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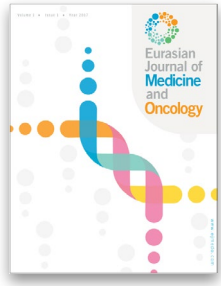

Research Article

The Higher Prevalence of Anemia among Diabetic Patients with Desirable Lipid Profile: A Retrospective Analysis

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Abstract

Objectives: Given the importance of anemia-induced adverse effects on progression of diabetes mellitus (DM), the main aim of this study is to evaluate anemia prevalence amongst diabetic patients hospitalized in a tertiary hospital. The impacts of some critical determinants, including age, gender, duration of diabetes, glycemic status (HbA1c), and lipid profile on anemia comorbidity or progression of DM, were also assessed.

Methods: In this cross-sectional study, all diabetic patients with anemia consecutively referred to the hospital in the first six months of 2018 were included. Data collection was performed according to the electronic medical records using a prepared checklist. Data analysis was also performed by SPSS. ver. 26.

Results: A total of 212 participants, 142 females (67%) and 70 males (33%), were included, with a mean age of 53.5±14.4. Based on the Hb and hematocrit measurements, anemia was observed in 71 (33.4%) and 76 (35.8%) patients, respectively. In addition, it was found that the prevalence of anemia directly correlates with aging in diabetic patients. Besides, the prevalence of anemia was higher in the patients with a diabetes duration ranging 5 to 10 years, while its prevalence was remarkably less common in those with diabetes duration of ≥20 years. Notably, anemia was reported more frequently in diabetic patients with desirable lipid profiles.

Conclusion: Based on our findings, lipid profile measurement should not be considered a reliable indicator to determine anemia prevalence. In this regard, early diagnosis of anemia by applying a simple hematologic test is highly recommended, which can be more helpful in preventing subsequent renal and cardiovascular adverse events.

Keywords: Anemia, diabetes mellitus, duration of diabetes, glycemic status, lipid profile

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Diabetes mellitus (DM) is considered a chronic metabolic disorder and one of the leading causes of morbidity and mortality with an epidemic growth pattern.[1] According to recent epidemiological reports in 2021, it is estimated that 537 million adults have DM globally and it is predicted to rise to 643 million by 2030 and 783 million by 2045.[2] As another global public health issue, anemia has become an increasingly recognized clinical entity among patients with DM.[3] In other words, the development of macro and -microvascular complications can be exacerbated by anemia, particularly in those with poorly-controlled DM.

Based on the National Kidney Foundation criteria, anemia is defined as the inadequate number of red blood cells (RBC) considered hemoglobin (Hb) limit values less than 130 g/L for men and 120 g/L for women,[4] which is ob-

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served in 24.8% of the individuals.[1] Having a negative impact on the quality of life and a further burden on the health of diabetic patients, anemia is unfortunately unrecognized in approximately 25% of the diabetic population due to similar symptoms between DM and anemia, such as chest pain, pale skin, headache, dyspnea, and numbness in the extremities.[5] Following some anemic conditions, in which the RBC turnover is modified, a false dynamic change of the glycosylated hemoglobin (HbA1C) is even expectable.[6] In general, the main mechanisms in anemia encompass iron deficiency (nutritional deficiencies), uncoupling of the Hb concentration from renal erythropoietin (EPO) synthesis and subsequent reduction in oxygen-carrying capacity, systemic inflammation with increased levels of oxidative stress and anti-erythropoietic action, functional hematinic and immune deficiencies status, erythropoietin resistance (dyserythropoiesis), and some medications, such as angiotensin-converting enzyme (ACE) inhibitors.[1] Besides, the comorbidity of chronic kidney diseases (CKD) and DM exerts a key promoter for the development of anemia,[7] in which subsequently reduced levels of Hb make them more susceptible to latter adverse events, such as the increased risk of microvascular complications, cardiovascular disease (CVD), and other life-threatening conditions.

