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Original Article

Prevalence of anemia in patients with type 2 diabetes

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Abstract

Background

Diabetes mellitus (DM) has a high prevalence worldwide. It leads to various complications, including microvascular and macrovascular complications. The nephropathy may undermine the renal production of erythropoietin, positively contributing to an increased anemia framework. The inflammatory situation created by kidney disease also interferes with intestinal iron absorption. Therefore, diabetic patients with kidney disease have higher risk for developing anemia.

Aim

The aim of this work was to determine the prevalence and various types of anemia in patients with type 2 DM.

Patients and methods

After obtaining informed written consent, all diabetics as well as control individuals were subjected to detail history, clinical examination, and investigations as follows: fasting blood glucose, postprandial blood glucose, glycated hemoglobin, complete blood count, peripheral smear for type of anemia, reticulocyte count and renal function test, creatinine clearance, urine examination, albuminuria, and stool examination through routine and microscopic fecal occult blood test.

Results

The prevalence of anemia among our studied patients with type 2 DM was 65%, with significant increase compared with control group (10%). Diabetics had microcytic hypochromic anemia among 55.4%, whereas 44.6% had normocytic normochromic anemia. There was a significant negative correlation between hemoglobin level and degree of albuminuria and a significant positive correlation between hemoglobin level and creatinine clearance.

Conclusion

Anemia is a common finding in patients with type 2 DM when compared with the general population. Hence in diabetic patients, it would be desirable to evaluate the hemoglobin levels often, even when the renal parameters are within the normal limits, for better quality of life.

Keywords: Albuminuria, anemia, renal impaired, type 2 diabetes mellitus

Introduction

Diabetes mellitus (DM) has a high prevalence worldwide [1]. It leads to various complications when poorly controlled, such as nephropathy, neuropathy, and retinopathy as well as several metabolic disorders. Type 2 diabetes affects 7% of the population [2]. Epidemiological data showed that in 2010 there were 285 million people affected with the disease in the world, and it is estimated that in the year of 2030, we will have ~440 million diabetes cases [3].

Anemia is defined as a reduction of the total circulating red cell mass below reference limits. It reduces the oxygen-carrying capacity of the blood, leading to tissue hypoxia [4]. It is associated with increased perinatal mortality, immune incompetence, impaired mental development, and decreased performance at work [5]. It is a key indicator of chronic kidney disease and important cardiovascular risk factor [6]. It is said to be highly prevalent affecting developing and developed countries, causing public health problem [7].

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Hyperglycemia has a direct relationship with the development of an inflammatory condition showed by the increased expression of proinflammatory cytokines such as interleukin (IL)-6 and tumor necrosis factor-α. Studies show that the longer the duration of the disease and/or loss of glycemic control, the higher inflammatory process [8].

It should also be noted that, owing to the development of DM, nephropathy may arise, which further undermines the renal production of erythropoietin, positively contributing to an increased anemia framework [9]. The inflammatory situation created by kidney disease also interferes with intestinal iron absorption and mobilization of inventories [10]. Therefore, diabetic patients with kidney disease have higher risk for developing anemia [11].

Patients with diabetes also have nutritional deficiencies for cyanocobalamin, folate, and iron, which may result in different types of anemia. Metformin may interfere with cyanocobalamin absorption, resulting in vitamin B_{12}-deficiency anemia [12]. Because of the fact that both anemia and type 2 diabetes share similar symptoms like pale skin, chest pain, numbness or coldness in the extremities, shortness of breath, and headache [13], anemia remains unidentified in most diabetic patients. Hence, it is important to identify anemia in diabetic patients.

Patients and methods

This study was carried on 100 patients with type 2 DM attending inpatient and outpatient department of Internal Medicine Shebin El-Kom Teaching Hospital Menoufia, Egypt, and 100 individuals as control group. This study was conducted over a period of 1 year from January 2018 to January 2019 after obtaining informed written consent from the patients. Exclusion criteria were type 1 diabetics, gestational diabetics, patients on ACI inhibitors, hematinic, liver disease, and malignancy.

