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ORIGINAL RESEARCH

Prevalence of Anemia in Type 2 Diabetic Patients and correlation with Body Mass Index and Kidney function in Palestine

Alaa Elsayed Fathi[1,2], Moyad Shahwan[1,2], Nageeb Hassan[1,2], Ammar Abdulrahman Jairoun[3,4], Monzer Shahwan[5]

[1]Department of Clinical Sciences, College of Pharmacy and Health Sciences, Ajman University, Ajman, Ajman, 346, United Arab Emirates; [2]Centre of Medical and Bio-Allied Health Sciences Research, Ajman University, Ajman, Ajman, 346, United Arab Emirates; [3]Health and Safety Department, Dubai Municipality, Dubai, United Arab Emirates; [4]Discipline of Clinical Pharmacy, School of Pharmaceutical Sciences, Universiti Sains Malaysia (USM), Pulau Pinang, 11500, Malaysia; [5]Diabetes Clinic, AL-Swity Center for Dermatology and Chronic Diseases, Ramallah, 972, Palestine

Correspondence: Moyad Shahwan; Ammar Abdulrahman Jairoun, Tel +971558099957, Email Dr_ammar_91_@hotmail.com; m.shahwan@ajman.ac.ae

Background: The objective of this study was to determine the prevalence of anemia in patients with type 2 diabetes mellitus and to identify the set of anthropometric and biochemical factors that jointly influence the diabetic and anemic patients including body mass index and kidney function..

Methods: A retrospective cross-sectional design study that was carried out in a private medical center in Palestine. The study included a total of 453 patients with type 2 diabetes. Inclusion criteria included all patients (18 years or older) suffering from type 2 Diabetes mellitus attended the diabetic clinic from the 1st of January 2018, till 30th of December 2018..

Results: A total number of 453 diabetic patients were recruited in the study. Male constituted 48.5% (n=220) of the study sample and 51.4% (n=233) were female. Of total 453 diabetic patients, 38.4% (95% CI, 34%–43%) had anemia. The results of statistical modeling showed that female gender (AOR 18.5; 95% CI 9.35–21.97), presence of hypertension (AOR 2.11; 95% CI 1.98– 4.25), high BMI (AOR 1.101; 95% CI 1.045–1.159), high Serum Creatinine (AOR 1.72; 95% CI 1.22–2.13), high BUN level (AOR 1.22; 95% CI 1.145–1.301) and low e-GFR (AOR 0.571; 95% CI 0.271–0.872) are strong determents of anemia in type 2 diabetic patients..

Conclusion: The results of the current study revealed a high prevalence of Anemia among type 2 diabetes Mellitus patients. A significant association was reported between Anemia, kidney functions and body mass index..

Keywords: type 2 diabetes mellitus, anemia, renal function, body mass index, erythropoietin

Introduction

Anemia is a health condition in which the Hgb levels, hematocrit and/or red blood cell (RBC) count are below normal and insufficient to carry enough oxygen for meeting the body tissues' physiological needs.[1] Anemia has a detrimental effect on the overall quality of life, impairing functional ability and labor productivity in adults, affecting children's cognitive and developmental growth, as well as anemia during pregnancy increases the risk of preterm birth, low weight in birth, and possibly poor neonatal health.[1,2] According to the WHO's gender-specific criteria, anemia is defined as men with Hgb levels of < 13 g/dL (7.7 mmol/l), non-pregnant women with < 12 g/dL (7.4 mmol/l) and pregnant women with <11 g/dl (6.83 mmol/l).[3]

Anemia is considered the most prevalent micronutrient deficiency globally, which is thought to be caused primarily by poverty in the lower socioeconomic segments of society. In 2013, the Global Burden of Disease, Injury, and Risk Factors Study estimated that anemia affects 27% of the world's population, or approximately 1.93 billion people worldwide.[2] Specific groups, such as pregnant women, young children, and those residing in low- and middle-income countries, face higher risks.[4] Factors contributing to this widespread occurrence include nutritional deficiencies (eg, folic acid, and vitamin B12), infectious diseases such as malaria, parasitic infections (eg, hookworm infection, and schistosomiasis), chronic illnesses like malignancies or kidney diseases, hereditary hemoglobinopathy (eg, sickle disease, and

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thalassemia) and socioeconomic disparities. Among the causes of anemia, Iron deficiency (IDA) has been the leading cause of more than 50% of the world's anemia cases.[5,6] Gastrointestinal bleeding, menstruation, reduced dietary iron intake and absorption are considered the most common causes of IDA.[7] Additionally, there are several chronic illnesses that frequently accompanied IDA which include cancer, inflammatory bowel disease, chronic kidney disease (CKD), and congestive heart failure (CHF).[8]

