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Prevalence and associated Factors of Anemia in Diabetic Patients

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Abstract

Introduction: Diabetes presents a significant global health challenge due to its association with a range of pathological changes, such as metabolic, cellular, and blood disturbances, that lead to long-term microvascular and macrovascular complications. Healthcare providers often underestimate anemia as a co-morbidity in diabetes, despite the wide range of prevalence estimates reported in the literature.

Aim of the study: To estimate the prevalence of anemia and its associated factors among patients with type 2 diabetes mellitus (T2DM).

Method: This is a cross-sectional prospective study with a retrospective review of diabetic patient medical records attending family medicine clinics at four Royal Medical Services Military Hospitals. Sociodemographic and clinical characteristics, anthropometrics, medical history, and laboratory data, including CBC and HbA1c, were collected. We used univariate and binary logistic regression to explore factors associated with anemia in T2DM patients.

Results: A total of 251 patients, with a mean age of 53.23 (12.45), were included in the study. The prevalence of anemia was 23.1%. Binary logistic regression analysis showed that glucose-lowering drugs (oral plus insulin) (OR, 5.016 [95% CI, 1.902–13.22]), poor glycemic control (OR, 5.587 [95% CI, 2.51–12.43]), and disease duration greater than five years (OR, 3.05 [95% CI, 1.69–10.65]) were reported as significant risk factors for anemia development among patients with T2DM (P<.05).

Conclusion: Anemia was highly prevalent among patients with type 2 diabetes. The current evidence suggests that all healthcare facilities should include hemoglobin testing in their routine evaluations of patients with type 2 diabetes at regular intervals.

Keywords: diabetes mellitus, anemia, risk factors, prevalence, glycemic control

Introduction: Diabetes comprises a heterogeneous group of metabolic disorders that is considered a rapidly expanding global health crisis (1,2). It is marked by abnormalities in the insulin secretion process in pancreatic β-cells and the failure of insulin-sensitive tissues to respond appropriately to insulin, resulting in changes in carbohydrate, lipid, and protein metabolism, along with sustained high blood glucose levels (3). The American Diabetes Association (ADA) categorizes diabetes into many subtypes, such as type I, type II, gestational diabetes, and other forms caused by substances like medications, chemicals, and pancreatic diseases (4). 90–95% of diabetes cases are classified as having type 2 diabetes mellitus (T2DM) (4).

Chronic hyperglycemia, along with other metabolic abnormalities in diabetes patients, may adversely impact different organ systems, resulting in a variety of severe and potentially fatal health complications. These include microvascular (retinopathy, nephropathy, and neuropathy) (5-7) and macrovascular complications (8). Anemia, an additional underrecognized complication, is frequently associated with diabetes; however, prevalence estimates vary considerably (9). This might be explained by shared symptoms of diabetes mellitus and anemia, such as pale skin, shortness of breath, fatigue and weakness, and numbness or coldness in the limbs, which overwhelmed the diagnosis (10). Anemia onset in patients with DM is reportedly twice as prevalent as in the general population without DM (10,11). A recent meta-analysis of twenty-four studies

with a total number of 19,118 diabetic patients reported the pooled prevalence of anemia as 27% (12). However, complications such as renal impairment in included patients may lead to an overestimation of anemia prevalence in T2DM, suggesting that available data may overestimate the actual prevalence (13-15). In Jordan, the prevalence of anemia was reported as 4.9% in males, 19.3% in non-pregnant females, and 27.4% in pregnant females in the general population (16); however, there are no previous statistics about diabetic patients.

A wide range of factors are associated with the onset of anemia in T2DM, including hormonal imbalances, oral hypoglycemic medications such as metformin, oxidative stress resulting from free radicals (especially reactive oxygen species), advanced age, poor glycemic control, inflammation, and reduced renal function (17-21).

Even though the impact of diabetes on anemia onset is well documented in the literature, there is a lack of studies in Jordan that investigate its prevalence and related factors. Thus, the study aims to determine the prevalence of anemia and its related factors in patients with T2DM.

Method

This is a cross-sectional prospective study with a retrospective review of diabetic patient medical records attending family medicine clinics at four military hospitals (King Hussien Medical Center, Prince Rashed Military Hospital, Queen Aliah Military Hospital, and Prince Hashem Military Hospital) at Royal Medical Services. The study included adult patients over the age of 18 who had been diagnosed with type 2 diabetes mellitus for more than a year. However, patients with diseases (such as thalassemia and leukemia) or other systemic disorders (such as infectious diseases) that could result in anemia, those with acute conditions such as acute hemorrhage, those who received blood transfusions in the last three months, pregnant women, or type 1 diabetes were excluded.