In this regard, anemia, as a multifactorial phenomenon, can be developed following several reasons in diabetic patients, including diabetic nephropathy, CKD, decreased EPO production, diabetic neuropathy, and chronic inflammatory bowel disease (IBD)- induced by DM, hemolysis and anti-diabetic drugs.[8] Long-term exposure to hyperglycemia can also induce vasoconstriction, tubular ischemia, and apoptosis in renal tubular epithelial cells in the tubulointerstitium.[9] Reduced oxygen sensing emerges upon hypoxia-inducible factor 1-alpha (HIF-1α) dysregulation through interstitial fibrosis or vascular lesions, which is considered a significant risk factor for anemia development accompanied by hyperglycemia via targeting the EPO gene in diabetic patients.[9]

It is well-known that anemia can lead to worse outcomes in diabetic patients, even without renal impairment.[10] Hence, regular and early screening may efficiently postpone the progression of vascular complications in patients.[4] In the current study, the main objective is to evaluate the prevalence of anemia in hospitalized patients with DM. Moreover, a possible association between the incidence and risk of anemia in diabetic patients and demographic characteristics including glycemic control status, duration of DM, and lipid profile were assessed for the first time in Iran.

Methods

Study Population

In this cross-sectional study, all diabetic patients with anemia consecutively referred to the tertiary hospital in the first six months of 2018 were included according to the inclusion criteria. Data collection was performed using a prepared and standard checklist based on electronic medical records. The prevalence of anemia among patients was determined according to the World Health Organization (WHO) criteria. Moreover, the type of anemia in patients was determined based on serum ferritin and mean corpuscular volume (MCV) levels.

Inclusion/Exclusion Criteria

The patients with a medical history of DM and anemia were included. Diabetic patients with hematological diseases, such as iron deficiency, hemolytic anemia, aplastic anemia, thalassemia, and glucose-6-phosphate dehydrogenase (G6PD) deficiency, were excluded. In addition, a recent history of acute or chronic blood loss, blood transfusion, a history of cancer or active cancer, pregnancy, uremia, medications affecting Hb level, nephropathy, advanced renal impairment, serum creatinine <2 mg/dL, hepatic cirrhosis, thyroid disorders, infectious diseases, chronic inflammatory diseases, rheumatoid arthritis, and pancreatitis were excluded. As inclusion criteria, diagnosis of anemia in patients with DM was performed as per the WHO definition as follows; Hb concentration < 130 g/L in men and <120 g/L in women. Other biochemical parameters assessed in this study consisted of serum ferritin, serum hematocrit, MCV, fasting serum glucose (FBS), serum glycosylated Hb (A1C), and lipid profile, including high High-density lipoprotein (HDL), low-density lipoprotein (LDL), serum triglyceride (TG), and total cholesterol.

Data Processing and Statistical Analysis

Quantitative and qualitative variables were reported as mean±standard deviation (SD) and percentage, respectively. Data analysis was performed using SPSS software. ver. 26.0. The P value less than 0.05 was considered statistically significant.

Results

Baseline Characteristics

In this study, among 412 diabetic patients with anemia, 212 cases met the inclusion criteria. Of the 212 patients, 142(67%) were females and 70(33%) were males, indicating a higher prevalence of DM-anemia comorbidity among females. In this study, the average age of patients was

53.35±14.4 (min=12, max= 87 years old). Forty patients were under 45 years old (18.86%), 78 patients were between 45 and 59 years old (36.79%), and 94 patients were ≥ 60 years (44.35%). Duration of DM was < 1 year in 55 patients (25.9%), 1-10 years in 107 patients (57.6%), 11-20 years in 29 patients (13.7%), and >20 years in six patients (2.8%). The mean duration of DM was 6.63±0.74 years.