Diabetes mellitus is a term used to represent a chronic disorder of carbohydrate metabolism that poses a significant threat to various individuals' health due to its increasing prevalence and long-term morbidity .[9] It is fundamentally diagnosed by abnormally elevated levels of blood glucose. The hyperglycemia observed in diabetes is primarily due to insulin deficiency, whether absolute or relative, stemming from beta-cell dysfunction and insulin resistance. Insulin resistance occurs when tissues fail to respond properly to the insulin produced, despite its adequate levels in the body.[10] Diabetes, particularly when inadequately managed, results in complications like nephropathy, retinopathy, and neuropathy, alongside various disrupted metabolic processes, including oxidative stress, which leads to tissue and cellular oxidative damage.[11,12]

Among the known types of diabetes, approximately 90–95% of all diabetes cases can be traced back to type 2 diabetes mellitus (T2DM) .[13]

According to several studies, diabetic patients are twice as likely as non-diabetics to suffer from anemia, in fact, 25% of diabetic patients have undiagnosed anemia. The manifestation of anemia in diabetic patients has a multifactorial etiology including chronic inflammation, malnutrition, concurrent autoimmune diseases, medication use, and renal disease.[14]

Evidence from previous studies shows that anemia prevalence in T2DM patients is magnified among patients with kidney impairment. In other words, patients who have diabetic nephropathy or diabetic kidney disease often have higher levels of anemia relative to their degree of renal dysfunction compared to those who are identified with other reasons for renal failure.[15–17] A well-known mechanism, that explains this relationship, is the failure of the kidneys to produce adequate amounts of erythropoietin (EPO). EPO can be referred to as the hormone produced primarily by kidneys in the promotion of the process of differentiation and proliferation of red blood cells (RBCs) which are presented in the bone marrow.[18] The strong correlation between the kidney and anemia in diabetes most likely reflects the distinctive vulnerability of the renal microcirculation to the damage caused by prolonged hyperglycemia.[19]

Furthermore, there is increasing evidence that anemia in T2DM is strongly correlated to the increased amount of risk for the development and progression of macrovascular and microvascular diseases in diabetes.[19–21] It contributes to the very first onset and quick progress of some particular conditions like nephropathy, retinopathy, neuropathy, ischemic heart disease, diabetic foot ulcers and end stage renal disease (ESRD). These complications can also exacerbate anemia progression, creating a brutal cycle .[22]

The WHO defines overweight as having a BMI between 25 and 30 kg/m^2, and obesity as having a BMI above 30 kg/m^2.[23] Both anemia and obesity are prevalent epidemics that affect billions of people worldwide. It has been demonstrated that iron deficiency anemia and obesity are physiologically connected and influence one another, rather than being two common diseases that coexist with each other. A National Health and Nutrition Examination Survey (NHANES) analysis found that adolescents who are overweight have a doubled risk of having iron deficiency, which is characterized by low serum ferritin and transferrin saturation. Furthermore, obesity is frequently linked to higher rates of T2DM, cardiovascular disease, and other chronic illnesses.[24]

Although there have been many studies on the prevalence of anemia in diabetic patients with renal impairment, there have been few studies demonstrating a possible link between the prevalence of anemia in patients with T2DM and other potential contributing factors such as BMI, gender, age, and blood pressure control, necessitating further research in this area.

Therefore, this study aims to determine the prevalence of anemia in patients with T2DM and to assess its significant association with BMI and kidney function.

Methodology

Subjects, Materials, and Methods

A retrospective cross-sectional study that was carried out in a private medical center in Palestine. Participants were outpatients recruited sequentially by a diabetes specialist for regular follow-up. All patients aged 18 years or older with

T2DM who attended the diabetic clinic between January 1st and December 30th, 2018 were included in the study group. The study enrolled 453 type 2 diabetes patients, 220 of whom were male and 233 of whom were female and all participants were informed about the study in accordance with the Declaration of Helsinki.[25]

Patients' confidentiality was held in high regard; all patients were screened privately, and data were collected using their registration number and coding. Furthermore, the principal investigator was exclusively responsible for data collection and entry, so there was no risk or harm to the patient.

Patients' anthropometric and biochemical information was collected from patient medical records, including age, gender, BMI, HbA1c, FBS, serum creatinine, e-GFR, BUN, systolic BP and diastolic BP.

Data Collection

The data collected included the following variables: age, gender, weight, height, BMI, physical activity and blood pressure. Whereas the laboratory tests included HbA1c, FBS, Hgb, serum creatinine, BUN, e-GFR, triglycerides (TG), total cholesterol (TC), high-density lipoprotein (HDL), and low-density lipoprotein (LDL).

