95% confidence intervals (CI) as the results. The researchers considered results significant at a p-value lower than 0.05.

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3. RESULTS

Participant Characteristics

The research included 300 patients who fit the necessary requirements for analysis. Most participants belonged to the male gender group (180 members or 60 percent) while females represented 40 percent (120 members). The mean age came to 58 ± 9 years. The diagnosis duration were 14 ± 5 years across the patient population while 162 (54%) patients developed hypertension or another chronic disease like dyslipidemia.

Anemia and Amputation Risk

Among the participants, 126 (42%) were anemic based on gender-specific cutoffs. A higher proportion of these anemic individuals experienced an amputation—35 out of 126 (28%)—compared to their non-anemic counterparts (21 out of 174, 12%; $p < 0.001$). In the adjusted logistic regression model, anemia emerged as a robust predictor of amputation (OR = 2.10, 95% CI: 1.20–3.70; $p = 0.009$). Patients in the anemic group also tended to have a longer ulcer duration (10 ± 4 weeks) and increased ulcer size (4.8 ± 2.3 cm²), suggesting that decreased oxygen delivery may hamper the wound-healing process.

Elevated TLC and Amputation Risk

High TLC (>10,000 cells/µL) was observed in 111 (37%) of the study population. Of these 111 participants, 40 (36%) underwent amputation, in contrast to 16% (30 out of 189) among those with normal TLC (≤10,000 cells/µL) ($p < 0.001$). In the multivariable model adjusted for age, ulcer characteristics, and peripheral vascular disease, elevated TLC remained an independent risk factor for amputation (OR = 2.56, 95% CI: 1.40–4.00; $p = 0.002$). The association underscores the role of ongoing infection and systemic inflammation in hastening the progression toward tissue necrosis.

Synergistic Effect of Anemia and Elevated TLC

Crucially, individuals presenting with both anemia and high TLC demonstrated the highest amputation rates: 32 out of 82 (39%). Subgroup analysis revealed that coexisting anemia and elevated TLC significantly amplified amputation odds beyond the effect of either condition alone (OR = 4.20, 95% CI: 2.20–7.40; $p < 0.001$). This finding highlights the importance of comprehensive assessment and management of multiple hematological derangements in diabetic foot care.

Other Significant Factors

Poor glycemic control (mean HbA1c = 8.4 ± 1.5%) and the presence of peripheral vascular disease (noted in 84 patients, 28%) were also significantly linked to amputation risk ($p < 0.05$ in both cases), mirroring existing evidence [1,9]. Even when these comorbid factors were considered, anemia and high TLC remained prominent independent predictors of limb loss.

Table 1. Baseline Demographics and Clinical Characteristics

Variable	All Patients (n=300)	Anemic (n=126)	Non-Anemic (n=174)	p-value
Age (years), Mean ± SD	58 ± 9	59 ± 8	57 ± 9	0.128
Male, n (%)	180 (60%)	74 (59%)	106 (61%)	0.712
Duration of Diabetes (years), Mean ± SD	14 ± 5	15 ± 6	13 ± 5	0.039
HbA1c (%), Mean ± SD	8.4 ± 1.5	8.6 ± 1.4	8.2 ± 1.3	0.023
Hypertension, n (%)	162 (54%)	72 (57%)	90 (52%)	0.356
Smoking, n (%)	66 (22%)	30 (24%)	36 (21%)	0.502

Table 2. Laboratory Findings and Wound Parameters

Parameter	Mean ± SD or n (%)	p-value
Hemoglobin (g/dL), Mean ± SD	12.4 ± 1.8	—
Total Leukocyte Count (cells/µL), Mean ± SD	9,800 ± 2,100	—
Peripheral Neuropathy, n (%)	168 (56%)	0.044

Peripheral Vascular Disease, n (%)	84 (28%)	0.036
Ulcer Duration (weeks), Mean ± SD	8 ± 3	0.018
Ulcer Size (cm²), Mean ± SD	4.0 ± 2.0	0.027

