Scientific Research Publishing

Open Journal of Blood Diseases, 2021, 11, 31-45
https://www.scirp.org/journal/ojbd
ISSN Online: 2164-3199
ISSN Print: 2164-3180

# Clinical Predictors of Iron Deficiency Anemia in Emirati Population with T2DM

**Aml Mohamed Nada[1,2*], Mariam Adel Younan[2,3]**

[1]Internal Medicine and Endocrinology, Faculty of Medicine, Mansoura University, Mansoura, Egypt
[2]Zulekha Hospital, Sharjah, UAE
[3]Clinical Pathology, Faculty of Medicine, Cairo University, Cairo, Egypt
Email: *aml_nadanoha@yahoo.com

**How to cite this paper:** Nada, A.M. and Younan, M.A. (2021) Clinical Predictors of Iron Deficiency Anemia in Emirati Population with T2DM. *Open Journal of Blood Diseases*, **11**, 31-45.
https://doi.org/10.4236/ojbd.2021.112005

**Received:** December 31, 2020
**Accepted:** April 9, 2021
**Published:** April 12, 2021

Copyright © 2021 by author(s) and Scientific Research Publishing Inc.
This work is licensed under the Creative Commons Attribution International License (CC BY 4.0).
http://creativecommons.org/licenses/by/4.0/

Open Access

## Abstract

**Aim:** To establish the prevalence of iron deficiency anemia and its clinical predictors in Emirati patients with type 2 diabetes. **Patients & Methods:** 237 patients were included in the study. A full blood count was obtained in addition to routine blood and urine tests for all patients. Hemoglobin level and iron studies were done for diagnosis of anemia. Statistical analysis was done to find out the prevalence and independent predictors of anemia in the study population of Emirati type 2 diabetic patients. **Results**: Of the studied 237 patients; 36.3% had iron deficiency anemia as per the WHO criteria. Independent predictors of iron deficiency anemia were age ≥ 60 years, female gender and wide pulse pressure ≥ 60 mmHg. Hemoglobin level was directly proportionate to e GFR ($p < 0.001$). Participants with age ≥ 60 years had 4.2 times higher odds to exhibit anemia. Female participants had 1.95 times higher odds to exhibit anemia. Participants with wide pulse pressure ≥ 60 mmHg have 2.4 higher odds to exhibit anemia. **Conclusion:** Iron deficiency anemia is common in type 2 diabetic patients. Testing the patient for iron deficiency anemia should be considered in type 2 diabetes patients especially with age ≥ 60 years, female patients and those with wide pulse pressure ≥ 60 mmHg.

## Keywords

Anemia, HbA1c, Pulse Pressure, Age, Diabetes

## 1. Introduction

Anemia is a global health problem which has negative impacts on the quality of life [1]. Anemia leads to fatigue, reduced physical fitness, anorexia, depression, impaired cognitive function and decreased libido. These effects increase the car-

diac risk and impair the quality of life [2]. Diabetes patients who have anemia should be treated immediately with careful follow up of response to treatment. Anemia in this group of population contributes to the development and progression of cardiovascular, retinal and renal complications of diabetes. Complete blood count should be part of routine blood tests for patients with diabetes to avoid the higher risk of development of diabetes associated complications [3].

Bosman *et al.* identified increased cardiovascular and end stage kidney disease in diabetes patients who had anemia [4]. Keane and Lyle' study [5], anemia was significantly associated with increased risk of hospitalization and premature death. In cardiac diseases, one gram reduction of hemoglobin was considered as an independent predictor of morbidity and mortality [6].

Iron deficiency anemia is the most common form of malnutrition anemia in both developed and developing countries [7] [8] [9]. It results from inadequate iron intake, malabsorption, increased iron requirement or chronic blood loss [10] [11] [12]. Iron deficiency leads to declined red cell production and microcytic hypochromic anemia [9] [13].

Worldwide prevalence of anemia is about 25% [14] [15] [16] [17] with 50% of anemic individuals having iron deficiency [14] [18]. The WHO recommends investigation of anemia when the Hb concentration is <12 g/dl in women and <13 g/dl in men [19].

Some studies suggest that anemia is two times more common in patients with diabetes compared with people without diabetes [20]. However, 25% of diabetes patients have unrecognized anemia [21].

Most studies focused on the prevalence of anemia in patients with diabetes and renal insufficiency. Patients with renal impairment or chronic kidney disease due to diabetes mellitus develop more reduction of hemoglobin level and more serious anemia when compared to other patients with the same degree of renal impairment but due to causes other than diabetes [22] [23] [24] [25].

In the present study we investigated the prevalence of anemia in type 2 diabetes mellitus patients with normal kidney function. We also tried to find out the clinical predictors that necessitate testing blood for anemia and iron deficiency in patients with type 2 DM.