Inclusion Criteria

All patients aged 18 years and older with type 2 diabetes who had frequent follow-up visits in 2018 and were willing to participate were included in the study, regardless of disease duration or treatment.

Exclusion Criteria

Patients with other types of diabetes (eg, type 1 diabetes, gestational diabetes, etc.), pregnant women, children, and patients with chronic medical history of renal, cardiovascular, or neurological diseases unrelated to diabetes were excluded from the study.

Definitions

- HbA1c > 6.5% were used as the diagnosis criteria for T2DM.[26]
- Hemoglobin level in men of < 13 g/dL and in women < 12 g/dL were used as a diagnostic criterion for anemia based on the WHO definition.[3]

Statistical Analysis

The SPSS version 26 was used to analyze the data. The qualitative variables were summed up using frequencies and percentages. The chi-square test was used to evaluate the association between the prevalence of the anemia and other categorical variables. Univariate and multivariate logistic regression was used to identify the significant anthropometric and biochemical factors that associated with Anemia. The threshold for determining statistical significance was set at a p value of 0.05.

Results

Anthropometric and Biochemical Information of the Patients

Table 1 shows the clinical parameters of the study participants'. A total number of 453 diabetic patients were recruited in the study. Male constituted 48.5% (n=220) of the study sample and 51.4% (n=233) were female. Of the total, 74.4% had hypertension and 69.5% had Hyperlipidemia. The mean age ± S.D of the patients was 54.5 ± 10.2. The mean ± S.D of BMI, HbA1c, Fasting blood glucose, Creatinine serum, e-GFR, BUN, Systolic BP, Diastolic BP and Hemoglobin were 29.3 ± 4.1, 7.8 ± 1.2, 159 ± 14.5, 0.84 ± 0.5, 99.6 ± 31.4, 14.8 ± 6.8, 129.5 ± 14.3, 80.7 ± 8, 13.6 ± 6 respectively.

Prevalence of Anemia and Its Correlations Among Type 2 Diabetes Mellitus

Of the total 453 diabetic patients, 38.4% (95% CI, 34%–43%) had anemia. Table 2 displays the prevalence of anemia according to clinical characteristics. In the present study, significantly increased risks of anemia among type 2 diabetic patients were observed in female gender (P < 0.001), older participants (P=0.014), patients with hypertensive (P=0.002)

Table 1 Anthropometric and Clinical Characteristics of the Patients (N= 453)

Characteristics	All Patients (n=453)	
Gender, n (%)	Male	220 (48.6)
	Female	233 (51.4)
Hypertension, n (%)	Yes	216 (47.7)
	No	237 (52.3)
Hyperlipidemia, n (%)	Yes	315 (69.5)
	No	138 (30.5)
Age (years), means ± SD		54.5 ± 10.2
Body mass index, means ± SD		29.3 ± 4.1
HbA1c (%), means ± SD		7.8 ± 1.2
Fasting blood glucose (mg/dl), means ± SD		159 ± 14.5
Creatinine Serum (mg/dl), means ± SD		0.84 ± 0.5
e-GFR (mL/min/1.73 m2), means ± SD		99.6 ± 31.4
BUN, means ± SD		14.8 ± 6.8
Systolic BP (mmHg), means ± SD		129.5 ± 14.3
Diastolic BP (mmHg), means ± SD		80.7 ± 8
Hemoglobin (g/dl), means ± SD		13.6 ± 6

Abbreviations: BUN, blood urea nitrogen; HbA1c, Hemoglobin A1C; BMI, body mass index; e-GFR, estimated glomerular filtration rate.

Table 2 Prevalence of Anemia According to Clinical Characteristics Among Type 2 Diabetes Mellitus

Characteristics	Anemia 174 (n=174)	No Anemia (n=279)	P–value
Gender, n (%)			< 0.001*
Male	17 (7.7%)	203 (92.3%)	
Female	157 (67.4%)	76 (32.6%)	
Hypertension, n (%)			0.002*
Yes	99 (45.8%)	117 (54.2%)	
No	75 (31.6%)	162 (68.4%)	
Hyperlipidemia, n (%)			0.835
Yes	120 (38.1%)	195 (61.9%)	
No	54 (39.1%)	84 (60.9%)	
Age (years), means ± SD	56 ± 11	53 ± 10	0.014*
Body mass index, means ± SD	30.3 ± 5	28.7 ± 4	0.001*
HbA1c (%), means ± SD	7.7 ± 1.1	7.9 ± 1.3	0.11

(*Continued*)

Table 2 (Continued).