Anemia is defined as a hemoglobin level < 13 g/dl in male and 12 g/dl in females (22). Type 2 DM is defined by glycated hemoglobin (HbA1c > 6.5%), fasting blood glucose (FBG > 126 mg/dl), and random blood glucose (RBG > 200 mg/dl) (23).

Patients' medical records were reviewed for patient medications, diabetes duration, and glycemic control. Furthermore, to exclude any patients who have one or more of the aforementioned conditions reported in the exclusion criteria, Meanwhile, researchers collected the following data in the clinic after patients' agreement to participate in the study: age, sex, marital status, smoking status, comorbidities, and anthropometric measurements, including weight, height, and body mass index (BMI). Moreover, patients were asked to withdraw a complete blood count (CBC) blood sample, which includes hemoglobin, for diagnosing anemia if it was present.

Patients were divided into two groups based on the presence of anemia: the anemic group and the non-anemic group. Regarding study variables, glycemic control was classified into two categories based on HbA1c results: the controlled diabetic group comprised those whose HbA1c level ≤7.5%, and the poorly controlled diabetic group comprised those whose HbA1c level was >7.5%. Body mass index (BMI) was classified according to the Centers for Disease Control (CDC) as follows: BMI score < 18.5 kg/m^2 is underweight, 18.5–24.9 kg/m^2 is normal, 25–29.9 kg/m^2 is overweight, and BMI ≥ 30 kg/m^2 is obese (24).

The sample size was calculated based on Cohran's sample size formula as: $n=Z^2\ pq\ /e^2$. Here, p will be the anticipation of anemia prevalence in the diabetic population, q=1 - p; e is an acceptable error (5%); and Z = 1.96. We used a simple random sampling (systematic procedure) to select patients with type 2 diabetes to minimize the risk of selection bias. With this technique, we randomly choose the first subject and then select the next subjects in a periodic manner according to K (interval). K was determined based on the sampling frame prepared by researchers, divided by n. The required sample size was determined to be equal to 250 patients.

The Royal Medial Services' Ethics Review Board granted ethical approval. Every participant in the study provided written informed consent, which encompassed the study's title, objectives, potential risks, and benefits. The study maintained anonymity by substituting a code for each participant's name. The study granted the participants the voluntary right to discontinue their involvement at any time.

Descriptive analysis is used with the mean (standard deviation) for continuous variables and frequency and percentage for categorical variables. The t-test was used to compare the baseline characteristics of quantitative variables between anemic and non-anemic groups. Categorical variables were compared between the groups using the chi-square test or Fisher exact test as appropriate. Logistic regression analyses were employed to find out how these variables are associated with anemia. The results are given as odds ratios (ORs) with a 95% confidence interval (CI). We selected only covariates with a p-value ≤0.20 in the univariate analysis to enter the logistic analysis.

Results

A total of 251 T2DM patients with a mean age (SD) of 53.23 (12.45) were included in this study. Among those patients, the prevalence of anemia was 23.1%. Most of them were married (64.5%) and held a primary degree of education (41.8%). Education was significantly differed between anemic and non-anemic groups (P = .001). 34.7% of patients had comorbidities. The mean diabetes duration was significantly higher in the anemic group (M = 3.48, SD = 3.10) compared to the non-anemic group (M = 2.34, SD = 1.78) (P =.001). The mean of HbA1c was significantly higher in the anemic group (M = 8.41, SD = 1.36) compared to the non-anemic group (M = 7.03, SD = 0.47). (P <.001). Table 1 shows the socio-demographic and clinical characteristics of the study population.

The prevalence of anemia among T2DM patients was significantly higher in underweight (33.3%) and overweight (33.3%) patients than other subgroups (P = .032). In terms of diabetes duration, most patients (83.3%) had diabetes duration greater than five years, which significantly differed from those with diabetes duration less than or equal to five years (P<.001). Of those patients with poorly controlled diabetes, 46.1% were anemic, while among those who had controlled diabetes, only 13.1% were anemic (P < .001). Table 2. Show the prevalence of anemia among patient with T2DM regarding different subgroups.