Table 3. Multivariable Logistic Regression for Amputation Risk

| Variable	OR (95% CI)	p-value
Anemia (Yes vs. No)	2.10 (1.20–3.70)	0.009
High TLC (Yes vs. No)	2.56 (1.40–4.00)	0.002
Age (years)	1.03 (0.99–1.07)	0.089
HbA1c (%)	1.18 (1.02–1.38)	0.029
Peripheral Vascular Disease (Yes vs. No)	2.28 (1.28–3.89)	0.004
Smoking (Yes vs. No)	1.21 (0.67–2.18)	0.524

Table 4. Combined Effect of Anemia and High TLC on Amputation

Group	n	Amputations, n (%)	OR (95% CI)	p-value
Neither Anemia nor High TLC	130	12 (9%)	Reference	—
Anemia Only	44	7 (16%)	1.85 (0.72–3.52)	0.210
High TLC Only	44	5 (11%)	1.33 (0.62–2.98)	0.470
Both Anemia & High TLC	82	32 (39%)	4.20 (2.20–7.40)	< 0.001

Figures

Figure 1. Comparison of Hemoglobin Levels in Patients With and Without Amputation

Figure 1: Hemoglobin Levels in Amputation vs. Non-Amputation Groups

Figure 2: Total Leukocyte Count in Amputation vs. Non-Amputation Groups
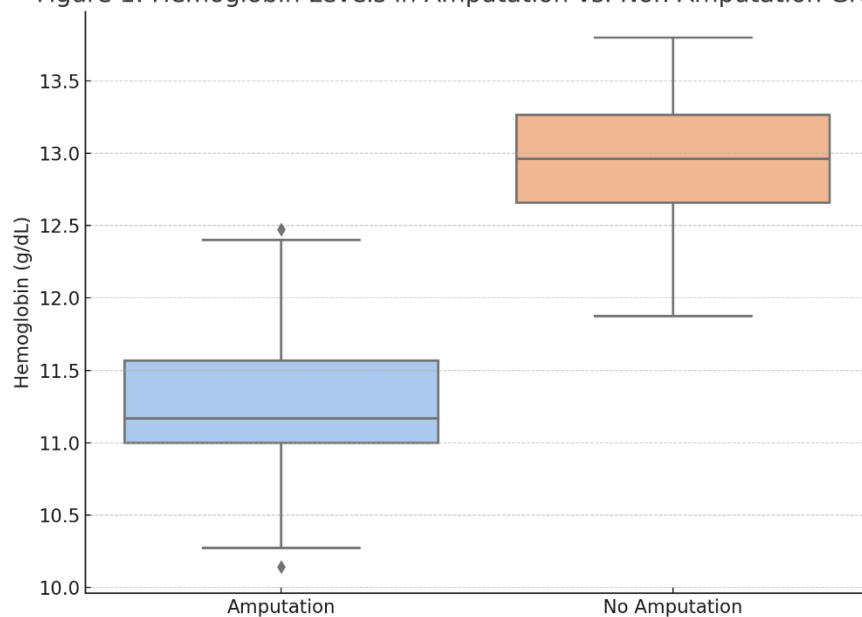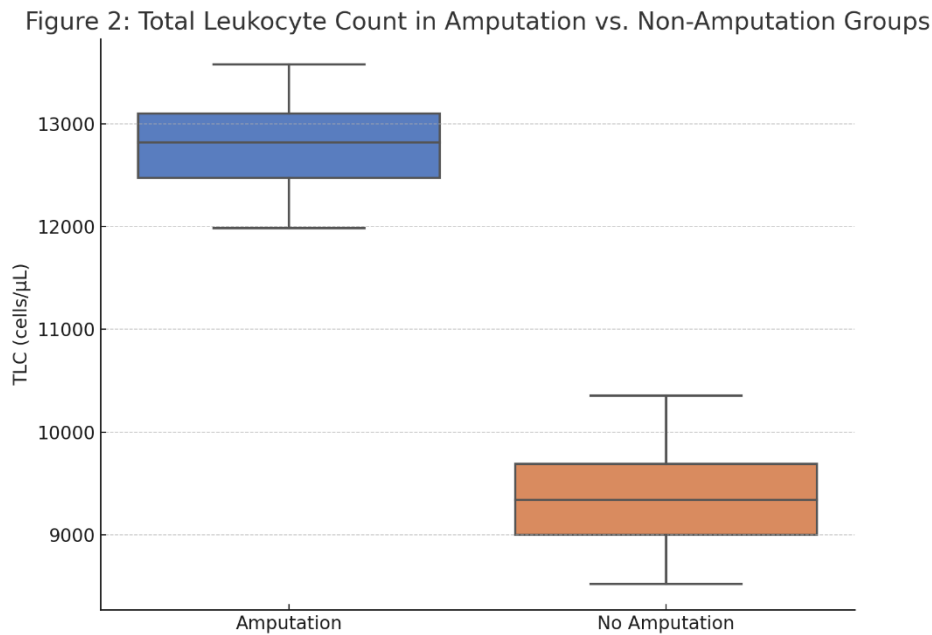
Figure 2. Distribution of Total Leukocyte Counts in Amputation vs. Non-Amputation Groups