Characteristics	Anemia 174 (n=174)	No Anemia (n=279)	P–value
Fasting blood glucose (mg/dl), means ± SD	160.5 ± 41	156.1 ± 54	0.372
Creatinine Serum (mg/dl), means ± SD	0.80 ± 0.22	0.73 ± 0.33	0.009*
e-GFR (mL/min/1.73 m2), means ± SD	88.6 ± 21.4	105.3 ± 31.2	0.001*
BUN, means ± SD	18.5 ± 12.3	14.8 ± 5.7	< 0.001*
Systolic BP (mmHg), means ± SD	131 ± 12.3	128 ±11.4	0.053
Diastolic BP (mmHg), means ± SD	79.6 ± 9.3	81.4 ± 6.5	0.016*

Notes: *P-values < 0.05 considered statistically significant.

and participants with higher BMI (P=0.001). Anemic patients were more likely to have higher serum creatinine level (P=0.009), higher BUN levels (P < 0.001), low e-GFR (P=0.001) and lower Diastolic BP (P=0.016).

Factors Associated with Anemia Among Type 2 Diabetes Mellitus

The results of statistical modeling showed that female gender (AOR 18.5; 95% CI 9.35–21.97), presence of hypertension (AOR 2.11; 95% CI 1.98–4.25), high BMI (AOR 1.101; 95% CI 1.045–1.159), high Serum Creatinine (AOR 1.72; 95% CI 1.22–2.13), high BUN level (AOR 1.22; 95% CI 1.145–1.301) and low e-GFR (AOR 0.571; 95% CI 0.271–0.872) are strong determents of anemia in type 2 diabetic patients (Table 3).

Table 3 Univariate and Multivariate Analysis for the Factors Associated with Anemic Type 2 Diabetes Mellitus Patients

Demographics	Prevalence of Anemia						
	COR	95% CI		P-value	AOR	95% CI		P-value
Gender (Ref. Male)								
Female	12.63	4.01	16.42	< 0.001*	18.5	9.35	21.97	< 0.001*
Hypertension (Ref. No)								
Yes	1.82	1.25	2.68	0.002*	2.11	1.98	4.25	0.036*
Age (years)	1.023	1.01	1.043	0.015*	1.082	0.946	1.109	0.326
BMI	1.077	1.031	1.124	0.001*	1.101	1.045	1.159	0.001*
HbA1c (%)	1.81	1.69	1.95	0.031	0.959	0.896	1.026	0.227
Fasting blood glucose (mg/dl)	0.998	0.994	1.002	0.371	0.997	0.990	1.005	0.472
Creatinine Serum (mg/dl),	1.39	1.19	1.81	0.001*	1.72	1.22	2.132	0.001*
e-GFR (mL/min/1.73 m2),	0.64	0.43	0.95	0.021*	0.571	0.27	0.872	0.008
BUN	1.047	1.023	1.072	< 0.001*	1.221	1.145	1.301	< 0.001*
Systolic BP (mmHg)	1.013	1.00	1.026	0.054	1.017	0.989	1.047	0.238
Diastolic BP (mmHg)	0.97	0.95	0.99	0.017*	0.94	0.85	1.09	0.071

Notes: *P-values < 0.05 considered statistically significant.
Abbreviations: COR, crude odd ratio; AOR, adjusted odd ratio; BUN, blood urea nitrogen; HbA1c, Hemoglobin A1C; BMI, body mass index.

Discussion

Anemia is a common complication of uncontrolled diabetes, affecting a growing number of diabetic patients each day.[27] Various factors may contribute to the development of anemia in patients with T2DM. Therefore, the aim of this study was to determine the prevalence of anemia in patients with T2DM attending a private clinic in Palestine and how significantly it associates with BMI and renal function.

Several studies have examined the prevalence of anemia in T2DM patients and found a positive correlation between T2DM and an increased risk of anemia. Data from the current study revealed a high prevalence of anemia among T2DM patients. Out of a total of 453 diabetic patients included, 38.4% (95% CI, 34%–43%) had anemia, this is consistent with studies conducted in Brazil (34.24%),[28] Iran (30.4%),[29] Malaysia (39.4%)[30] and eastern Ethiopia (34.8%).[31] On the other hand, compared to other studies carried out in Pakistan (63%),[32] Egypt (63%)[33] and UK (59%),[34] our finding was relatively lower. Such variation in the level of anemia among T2DM patients may be attributed to variations in the age, ethnicity, duration of diabetes, comorbidities, country level of development, selected sample size, and nutritional status of participants.