The Evaluation of Hematological Profile in Diabetic Patients with Anemia

Of the 212 patients, 71 patients (33.4%, 22 males, 49 females) were detected to have anemia based on Hb values. The hematocrit (HCT) values ranged from 27.5 to 70.6, with a mean level of 38.24±4.29. The prevalence of anemia based on HCT values was also assessed and the results showed that 76 diabetic patients (35.8%, 26 males, and 50 females) had anemia based on HCT level. In Table 1, the percentages of anemic patients by Hb and HTC levels were shown in detail. Also, in Table 1, anemia classification by MCV was performed in 211 patients. The MCV level ranged from 69.08 to 114.80, and the mean MCV was 85.25 ± 5.83. Given that most patients had normocytic anemia, the MCV level would not be an applicable indicator for anemia diagnosis in those with DM. Moreover, 141 (66.5%) and 54 (25.5%) patients with anemia have high (7-10) and severe (10 <) HbA1c levels, respectively.

Table 1. Baseline Characteristics in Diabetic Patients with Anemia

Demographic Data	**Mean±SD**	**Min-Max**
Age	53.35±14.4	12-87
FBS (mmol/l)	349.9±133.76	55-794
HbA1C (mmol/mol)	9.43±1.63	6.4-18.2
	N-number	**Percentage (%)**
Gender		
Male	70	33
Female	142	67
	N-number	**Percentage (%)**
MCV		
Microcytic	17	8.05
Normocytic	191	90.52
Macrocytic	3	1.43
Total	211	100
Anemia prevalence based on Hb		
Male	22	31.4
Female	49	34.5
Anemia prevalence based on HTC		
Male	26	37.1
Female	50	35.2

The Assessment of Lipid Profile in Diabetic Patients with Anemia

As shown in Table 2, the HDL levels ranged from 15 to 388, with a mean level of 43.58±31.29. Of note, the prevalence of anemia in diabetic patients was detected to be remarkably lower in groups with desirable HDL level (55 patients, 25.9%) than those in the patients with borderline (75 patients, 35.4%) and high-risk HDL level (73 patients, 34.4%). However, the prevalence of desirable LDL (87.7%), TG (46.2%), and total cholesterol levels (69.8%) were found to be more frequent than the prevalence of high and borderline counterparts in patients with DM and anemia.

Correlation between Anemia Prevalence and Multiple Variables

In this study, we found a positive relation between anemia and aging, in which the prevalence of anemia increases with advanced age. For example, in diabetic patients aged <45 years, 45-59 years, and >60 years, anemia prevalence was recorded 5.64 %, 42.25%, and 52.11%, respectively (Fig. 1a). Considering the prevalence of anemia by duration of DM, the prevalence of anemia was observed more frequent in patients who had DM for 5 to 10 years than those in other groups. (29.23% vs. 24.62% vs. 21.54%, respectively) (Fig. 1b). Notably, the highest prevalence of anemia was detected in patients with HbA1c levels between 7 and 10% (67.65%, Fig. 1c). It is worth noting that the prevalence of anemia in patients with DM was more frequent in group with high-risk HDL level (39.39%, Fig. 2a) and in those groups with desirable LDL (92.42%, Fig. 2b), TG (39.39%, Fig. 2c), and total cholesterol level (79.10%, Fig. 2d).

Discussion

Anemia is considered as one of the most common findings among diabetic patients, which can grow by 5% per year during the course of DM.[11] In the current study, we aimed to explore the prevalence of anemia during the hospitalization of diabetic patients. Regardless of kidney function, we evaluated a possible correlation between anemia and potential determinants, such as age, gender, duration of diabetes, the levels of HbA1c, and lipid profile. According to our findings, the prevalence of anemia was higher among females and was observed in 71 (33.4%) and 76 patients (35.8%) according to Hb and HTC measurements, respectively. We also reported that anemia is an age-dependent complication, predominantly observed in patients ≥60 years, with a DM duration of 5 to 10 years. Besides, it is worth noting that anemia was common among subjects with HbA1c between 7 and 10 (67.65%). In better words, the possibility of anemia development is reported to be less in patients with well-controlled DM. Notably, the prev-