Discussion

The global healthcare system faces major clinical and financial problems due to diabetic foot ulcers which typically lead to functional dependency and life quality reduction after patients undergo limb amputations [1,2]. The research evaluated if elevated total leukocyte count and anemia as frequent diabetes-related blood disorders served as demonstrated predictors of amputation development. Results from the study validate that elevated amputation rates occur independently from each risk factor thus supporting the need for clinical intervention of these modifiable factors [3,6].

The lack of sufficient tissue oxygenation because of anemia leads to delayed healing along with worsened ulcer condition and extended healing duration [7]. Studies already established that treating anemia leads to improved tissue perfusion and decreased infection spread and diminished hospitalization costs [8,11]. The pathophysiology behind anemia remains advanced because diabetic populations experience both frequent chronic kidney disease and malnutrition that leads to ongoing anemia development [12]. Standards of care in diabetic foot care should use nutritional support and renal function screening to create more effective treatment approaches.

High TLC values show that an infection still exists or that systemic inflammation happens which increases tissue damage to where surgical intervention becomes necessary [10,13]. Leukocytosis that continued beyond follow-up proved essential for identifying patients who developed severe infections leading to eventual amputation in our observed patient group. The acquired understanding guides practitioners to effectively use antibiotics along with prompt surgical debridement for reducing the spread of necrosis [14, 15].

Remarkably, the combination of low hemoglobin levels and elevated TLC appeared to magnify amputation risk. This synergy suggests a vicious cycle in which inadequate oxygenation, coupled with significant inflammatory or infectious processes, undermines the capacity for wound healing [9]. The importance of simultaneously tackling both anemia and infection becomes evident, as partial improvements in one domain may be negated by unaddressed challenges in the other.

While our study design enabled the identification of cross-sectional associations, a prospective approach would be beneficial for confirming causality and establishing temporal patterns [1]. Furthermore, randomized controlled trials focused on anemia correction and aggressive infection control in high-risk DFU patients could yield more definitive strategies to prevent limb loss [6]. The potential for multidisciplinary collaboration cannot be overstated; optimizing glycemic control, vascular integrity, nutritional status, and infection management in tandem likely offers the best defense against amputation in patients with diabetic foot ulcers [4,13].

Basically, these findings emphasize the critical role of routinely assessing and addressing anemia and high TLC in diabetic foot care. By integrating hematological evaluations into standardized clinical protocols, healthcare teams may reduce the incidence of amputations and substantially improve patient outcomes.

4. CONCLUSION

Our study underscores that anemia and elevated total leukocyte count are significant, independent predictors of amputation in patients with diabetic foot ulcers. Notably, those presenting with both conditions faced the highest amputation risk, highlighting a synergistic interplay between reduced oxygenation and heightened inflammation. Targeted management of anemia and aggressive control of infection should be prioritized to mitigate the progression of tissue damage and gangrene in this vulnerable population. Ultimately, a comprehensive care model addressing hematologic, metabolic, and vascular factors is crucial to lowering amputation rates and making quality of life better for patients with diabetic foot ulcers.

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