## 2. Patients and Methods

This is a cross-sectional retrospective study that included 237 patients who were regularly visiting a single endocrine clinic at Zulekha Hospital, Sharjah, UAE. Patients visited the endocrine clinic from May 2018 to May 2019.

The study proposal has been reviewed and approved by the MOHAP Research Ethics Committee, Sharjah (Research Approval Reference No. MOHAP/DXB-REC/OON/No. 42 2019). All methods were performed in accordance with the relevant guidelines and regulations of Zulekha Hospital, Sharjah (ZHS). The ethics committee waived the need to obtain informed consent for this study.

Data, including age, sex, body weight, BMI, type and duration of diabetes

were traced from patient records. All patients had T2DM, age more than 18 years and eGFR more than 90 ml/min/1.73m$^2$.

Exclusion criteria included pregnancy, hospitalization, hemoglobinopathies, hemolytic anemia, hypothyroidism, abnormal renal function test (high serum creatinine, eGFR < 90/ml/1.73 m$^2$). Patients with micro or macroalbuminuria were also excluded from the study. Normoalbuminuria was defined by two of three urine albumin/creatinine ratio < 30 mg/gm [26].

Serum iron was determined by quantitative method on Roche/Hitachi cobas c systems is by a colorimetric assay in which liberation of $Fe^{3+}$ ions from the transferrin complex under acidic conditions takes place followed by reduction by ascorbate of $Fe^{3+}$ ions to $Fe^{2+}$ ions which then react with FerroZine to give a colored complex. Iron concentration is measured photometrically (For **cobas c** 311/501 analyzers: **IRON2:** ACN 661).

Quantitative measurement of serum Unsaturated Iron-Binding Capacity (UIBC) was done on Roche/Hitachi cobas c systems is by direct determination with FerroZine. The color intensity is directly proportionate to the unbound excess iron concentration and indirectly proportionate to the unsaturated iron binding capacity. It is determined by measuring the increase in absorbance photometrically. The sum of the serum iron and UIBC represents total iron-binding capacity (TIBC). TIBC is a measurement for the maximum iron concentration that transferrin can bind. (For cobas c 311/501 analyzers: UIBCI: ACN 779)

Serum ferritin was measured by the electrochemiluminescence immunoassay "ECLIA" on Elecsys and cobas e immunoassay analyzers. This is done by a sandwich principle. First incubation: the sample, a biotinylated monoclonal ferritin-specific antibody, and a monoclonal ferritin-specific antibody labeled with a ruthenium complex form a sandwich complex. Second incubation: after addition of streptavidin-coated microparticles, the complex becomes solid phase-bound through an interaction between biotin and streptavidin. The resulting mixture is aspirated into the measuring cell where the microparticles are magnetically captured onto the surface of the electrode. ProCell/ProCell M removes the unbound substances. A voltage is applied to the electrode with induction of chemiluminescent emission that can be measured by a photomultiplier (Ferritin elecsys cobas e 411).

Complete Blood count was done using UniCel DxH 800 Coulter Cellular Analysis System. It is an automated analyzer with five part differential. RBCs, WBCs & platelets were measured by the Coulter Principle, Hemoglobin is measured photometrically, and Hematocrit, MCH & MCHC are calculated (Beckman Coulter).

Blood glucose, C Reactive Protein (CRP), urine albumin and urine creatinine were determined on the same instrument by enzymatic hexokinase, turbidimetric, immunoturbidimetric & kinetic Jaffe methods; respectively [27] [28].

HbA1c was measured by turbidimetric inhibition immunoassay (TINIA) using COBAS INTEGTRA 400 plus machine; Roche Diagnostics. HbA1c percent was calculated as per the equation: HbA1c (%) = (HbA1c/Hb) × 91.5 + 2.15 [28].

Fasting plasma glucose was measured on Roche Hitachi P800/917 chemistry analyzer, Roch Diagnostics.

The latest full blood count was used for statistical analysis. The Modification of Diet in Renal Disease (MDRD) study formula was used for calculation of eGFR [29] [30]. As per WHO, sex specific definition of anemia was used; Hb < 13 g/dl in men and <12 g/dl in women [19].

Iron studies diagnostic for iron deficiency anemia consisted of a serum ferritin concentration less than 50 μg/L, a low serum iron (<7.1 μg/L) and a high TIBC (>13.1 μmol/L) [13] [31] [32] [33].

