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Finding strongly linked between anemia and diabetic foot ulcers: A multi center study

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***Abstract*---**Objective: Diabetic foot ulcers and anemia are two typical complications of diabetes. For this reason, we setout to gather data on the prevalence of anemia in persons with and without diabetic foot ulcers (DFUs) of similar ages and sex. Method: The Department of Medicine HMC hospital Peshawar conducted this multi-center study from October 2020 to October 2021 in their interdisciplinary diabetic foot clinic. Those who took part in the studywere split into two groups: those with DFUs (the Case group) and those without (the Control group) (peoplewithout DFUs). Biochemical and hematological markers, as well as demographic data, were collected from the outset. DFU in the case group was categorized and staged using the UT system. Anemic subjects with other obvious explanations were not included. Controls were recruited from a diabetes clinic that offered presentations during the same time frame. SPSS version 24 was used

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for the statistical analysis of the data. Results: A total of 80 people were studied, split evenly between the case and control groups regarding age and gender. Men made up the majority of the 60 participants (74%). Case and control groups were similar in age and sex, except for diabetes duration, body mass index (BMI), and high-density lipoprotein (HDL) values. Anemia affects about 86% of the case group (males, 65%), 11.10% of the females, and 18.03% of the control group (males, 11.09% of the females, 11.04%). In the case group, the average Hb was [10.49g/dl], whereas, in the control group, it was [13.40g/dl]. Several other blood markers also showed statistically significant changes. Conclusion: Based on our findings, we can say that anemia is highly linked to DFU disease. When caring for patients with foot ulcers, it is important to consider the possibility of anemia and treat it accordingly.

***Keywords*---**type 2 diabetes, diabetic foot ulcer, anemia, causes.

Introduction

The development of diabetic foot is a leading cause of hospitalization and catastrophic complications for people with diabetes. Diabetic foot ulcers affect between 4 and 10 percent of the population. Foot ulceration is associated with an 8-21% probability of lower extremity amputation (LEA)[1]. Second and third, the psychological and financial toll of diabetic foot illness is substantial. 4,5Common risk factors for foot ulceration include peripheral vascular disease, neuropathy severity, structural foot deformity, concurrent infection, high plantar pressure, poor glycemic control, duration of diabetes, being male, and the presence of other micro- and macro vascular A. M. Shareef et al.complications.DFU outcomes are highly correlated with illness severity[2]. Anemia is one of the most prevalent risk factors and a strong predictor of DFU prognosis. The pathophysiology of anemia in patients with diabetes and DFU may have various unfavorable effects. Despite being twice as prevalent in those with diabetes as those without the disease, anemia in diabetes is often misdiagnosed[3]. Anemia has also been demonstrated to increase the risk of morbidity and death in those with DFU compared to those without DFU. This study compared the incidence of anemia in DFU patients to age- and sex-matched controls without DFUs[4].

Foot ulcer sufferers must be diagnosed and treated for anemia. Anemia reduced DFU wound healing, according to Bates et al. Studies by Sharif A. et al., Wright JA. et al. and Costa R.H. et al. found that individuals with DFU were more likely to have anemia, and 89.6% of frail DFU patients had amputations[5]. DFU's link to anemia needs to be better-studied. 8,11,12. 13 No Pakistani studies have shown this. In addition, there are no data on the incidence or absence of anemia among age- and sex-matched type 2 diabetics without foot ulcers. This research compared DFU-infected anemics to age- and sex-matched healthy controls[6].

Methods

The Department of Medicine HMC hospital Peshawar conducted this multi-center study from October 2020 to October 2021. People with diabetes admitted to the OPD or DFU were recruited. Diabetes clinic volunteers who are age and gender-matched. Cases were given OHA, insulin, or both. Ethics-approved Non- diabetic, Type 1 diabetic, and pregnant women were not included. Hematological issues, as well as supplement users, were removed. Individuals with DFUs due to significant trauma or other anemic causes were excluded from this investigation (chronic liver disease, malabsorption, inadequate meat intake, strict vegetarianism). Patients with CRF-DFU were omitted. The doctor's helper completed the survey. Control and Case (people with diabetes without DFU). Simple examples. Gender, age, diabetes duration, family history, BMI, and blood pressure were all reported by the researchers. Before DFU debridement, which may cause blood loss and anemia, CBC samples were collected. HbA1c, lipids, creatinine, and CBC were all measured. Men have anemia of 13g/dL, whereas women have anemia of 12g/dL. The familial, dietary, lifestyle, and pharmacological histories of 14 comorbidities. MCV 80, normocytic (80-100), or macrocytic (>100). Ferritin and iron levels in 15 microcytic anemia patients were measured. Foot ulcers in the case group were examined using the UT diabetic wound classification. Grade 0 wounds are epithelialized or at-risk feet, Grade I wounds are superficial, Grade II wounds have tendons but no bone, and Grade III wounds have a bone. Infection and ischemia in D (stage D). Celtic CBC MEK-6450 Automated. The BIO-RAD D-10 HbA1c test determined glycemic Control. On a selectra Pro Sa, GOD-PAP assessed triglycerides. Selectra Pro S total cholesterol was assessed with Chod-Pap. Enzymatic colorimetry is used to measure HDL cholesterol, while the direct measurement is used for LDL cholesterol. The standing height and weight of subjects were measured to 0.1cm (kg). Squared weight (kg) BMI equals (m2). Asians regard a BMI of 25 to be fat. 19 Taking blood pressure