The results of the current study revealed that gender, specifically female gender ($P < 0.001$), was significantly associated with anemia. Female patients (67.4%) have a higher chance of developing anemia than male patients (7.7%). Similar results have been noted in Pakistan.[35] However, our study's findings did not agree with those of the Ethiopian study, which revealed that anemia was present in 10.56% and 6.52% of type 2 diabetic males and females respectively. This disparity can be attributed to the proportion of female patients who are menopausal as a result of how menstruation affects iron reserves in the body.[36]

Additionally, according to our results, anemia predominated among older diabetic patients (P=0.014). Participants in the current study who were anemic had a mean age ± SD of 56 ± 11; this result was anticipated as age is associated with the deterioration of hemoglobin levels and consequent anemia regardless of health status. Likewise, anemia might be linked to vitamin deficiencies (eg, folate), bone marrow abnormalities, and co-morbidities, all of which are common among elderly.[37] Other studies conducted in Korea,[37] California,[38] and Australia[39] found similar results.

Our study also found that kidney function is a major predictor for anemia in T2DM patients. Anemic patients were more likely to have abnormal readings of kidney function tests especially, higher serum creatinine level (P=0.009), higher BUN levels ($P < 0.001$), and lower e-GFR (P=0.001). The correlation between anemia and kidney has been established in numerous studies.

The main findings of these studies support the fact that anemia is very common among T2DM patients with kidney disease, in the form of renal failure and/or proteinuria.[17,40–42] Results from a relatively newer cross-sectional study showed that two out of every five patients with T2DM had anemia and that diabetes complications such as nephropathy were primarily responsible for this high prevalence (Feteh et al, 2016).[43] Additionally, a nested case-control study done in 2016 by Loutradis et al concluded that the incidence of anemia increases with the progression of chronic kidney disease, particularly stage 3, and is more common in diabetic than in non-diabetic chronic kidney disease patients.[44] Possible contributors to the prevalence of anemia in T2DM and kidney disease include EPO deficiency, chronic inflammation and increased utilization of RAAS-inhibitors (eg, ACE inhibitors and ARBs) in diabetic patients. These medications' inhibition of the biological erythropoietic action of angiotensin II may be linked to the emergence of anemia.[45]

Another variable that was evaluated was the participants' blood pressure. In this study, we observed that among T2DM patients, hypertension was a substantial risk factor for anemia (P=0.002). The deteriorating renal function caused by chronic uncontrolled hypertension together with the chronic inflammatory status brought on by diabetes may be the key causes.[46] This result is in line with a cross-sectional study carried out in Northwest Ethiopia.[36]

In terms of BMI, the mean BMI ± S.D of the individuals in the study was 29.3 ± 4.1. Anemia prevalence was observed to be significantly linked with increasing BMI in T2DM (P=0.001). A study conducted by Barbieri et al in 2015 in Brazil found that anemia in diabetic patients is positively related to obesity, BMI, and high waist circumference ($P < 0.05$).[47] Other studies, however, failed to find any association between BMI and anemia in T2DM patients. Studies conducted in East Africa[48] and North America[49] found no correlation between BMI and anemia. Over-nutrition in those regions where higher consumption of iron, protein, and other micronutrients may be protective against IDA could be a plausible explanation for this variance in outcomes.[49]

Limitations and Strengths

There are some limitations to this study. Firstly, the study was limited to a single geographic region, therefore; the sample is not representative and cannot be generalized internationally. Secondly, this study demonstrates a common limitation of cross-sectional epidemiological studies, which is it hinders the determination of causality. Finally, no investigation was done concerning the possible correlation between patients' medication and the prevalence of anemia. Given that ACE inhibitors, which are advised for diabetics, are known to suppress erythropoiesis.[50]

On the other hand, this study has a couple of strengths, including the fact that it was retrospective cross sectional study, which allowed for simultaneous evaluation of several outcomes and eliminated the need for lengthy patient follow-up.

Conclusion

In conclusion, this study revealed a high prevalence of Anemia among type 2 diabetes Mellitus patients. A significant association was reported between Anemia, kidney functions and body mass index. Given the high prevalence of anemia in Type 2 diabetic patients, hematological tests should be included in routine testing for all diabetics. Additionally, attention should be paid to proper diabetes care, anemia management, and maintaining regular physical activity to prevent the progress of diabetes complications.

Data Sharing Statement

All data will be provided upon request. Further inquiries can be directed to the corresponding authors (Ammar Abdulrahman Jairoun and Moyad Shahwan).

Ethical Approval

The study received approval from the health and ethics committee (AL-Swity Medical Center, Palestine) of the participating healthcare center, and all participants provided informed consent following the Declaration of Helsinki.

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Disclosure

All authors declare no conflicts of interest.

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