Table 2. Lipid Profile in Diabetic Patients with Anemia

Lipid profile	N Number	Percentage (%)	Mean±SD	Min-Max
HDL				
High-risk (<35 mg/dl)	73	34.4	43.58±31.29	15-388
Borderline (35-45 mg/dl)	75	35.4		
Desirable (> 60mg/dl)	55	29.5		
LDL				
High (160-189 mg/dl)	2	0.9	92.21±36.99	43-382
Borderline (131-159 mg/dl)	14	6.6		
Desirable (60-130 mg/dl)	186	87.7		
TG				
Very High (500 mg/dl<)	8	3.8	195.98±130.73	46-766
High (200-499 mg/dl)	66	31.1		
Borderline (150-199 mg/dl)	34	16.6		
Desirable (<150 mg/dl)	98	46.2		
Total Cholesterol				
High (240 mg/dl<)	22	10.4	176.39±53.99	86-561
Borderline (200-239 mg/dl)	34	16		
Desirable (<200 mg/dl)	148	69.8		

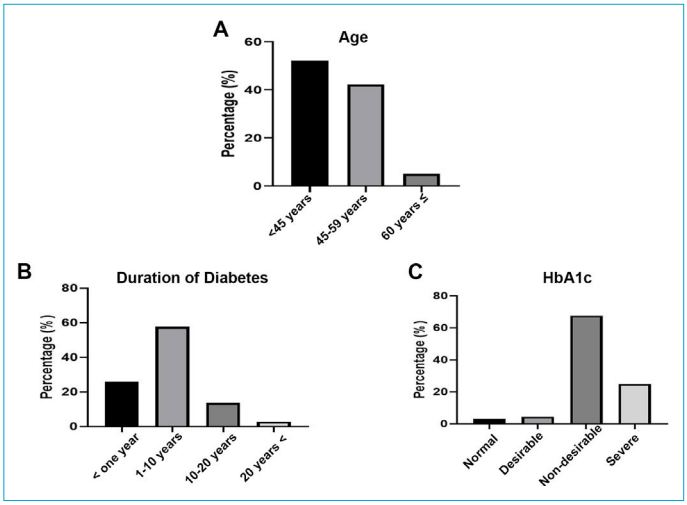

Figure 1. The assessment of anemia prevalence in diabetic patients considering major risk factors.

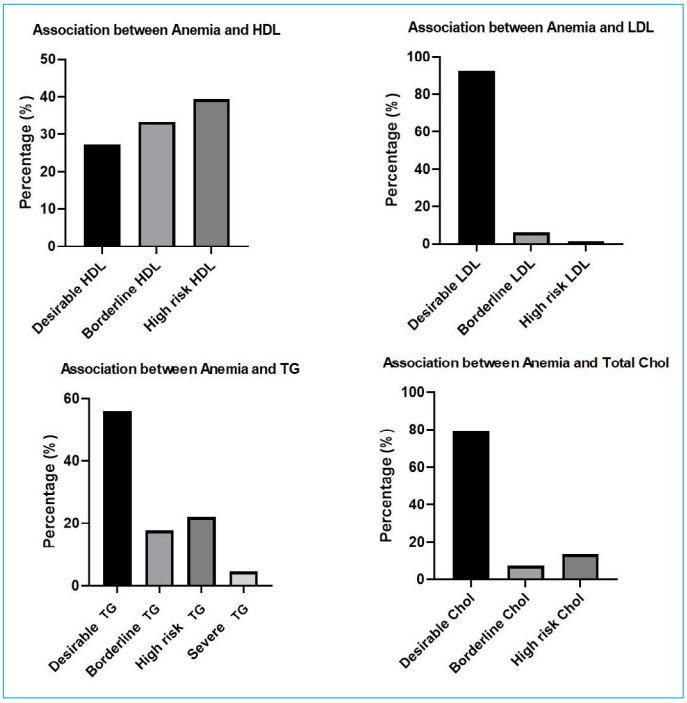

Figure 2. The assessment of lipid profile in diabetic patients with anemia.

alence of anemia was observed more frequent among diabetic patients with desirable LDL, TG, and cholesterol levels, indicating widespread consumption of lipid-lowering medication by diabetic patients.