Inclusion criteria

Type 2 diabetics, good controlled DM [glycated hemoglobin (HbA1c)=6–7], and patients on sulfonylureas and metformin were included. Anemic patients, with hemoglobin level less than 13 g/dl for male and less than 12 g/dl for female, were included as well.

All diabetics as well as control individuals were subjected to detail history, clinical examination and investigations as following

(1) Blood sugar levels (fasting blood glucose and postprandial blood glucose) and HbA1c by Siemens kit
(2) Complete blood count
(3) Peripheral smear for type of anemia
(4) Reticulocyte count
(5) Renal function test
(6) Creatinine clearance (ml/min) was calculated using the Cockcroft–Gault equation [(140 − age)×weight (kg)/serum creatinine (mg/dl)×72]×0.85 (if female)
(7) Urine examination and albuminuria by nephelometry using first urine samples in the morning
(8) Stool examination: routine and microscopic fecal occult blood test.

Statistical analysis

Interpretation and analysis of data obtained were carried out using standard test of significance. The difference of mean between anemic and nonanemic diabetic patients was evaluated by unpaired Student's *t*-test. Finally, correlation between the level of hemoglobin and index of renal damage (albumin–creatinine ratio) was assessed by Pearson's correlation. Statistical software of SPSS, version 10 and EXCEL (Office 9) SPSS 16, SPSS Inc.SPSS for Windows, Version 16.0. Chicago, (Microsoft, Redmond, WA, USA) were used to analyze the data.

Results

Table 1 shows significant increase in the number of anemic patients and level of HbA1c in diabetic patients versus control group.

Table 2 shows percentage of anemia in type 2 DM. Overall, 65% of all patients were anemic and 35% of all patients were found to be nonanemic.

Table 3 shows classification of anemia in patients with type 2 DM. Diabetic patients had microcytic hypochromic anemia

Table 1: Comparative study between studied diabetics and control groups

Variables	Control group (*n*=100)	Diabetic group (*n*=100)	*P*
Age	50.43±7.6	51.35±9.1	>0.05
Sex (male/female)	65/35	67/33	>0.05
BMI	30.3±8.9	30.9±9.1	>0.05
Number of anemic patients (%)	10	65	<0.05
Glycated hemoglobin	5.1±0.83	6.9±0.71	<0.05
Serum creatinine (mg%)	0.9±0.56	0.96±0.074	>0.05
Hemoglobin (g/dl)	13.9±1.9	11.7±1.1	<0.05

Table 2: Percentage of anemia in type 2 diabetes mellitus

Variants	Males [*n* (%)]	Females [*n* (%)]	Total [*n* (%)]
Anemia present	44 (65.7)	21 (63.6)	65 (65)
Anemia absent	23 (34.3)	12 (36.4)	35 (35)
Total	67 (67)	33 (33)	100 (100)

Table 3: Classification of anemia in type 2 diabetes mellitus

Type of anemia	*n* (%)		
	Males	Females	Total
Microcytic hypochromic	23 (52.3)	13 (61.9)	36 (55.4)
Normocytic normochromic	21 (47.7)	8 (38.1)	29 (44.6)
Macrocytic	0	0	0
Total	44 (67.7)	21 (32.3)	65 (100)

among 55.4%, whereas 44.6% had normocytic normochromic anemia. None of them had macrocytic type of anemia.

Table 4 shows there was a significant negative correlation between creatinine clearance and prevalence of anemia in patients with type 2 DM. The prevalence of anemia was 100% in patients with creatinine clearance less than 30 ml/min.

Table 5 shows a significant positive correlation between number of anemic patients and degree of albuminuria. As the level of albuminuria increased, the prevalence of anemia also increased.

Table 6 shows the relation of albuminuria and creatinine clearance with hemoglobin level. There was a significant negative correlation between hemoglobin level and albuminuria and a significant positive correlation between hemoglobin level and creatinine clearance.