Binary logistic regression analysis showed that glucose-lowering drug (oral plus insulin) (OR, 5.016 [95% CI, 1.902–13.22]), poor glycemic control (OR, 5.587 [95% CI, 2.51–12.43]), and disease duration greater than five years (OR, 3.05 [95% CI, 1.69–10.65]) were reported as significant risk factors for anemia development among patients with T2DM (P<.05). Meanwhile, college and above education level (OR, .144 [95% CI,.029–.718]) were reported as protective factors among those patients. Table 3. Show factors associated with anemia in T2DM patients.

Table 1. Socio-demographics and clinical characteristics of patients with T2DM (n=251)

Variables		**Total**	**Non-anemic (n=193)**	**Anemic (n=58)**	**P-value**
Age (M±SD)		53.23 ± 12.45	53.08 ± 12.17	53.62 ± 13.45	.786
Sex, n (%)	Male	103 (41)	84 (43.5)	19 (32.8)	.171
	Female	148 (59)	109 (56.5)	39 (67.2)	
Marital, n (%)	Single	58 (23.1)	44 (22.8)	14 (24.1)	.959
	married	162 (64.5)	125 (64.8)	37 (63.8)	
	divorced	11 (4.4)	8 (4.1)	3 (5.2)	
	widow	20 (8)	16 (8.3)	4 (6.9)	

Education, n (%)	No formal education	21 (8.4)	8 (4.1)	13 (22.4)	.001
	Primary	105 (41.8)	82 (42.5)	23 (39.7)	
	Secondary	87 (34.7)	69 (35.8)	18 (31)	
	College and above	38 (15.1)	34 (17.6)	4 (6.9)	
Employment, n (%)	Employed	82 (32.7)	61 (31.6)	21 (36.2)	.526
	Unemployed	169 (67.3)	132 (68.4)	37 (63.8)	
Smoking, n (%)	non-smoker	157 (62.5)	117 (60.5)	40 (69)	.281
	smoker	94 (37.5)	76 (39.4)	18 (31)	
Comorbidities, n (%)	No	164 (65.3)	129 (66.8)	35 (60.3)	.432
	Yes	87 (34.7)	64 (33.2)	23 (39.7)	
BMI kg/m^2, (M±SD)		23.08 ± 3.11	22.94±2.93	23.54±3.65	.200
Diabetes duration (M±SD)		2.60 ± 2.24	2.34± 1.78	3.48± 3.10	.001
HbA1c (M±SD)		7.34 ± .93	7.03 ± 0.47	8.41 ± 1.36	<.001
Hb (M±SD)		13.18 ± 2.06	14.05 ± 1.29	10.3 ± 1.46	<.001

BMI: body mass index; Hb: Hemoglobin; Hb A1c: Hemoglobin A1c; T2DM: Type 2 diabetes mellitus

Table 2. prevalence of anemia among patients with T2DM in different subgroups

Subgroups	**Case/total**	**Prevalence**	**P-value**
Age, years			
< 50	21/91	23.1	.993
> 50	37/160	23.2	
BMI, kg/m^2			
Underweight	8/24	33.3	.032
Normal weight	26/154	16.9	
Overweight	22/66	33.3	
Obese	2/7	28.6	
GLD			
Oral	24/130	18.5	.063
insulin	18/76	23.7	
Oral plus insulin	16/45	35.6	
Diabetic duration			
<5 years	38/227	16.7	<.001
>5 years	20/24	83.3	
Glycemic control, n (%)			
Controlled	23/175	13.1	<.001
Poorly controlled	35/76	46.1	

BMI: body mass index; GLD: glucose lowering drug

Table 3. factors associated with anemia among T2DM patients.

Factors	**Odd ratio**	**Confidence interval**	**P-value**

Sex			
Male	1	-	
Female	2.05	.922 - 4.58	.078
BMI			
Underweight	1	-	
Normal weight	.316	.098 - 1.02	.055
Overweight	.451	.126 - 1.617	.222
Obese	.310	.026 – 3.537	.339
Education			
No formal education	1	-	
Primary	.261	.075 - .908	.065
Secondary	.351	.098 – 1.25	.107
College and above	.144	.029 - .718	.018
GLD			
Oral	1	-	
insulin	1.295	.534 - 3.14	.567
Oral plus insulin	5.016	1.902- 13.22	.001
Glycemic control			
Controlled	1	-	
Poorly controlled	5.587	2.51 – 12.43	< .001
Diabetes duration			
< 5 years	1	-	
>5 years	3.05	1.69 – 10.65	< .001