Regarding the gender differences, a study conducted by Kumar Panda et al. paradoxically reported that anemia was frequently observed in male patients. In line with our study, they also revealed that poor glycemic control has a potential to trigger anemia in these patients.[3]

In a similar study, Sajid et al. reported that female patients with DM are more prone to anemia. In addition, they could not find a significant difference in MCV levels, as a reliable blood index the diabetic patients with anemia when compared to non-diabetic patients.[13] Regarding the recent meta-analysis performed in Ethiopia, age > 60 years [odds ratio (OR), 95% confidence interval (CI): 3.73 (2.23–6.77)], GFR < 60 mL/min/1.73 m^2 [OR, 95% CI: 12.65 (8.71–18.37)], and being diabetic for >10 years (OR, 95% CI: 10.21 (7.00–15.04)] were considered the major risk factors in anemia

progression among diabetic patients,[14] which was in parallel with a clinical study conducted in Malaysia.[15] In multivariate logistic regression models, male gender, physical inactivity, a history of nephropathy, poor glycemic control, and a duration of diabetes of ≥5 are were directly associated with anemia prevalence in patients with T2DM.[16]

The results of 2 separate studies conducted by Sharif et al. and AlDallal et al. also demonstrated that female gender, poor glycemic control (HbA1c >7.5%), and aging should be considered as substantial risk factors for the development of anemia in T2DM subjects.[4, 16] Of note, it has been proposed that anemia can also accelerate the progression of diabetes-induced complications compared to non-anemic patients. For instance, Wang et al. indicated that anemia and CKD are jointly associated with increased risk of retinopathy, particularly in patients with T2DM.[17] In line with our findings, a clinical study in Nigeria reported that majority of patients (68.6%) had normocytic anemia,[18] while another study performed in Egypt showed that a higher prevalence of microcytic hypochromic anemia was observed among diabetic patients compared to normocytic normochromic anemia (55.4% vs. 44.6).[5] Based on Korean National Health and Nutrition Examination Survey VI (KNHANES VI), unadjusted OR was greater in adults with DM compared to the healthy population (OR=3.28; 95% CI: 2.27~4.73).[19] Noteworthy, a remarkable correlation between anemia and DM in females, advanced age, family outcome, and education level was not found. As a result, it was shown that there was no significant difference in anemia prevalence between diabetic and non-diabetic Korean adults upon adjusting for multiple risk factors.[19]

Besides, a recent cross-sectional study from the Korea National Health and Nutrition Examination Survey (2010–2016) indicated a strong association between DM and anemia in a sex-dependent manner, which was more prominent among men. However, the prevalence of anemia in our study was considerably higher among women [142 (67%) vs. 70 (33%)].[20]

A portion of anemic patients with incomplete medical records and a lack of additional laboratory tests were the major limitations of this study. Designing multi-center and large-scale studies by considering the renal function and anemia etiology are also recommended to further evaluate and verify the study outcomes.

In conclusion, our findings indicated that the prevalence of anemia was higher in females and in those who had DM for 5 to 10 years. In addition, anemia prevalence had a positive correlation with aging and glycemic status (HbA1c) in diabetic patients. Besides, the prevalence of anemia was higher among subjects with desirable LDL, TG, and total cholesterol levels but not desirable HDL level. In this regard, lipid profile measurement should not be considered a reliable indicator to determine anemia. However, early diagnosis by applying simple hematologic tests, as diagnostic criteria, is highly recommended, which can be more helpful in preventing subsequent kidney dysfunction and cardiovascular outcomes.

Disclosures

Ethics Committee Approval: The ethical approval for this research was issued from the xxxxxxxxxxx University of Medical Sciences with the ethics committee number: IR.UMSU.REC.1399.251. It should also be noted that the information of all patients was confidential and identified by an assigned code number. Also, no additional cost was incurred by the patients.

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Conflict of Interest: None declared.