Discussion

In this study, of 100 patients, 65% were anemic and 35% were nonanemic versus 10% anemic individual in the control group. In contrast, a study conducted by Kaushik *et al.* [14] showed 63% were anemic and 37% were nonanemic. In another study conducted by Ezenwaka *et al.* [15], 46.45% were anemic and 53.54% were nonanemic. Often, chronic disease, such as DM, are accompanied by mild-to-moderate anemia, often called anemia of inflammation or infection or anemia of chronic disease (ACD) [16]. The results found by the authors demonstrate that diabetic patients with anemia exhibit increased expression of proinflammatory cytokines as compared with patients with only diabetes. In an anemic patient, increase in IL-6 production, as well as B cell activity was confirmed which reinforced the association between IL-6 production and antierythropoietic action [17]. Moreover, the diabetic and anemic patients had high levels of C-reactive protein and ferritin ultrasensible; however, these diabetic and anemic patients had low iron contents, showing that ferritin increases were associated with chronic inflammatory process present in diabetes [18].

Table 4: Creatinine clearance in patients with type 2 diabetes mellitus

Creatinine clearance (ml/min)	*n* (%)				*P*
	≤30	31-60	61-90	>90	
Anemia (*n*=65)	8 (100)	33 (91.7)	22 (53.7)	2 (13.3)	<0.05
Nonanemia (*n*=35)	0	3 (8.3)	19 (46.3)	13 (86.7)	<0.05
Total (*n*=100)	8 (8)	36 (36)	41 (41)	15 (15)	<0.05

Table 5: Relation of number of anemic patients with albuminuria

Albuminuria (mg/day)	*n* (%)		*P*
	Anemic patients	Nonanemic patients	
<30 (*n*=18)	4 (22.2)	14 (77.8)	<0.05
30-300 (*n*=37)	16 (43.2)	21 (56.8)	<0.05
>300 (*n*=45)	45 (100)	0	<0.05

Table 6: Relation of albuminuria with creatinine clearance and hemoglobin level

Albuminuria (mg)	Mean±SD		*P*
	Creatinine clearance (ml/min)	Hemoglobin level (mg/dl)	
<30 (*n*=18)	109±12.4	12.5±3.4	<0.05
30-300 (*n*=37)	75.5±11.5	11.9±2.7	
>300 (*n*=45)	50.6±13.3	9.1±3.1	

In this study, of 65 anemic patient. 29 (44.6%) had normocytic normochromic anemia, characterized as ACD [19]. ACD is a mild-to-moderate anemia shortening the survival of red blood cells (~80 days instead of 120 days normal) [20]. This phenomenon is attributed to hyperactivity state mononuclear phagocyte system, triggered by the infectious, inflammatory, or neoplastic process, leading to the early removal of circulating red blood cells [21]. Inadequate bone marrow response observed is basically owing to inappropriately low secretion of erythropoietin, decreased bone marrow response to erythropoietin, and decreased erythropoiesis consequent to lower supply of iron to bone marrow [22]. In our study, 36 (55.4%) had microcytic hypochromic anemia. The higher prevalence of microcytic hypochromic anemia in DM was probably owing to malnutrition, iron deficiency, poverty, and increased frequency of pregnancy in females [14].

In this study, there was a significant negative correlation between creatinine clearance and prevalence of anemia in patients with type 2 DM. The prevalence of anemia in patients with creatinine clearance less than 30 ml/min was 100%, whereas prevalence of anemia in cases with creatinine clearance more than 90 ml/min was only 13.3%. Male and female diabetic patients also follow the same pattern. These findings were supported by Kaushik *et al.* [14], who showed that patients with type 2 DM with clearance less than 30 ml/min were 100% anemic, whereas prevalence of anemia in 16 cases with creatinine clearance more than 90 ml/min was only 18.75%.

In our study, there was a significant positive correlation between number of anemic patients and degree of albuminuria. As the level of albuminuria increased, the prevalence of anemia increased. In patients with normoalbuminuria, 22.2% of diabetic patients were anemia, whereas in patients with microalbuminuria, the prevalence of anemia was 43.2% of diabetic patients, and in patients with macroalbuminuria, the prevalence of anemia was 100% of diabetic patients. The study conducted by Kaushik *et al.* [14] reported that as the level of albuminuria increased, the prevalence of anemia increased.

Conclusion

Anemia is a common finding in patients with type 2 DM when compared with the general population. Hence in diabetic

patients, it would be desirable to evaluate the hemoglobin levels often, even when the renal parameters are within the normal limits, for better quality of life.

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Conflicts of interest

There are no conflicts of interest.

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