Results

One hundred four people with DFUs were included in the case group. Twenty-four of these instances couldn't be considered since other, more obvious causes of anemia were present. The remaining 80 patients in the case group were matched with 80 controls with type 2 diabetes but no DFU. There were more men than women in the study (74%, to be exact). There were 4% of participants in the age range of 25-45, 16% in the range of 46-55, and 81% in the age range of 55+. Control groups were similar in terms of age and sex. Systolic and diastolic blood pressure, total cholesterol, triglycerides, low-density lipoprotein, serum creatinine, and hemoglobin A1c all showed no significant changes between the two groups. (Table-I)

Table 01: Basic Demographic and Biochemicalcharacteristics of case and control group

[Variables]	*[Case]*	*[Control]*	*[P-value]*
N	80	80	-
1. Age (in years)			
*2.*30 – 40	03(04%)	03(3.7%)	[0.999]
*3.*0 -50	13(16%)	13(15.5%)	
4.≥ 50	65(81%)	65(80.7%)	
5. Gender			
6. Male	60(74%)	60(73.9%)	[0.999]
7. Female	21(26%)	22(26.1%)	
8. Duration of diabetes (in years)			
9.<5	14(17%)	18(21.1%)	[0.001]
*10.*5 – 10	14(18%)	25(31.1%)	
*11.*10-15	18(21%)	18(23.6%)	
12.≥ 15	37(44%)	19(24.2%)	
13. Family history of DM			
*14.*No	25(37%)	26(33.1%)	[0.512]
15. Yes	43(64%)	53(66.9%)	
16. Body mass index	24.14±5.80	24.53±4.85	[<0.000]1
17. (kg/m^2)			
18. Systolic blood pressure (mmHg)	135.51±19.7	136.88±20.45	0.567
19.			
*20.*Diastolic blood pressure (mmHg)	82.42±10.25	81.41±10.72	0.416
21. High density lipoprotein (mg/dl)	27.03±9.86	38.32±10.61	<0.0001
23.			
24. Low density lipoprotein (mg/dl)	90.94±28.94	103.24±41.94	0.087
25.			
*26.*Cholesterol (mg/dl)	166.01±59.97	172.57±49.27	0.563
*27.*Triglyceride (mg/dl)	143.58±65.76	159.45±67.57	0.252
28. Serum Creatinine (mg/dl)	1.33±0.66	1.19±0.68	0.240
*29.*HbA1c (%)	10.1±2.55	10.0±1.81	0.80
Mean SD or n (%)			
p0.05 was statistically significant.			

Mercury oximeter technique. Hypertension is 130/85mmHg. Stats Data was analyzed using SPSS 24.0. Categorical variables have rates and percentages computed. We calculated means and SDs for numerical variables. Chi-square tests with 95% confidence intervals compared category frequencies. Student t-tests compared the mean and standard deviation of numerical variables. Significant at p0.05.

Table 02: Complete Blood Count (CBC) comparison between experimental and Control groups.