### Statistical Analysis

**Sample size:** Based on a previous work by Barbieri *et al.* [34], anemia occurs in 34.2% of patients with type 2 diabetes with at least three predictors. Based on the work of Peduzzi *et al.* [35] the minimum number of cases to be included in this study can be calculated from the following equation: $N = 10\ k/p$, where $p$ is the smallest of the proportions of negative or positive cases in the population (in this study $p = 0.342$) and k represents the number of covariates or independent variables ($k = 6$ in this study which are age, sex, BMI, diabetes duration, diabetes control and renal function). Therefore, a minimum of 176 patients with type 2 diabetes is required.

Data were analyzed using IBM SPSS statistics 20. The data were presented as mean ± SD. A student's *t*-test was applied for comparison of group means. Pearson's coefficient of correlation was calculated to determine the correlation between the two variables. Categorical data was analyzed by $\chi^2$ test. Odds ratio and 95% confidence intervals were obtained by the use of logistic regression analyses. *P* value less than 0.05 was considered significant.

Binary logistic regression (multivariable) was run to ascertain the effects of old age (≥60 years), female sex and wide pulse pressure (≥60 mmHg) on the likelihood that participants with type 2 diabetes will exhibit anemia. The model was statistically significant in predicting anemia (WHO: $\chi^2$ 45.89 = and $P < 0.001$).

## 3. Results

Our study included 237 patients with a median age of 62 years (49.5 - 69.6) and a median duration of diabetes of 10 years (3.0 - 17). 139 patients were females (58.6% of the study sample) and 98 patients were males (41.4% of the study sample). Median HbA1c was 7.4% (6.7% - 8.55%) and median eGFR 99 ml/min/1.73m$^2$ (90.1 - 126). Basic characteristics of the study group are shown in **Table 1**.

Prevalence of iron deficiency anemia, as per WHO criteria; in the study population was 36.3% with significantly higher prevalence in females than males (47.9% vs 19.6% respectively, $p < 0.001$). Menopausal females showed higher prevalence than premenopausal females but this did not reach statistical significance (51.8% vs 30.8% respectively, $p < 0.058$) (**Table 2**).

**Table 1.** Basic characteristics of the study participants (n = 237).

| Characteristic | Statistic |
|---|---|
| Sex N (%) | |
| Male | 98 (41.4%) |
| Female | 139 (58.6%) |
| Age [years] | 62 (49.5 - 69.5) |
| Heart rate (Mean ± SD) | 82 ± 12 |
| SBP | 130 (120 - 141) |
| DBP Mean ± SD | 77 ± 8 |
| Pulse pressure | 50 (41 - 64) |
| Mean blood pressure Mean ± SD | 95 ± 9 |
| RPP | 10,560 (9240 - 12,026) |
| Duration of DM [years] | 10 (3.0 - 17) |
| BMI [kg/m$^2$] Mean ± SD | 30.6 ± 5.8 |
| Waist circumference Mean ± SD | 95.5 ± 14.5 |
| Hip circumference Mean ± SD | 109.6 ± 14.4 |
| Hemoglobin level [g/dL] Mean ± SD | 12.75 ± 1.87 |
| WBC count [per μL] Mean ± SD | 10,600 ± 1090 |
| Serum creatinine [μmol/l] | 76.5 (67 - 87) |
| eGFR ml/min/1.73m$^2$ | 99 (90.1 - 126) |
| HbA1c % | 7.4 (6.7 - 8.55) |

SBP: systolic blood pressure, DBP: diastolic blood pressure, HbA1c: glycated hemoglobin, eGFR: estimated glomerular filtration rate. RPP: rate pressure product, BMI: body mass index.

**Table 2.** Prevalence of iron deficiency anemia in different categories of the study sample.

| Cohort | Prevalence as per WHO criteria |
|---|---|
| **All cases N = 237** | 86 (36.3%) |
| **Male participants N = 97** | 19 (19.6%) |
| **Female participants N = 140** | 67 (47.9%) |
| **Premenopausal N = 26** | 8 (30.8%) |
| **Postmenopausal N = 114** | 59 (51.8%) |

Hemoglobin level negatively correlated with patient's age ($p < 0.001$) and pulse pressure ($p = 0.005$). It positively correlated with body weight ($p = 0.011$), diastolic blood pressure ($p = 0.004$) and eGFR ($p < 0.001$) (Table 3).