References

1. Kansal A, Chouhan M, Singh N, Trikha S, Verghese J. Study of anemia in diabetes and its association with diabetic retinopathy. IJAM 2017;4:1437–40.
2. IDF Diabetes Atlas. Diabetes around the world. Available at: https://diabetesatlas.org. Accessed Jan 16, 2023.
3. Panda AK, Ambade RA. Prevalence of anemia and its correlation with HBA1c of patients in type-II diabetes mellitus: a pilot study. Natl J Physiol Pharm Pharmacol 2018;8:1409–13.
4. AlDallal SM, Jena N. Prevalence of anemia in type 2 diabetic patients. J Hematol 2018;7:57–61.
5. Shaheen ES. Prevalence of anemia in patients with type 2 diabetes. J Med Sci Res 2019;2:114–7.
6. Sahay M, Kalra S, Badani R, Bantwal G, Bhoraskar A, Das AK, et al. Diabetes and Anemia: International Diabetes Federation (IDF) - Southeast Asian Region (SEAR) position statement. Diabetes Metab Syndr 2017;11:685–95.
7. El Minshawy O, El-Bassuoni E. Anemia and kidney dysfunction in type 2 diabetic patients. Int J Nephrol Urol 2010;2:543–52.
8. Martynov SA, Shestakova MV, Shilov EM, Shamkhalova MS, Vikulova OK, Sukhareva OY, et al. Prevalence of anemia in patients with type 1 and type 2 diabetes mellitus with chronic renal disease. Diabetes Mellitus 2017;20:318–28.
9. Angelousi A, Larger E. Anaemia, a common but often unrecognized risk in diabetic patients: a review. Diabetes Metab 2015;41:18–27.
10. Robles NR, Ramos JL, Chavez E, Gonzalez Candia B, Bayo MA, Cidoncha A, et al. Iron deficiency in chronic kidney disease patients with diabetes mellitus. Diabetes Metab Syndr 2018;12:933–7.
11. Gauci R, Hunter M, Bruce DG, Davis WA, Davis TME. Anemia complicating type 2 diabetes: Prevalence, risk factors and prognosis. J Diabetes Complications 2017;31:1169–74.

12. Sajid A, Waseem SMA. Study of anemia in diabetic and non-diabetic subjects: A hospital-based study in Lucknow, Uttar Pradesh. Natl J Physiol Pharm Pharmacol 2020;10:344–8.
13. Atlaw D, Tariku Z. Magnitude and factors associated with anemia among diabetic patients in Ethiopia: A systematic review and meta-analysis. SAGE Open Med 2021;9:20503121211031126.
14. Thambiah SC, Samsudin IN, George E, Ranjit LK, Saat NS, Hussein Z, et al. Anaemia in type 2 diabetes mellitus (T2DM) patients in Hospital Putrajaya. Malays J Med Health Sci 2015;11:49–61.
15. Bekele A, Teji Roba K, Egata G, Gebremichael B. Anemia and associated factors among type-2 diabetes mellitus patients attending public hospitals in Harari Region, Eastern Ethiopia. Plos One 2019;14:e0225725.
16. Sharif A, Younus S, Baig K, Ali NH. Prevalence and risk of anemia in type-2 diabetic patients. Health 2014;12:1415–9.
17. Wang J, Xin X, Luo W, Wang R, Wang X, Si S, et al. Anemia and diabetic kidney disease had joint effect on diabetic retinopathy among patients with type 2 diabetes. Invest Ophthalmol Vis Sci 2020;61:25.
18. Sumathi K, Dilliraj G, Shanthi B, Selvi VK, Rani AJ. Correlation between iron deficiency anemia and HbA1C levels in type 2 diabetes mellitus. Int J Clin Biochem Res 2020;7:400–2.
19. Lee A-R, Yun J-M. Relationship between diabetes mellitus and Anemia in Korean adults-based on the Korean National Health and nutritional examination survey VI. JKDA 2017;23:54–63.
20. Kim M, Lee SH, Park KS, Kim EJ, Yeo S, Ha IH. Association between diabetes mellitus and anemia among Korean adults according to sex: a cross-sectional analysis of data from the Korea National Health and Nutrition Examination Survey (2010-2016). BMC Endocr Disord 2021;21:209.