Complete Blood	*Case*	*Control*	*P-value*
N	80	80	-
Hemoglobin (g/dL)	10.44±02.06	13.31±2.06	<0.0001
Hemoglobin deficiency			
Males (<13 g/dL)	52(64.56%)	16(22.9%)	<0.0001
Females (<12 g/dL)	16(21.11%)	10(12.4%)	0.001
Hemoglobin levels			
Males (>13 g/dL)	07(9.32%)	80(50.93%)	<0.0001
Females (>12 g/dL)	04(4.97%)	20(13.66%)	<0.0001

RBC (x 10^6/µL)	03.74±0.64	04.73±0.63	<0.0001
MCV (fl)	84.12±7.41	83.84±7.7	0.130
MCH (pg)	26.28±5.95	27.07±3.29	0.141
MCHC (g/dL)	32.81±1.8	32.65±1.95	<0.0001
TLC (x 10^3/ul)	14.26±4.58	08.5±2.07	<0.0001
Neutrophils count (%)	80.21±9.16	67.33±8.81	<0.0001
Lymphocytes count (%) 18.67±8.84		26.45±8.78	<0.0001
Monocytes count (%) 01.5±0.65		01.95±0.64	<0.0001
Eosinophils count (%) 01.62±0.75		02.27±1.14	<0.0001
Platelets count 0345.3±123.82 244.5±83.08 <0.000(g10^3/ul)			

Statistics are shown as a mean + standard deviation. If the p-value was less than 0.05, it was deemed significant.

Table 03: Comparison of clinical parameters between the case and control groups, expressed asan odds ratio and a 90% confidence interval

[Parameters]		[Case]		Control	
	[OR 90% CI]		[P-value]	[OR (90% CI]	[P-value]
[Duration of DM]	[1.34 0.985-1.826]		[0.062]	01.10(0.782-1.54)	[0.583]
[BMI]	[1.0050.923-1.090]		[0.905]	01.049(0.974-1.129)	[0.208]
[HDL]	[1.025 0.957-1.097]		[0.487]	0.983(0.92-1.051)	[0.623]
[HbA1c]	[0.842 0.656-1.08]		[0.176]	01.006(0.731-1.385)	[0.97]

Anemia affects 86% of the case group (males 65%, females 21%) and 35% of the control group (males 23%, females 12%). The Case group's hemoglobin was 10.46 g/dL, and the Control was 13.36 g/dL. (p0.0001). Except for MCV and MCH, all other CBC values differed across groups. (Table-02) The UT grading system discovered Grade 0 (stage B 0.06%), Grade I (stages A, B, and C), and Grade II (stage B 13%). In Grade 3, pupils were at B (73%), C (3%), and D (7%). Table 03 shows the 90% confidence range for the case-control ratio of clinical parameters. Case and control groups had similar diabetes duration, BMI, HDL, and A1c.

Discussion

DFU was related to an increased risk of anemia (86% vs. 35% among age- and sex-matched individuals without DFU). The most prevalent kind of anemia was normocytic normochromic anemia (73%), followed by microcytic (25%) and megaloblastic (0.64%)[7]. Similar to other studies, 52–85 percent of DFU patients experienced anemia.21,22 A higher proportion of males than females reported DFU, consistent with previous findings[8]. 22 Our study found that glycemic Control (HbA1c)was poor across the board in both the patient and control groups. Anemia, but not diabetes, may affect HbA1c levels. Although there was no difference in HbA1c levels between the two groups, this may not indicate glycemic

management for individuals with anemia[9]. Although the control group had a higher body mass index and lower HDL levels, they were both obese and low in HDL, which indicates insulin resistance. Even though the case group included more people with 15 years of diabetes, the absence of anemia in the control group with an equivalent duration of diabetes highlights that anemiawas related to DFU and not just due to disease duration[10]. Although chronic kidney disease (CKD) is often mentioned in conjunction with diabetic anemia, both groups in our study started with healthy kidneys[11,12]. Anemia in DFU patients is caused by chronic inflammation, bone involvement leading to osteomyelitis, frequent debridement, inadequate nutrition, medicine, or a combination of these factors [13,14]. There is probably an iron deficiency, an Epo-Epo receptor deficit, and an erythroid precursor deficiency in chronic inflammation, all leading to anemia[15].Premature death of erythroid precursor cells may be averted with the help of erythropoietin (Epo), which generates signals within the cell[16]. Reduced circulating hemoglobin results from chronic inflammation in anemia, which increases proinflammatory cytokines such as TNF-, IL-1, and IL-6. 27 Healing is slowed, and morbidity and mortality increase in DFU patients with anemia[17].

The study's limitations

Microcytic anemia was more common, while normocytic anemia was morecommon overall. No more testing was performed on these instances to identify the root of the problem.

Conclusion

Finally, we found that anemia is significantly linked to DFU illness. Patients with foot ulcers whosuffer from anemia must have both conditions considered and addressed. Anemia in diabetic footulcer patients (DFUs)

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