T2DM: Type 2 diabetes mellitus; GLD: glucose lowering drug

Discussion

This multiple-center cross-sectional study evaluated the prevalence of anemia and related factors in adult T2DM patients who attended Royal Medical Services family medicine clinics. Anemia has been identified in 23.1% of adult patients with T2DM, indicating that approximately one in every four adults with T2DM has the condition. This finding is in accordance with the recent meta-analysis that reported the prevalence of anemia at 27% (12). However, the prevalence of anemia in our study is lower when compared with the findings of the study conducted in Sub-Saharan Africa (41.1%), Iran (33.4%), Malaysia (31.7%), Saudi Arabia (47.8%), and Pakistan (59%) (13, 25-28). These results may highlight the variability of healthcare quality in developing countries. However, several potential explanations for the discrepancy should be considered, which may impact the generalizability of the aforementioned studies, including selection bias, methodological discrepancies, and variations in participant characteristics like lifestyle, eating habits, type of GLD consumption, duration of T2DM, ethnicity, and age groups.

Females have a much higher probability of developing anemia (67.2%) than males (32.8%), according to our findings. Monthly physiological blood loss in the form of menstruation, multiple gravidaras (29) and the high prevalence of iron-deficiency anemia among Jordanian females (68%) (16) all contribute to this higher prevalence of anemia in this populations.

The presence of anemia is associated with the duration of diabetes in our study, which is consistent with the findings of previous studies (13,17, 30). Adult patients with T2DM for more than five years have a nearly three-fold higher risk of developing anemia when compared with T2DM patients who had diabetes for less than five years. Chronic hyperglycemia may cause a reduction in red blood cell production (erythropoiesis) and an increase in red blood cell destruction (RBCs). This is because chronic hyperglycemia exposes the body to greater inflammation and oxidative stress and impairs the functioning of the bone marrow (31,32).

In terms of glucose-lowering drugs (GLD), using insulin in combination with oral GLDs is associated with a five-fold increased risk of anemia compared to those patients on oral GLD alone. This finding is in line with a recent study conducted in Iran (30). However, the exact mechanism by which hemoglobin levels decrease

so rapidly is unknown; nevertheless, malabsorption of vitamin B12 and erythrocyte destruction resulting from the detrimental and synergistic effects of the medication may provide a plausible explanation. To mitigate this condition, there are different GLDs, like sodium-glucose cotransporter 2 (SGLT2) inhibitors or glucagon-like peptide-1 receptor agonists (GLP-1 RAs), that have been shown to help patients reach their glycemic goals, keep their kidneys functioning, and lower their risk of anemia (33).

Out of 251 patients included in the study, 76 patients (30.2%) demonstrated poor glycemic control (HbA1c > 7.5). Contrary, previous study conducted in Jordan reported a higher proportion of poor glycemic control among diabetic patients (65.1%) than our study and longer disease duration (> 7 years) was the main associated factors that increased the risk of poor glycemic control (34). Adult patients with poor glycemic control (HbA1c > 7.5) have a more than five-fold higher risk of developing anemia when compared with T2DM patients who had good glycemic control (HbA1c < 7.5). Furthermore, almost half of patients with poorly controlled diabetes (46.1%) have anemia in the current study. Similar results also reported in previous studies (10,30,35). Direct glucose toxicity to bone marrow erythrocyte precursors or oxidative stress to mature erythrocytes, damage to the renal interstitium, severe symptomatic autonomic neuropathy causing efferent sympathetic denervation of the kidney, and loss of appropriate erythropoietin are potential mechanisms that contribute to this anemia; however, their exact cause remains unknown (36). Finally, there is no evidence that age, sex, BMI, smoking, or comorbidities increase the risk of anemia onset among patients with type 2 diabetes mellitus (T2DM) in the current investigation. On the other hand, a higher level of education was considered a protective factor.

Limitations

Since our cross-sectional analysis was unable to reveal the casualty, a longitudinal investigation is necessary to evaluate the relationship over time. Second, our analysis did not account for dietary trends, especially iron consumption. Another limitation was that we could not determine the cause of anemia because we did not assess the subjects' levels of erythropoietin, B12, and folate. Continuing, we did not rule out patients whose jobs put them at risk of anemia due to exposure to blood toxins.

Conclusion

The findings of our study showed a high prevalence of anemia among patients with type 2 diabetes. Glucose-lowering drugs (oral plus insulin), poor glycemic control (HbA1c > 7.5), and disease duration greater than five years were reported as significant risk factors for anemia development among patients with type 2 diabetes. The current evidence suggests that all healthcare facilities should include hemoglobin testing in their routine evaluations of patients with type 2 diabetes at regular intervals, particularly for those patients who have the aforementioned risk factors.

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