Comparing anemic with non anemia groups showed significantly older age in anemic patients ($p < 0.001$), significantly higher prevalence in females than males ($p < 0.001$). No significant difference was found as regard to metabolic syndrome (IDF criteria $p = 0.588$, NHLBI/AHA criteria $p = 0.375$), body mass index ($p = 0.081$) or rate pressure product ($p = 0.264$). Diastolic blood pressure

**Table 3.** Comparison between those with and without anemia.

| Parameter | Without anemia | With anemia | *P* value |
|---|---|---|---|
| **N** | 151 | 86 | |
| **Age** | | | |
| **<60 years** | 79 (52.3%) | 19 (22.1%) | **<0.001** |
| **≥60 years** | 72 (47.7%) | 67 (77.9%) | |
| **Sex** | | | |
| **Male** | 78 (51.7%) | 20 (23.3%) | **<0.001** |
| **Female** | 73 (48.3%) | 66 (67.3%) | |
| **BMI category** | | | |
| **Ideal** | 20 (13.2%) | 14 (16.3%) | |
| **Overweight** | 54 (35.8%) | 27 (31.4%) | *0.081 |
| **Grade I obesity** | 51 (33.8%) | 29 (33.7%) | |
| **Grade II obesity** | 22 (14.6%) | 7 (8.1%) | |
| **Grade III obesity** | 4 (2.6%) | 9 (10.5%) | |
| **Presence of MS** | | | |
| **IDF criteria** | 74 (49%) | 39 (45.3%) | 0.588 |
| **NHLBI/AHA criteria** | 88 (58.3%) | 45 (52.3%) | 0.375 |
| **Rate pressure product** | | | |
| **≤10,000** | 62 (41.1%) | 29 (33.7%) | 0.264 |
| **>10,000** | 89 (58.9%) | 57 (66.3%) | |
| **Heart rate** | 81 ± 11 | 84 ± 13 | 0.111 |
| **SBP** | 130 ± 16 | 134 ± 20 | 0.156 |
| **DBP** | 78 ± 8 | 75 ± 8 | **0.008** |
| **PP** | 52 ± 15 | 58 ± 18 | **0.006** |
| **RPP** | 10,560 (9126 - 11,880) | 10,739 (9498 - 12,482) | *0.109 |
| **HbA1c** | 7.3 (6.5 - 8.2) | 7.75 (7 - 8.9) | *0.072 |
| **Serum creatinine** | 76 (66 - 86) | 77 (68 - 87) | *0.388 |
| **eGFR** | 110.2 (97.7 - 128) | 92.7 (90.1 - 102.9) | ***<0.001** |

SBP: systolic blood pressure, DBP: diastolic blood pressure, PP: pulse pressure, HbA1c: glycated hemoglobin, eGFR: estimated glomerular filtration rate, BMI: body mass index.

was significantly lower in anemic patients ($p = 0.008$). Pulse pressure was significantly wider in anemic than non anemic individuals ($p = 0.006$). eGFR was significantly lower in anemic than non anemia persons 92.7 (90 - 102.9) vs 110.2 (97.7 - 128), $p < 0.001$. There was a tendency towards higher HbA1c in anemic patients but did not reach a statistical significance ($p = 0.07$) (Table 4).

In the present study, significant and independent clinical predictors of iron deficiency anemia in diabetic patients are age, female gender and wide pulse pressure ≥ 60 mmHg (Table 5).

T2DM patients with age ≥ 60 years had 4.2 times higher odds that participants will exhibit anemia. Females had 1.95 times higher odds that to exhibit anemia. T2DM patients with wide pulse pressure ≥ 60 mmHg had 2.4 times higher odds that participants will exhibit anemia.

**Table 4.** Correlation of hemoglobin with clinical and laboratory parameters.

| Parameter | $r_s$ | *p* value |
|---|---|---|
| **Age (years)** | −0.440 | **<0.001** |
| **DM duration** | 0.057 | 0.386 |
| **Body weight (kg)** | 0.211 | **0.011** |
| **BMI (kg/m²)** | −0.120 | 0.065 |
| **Waist circumference (cm)** | −0.005 | 0.937 |
| **Hip circumference (cm)** | −0.261 | 0.067 |
| **Waist to hip ratio** | 0.247 | 0.130 |
| **Heart rate (beats/minute)** | −0.027 | 0.678 |
| **SBP (mmHg)** | −0.075 | 0.249 |
| **DBP (mmHg)** | 0.185 | **0.004** |
| **Pulse pressure (mmHg)** | −0.182 | **0.005** |
| **Rate pressure product (RPP)** | −0.070 | 0.284 |
| **HbA1c%** | −0.111 | 0.179 |
| **Serum creatinine** | −0.069 | 0.312 |
| **eGFR** | 0.377 | **<0.001** |

SBP: systolic blood pressure, DBP: diastolic blood pressure, PP: pulse pressure, HbA1c: glycated hemoglobin, eGFR: estimated glomerular filtration rate, BMI: body mass index.

**Table 5.** Predictors of the likelihood of iron deficiency anemia in T2DM.

| Predictor | Univariate | | Multivariate | |
|---|---|---|---|---|
| | *P* value | COR (95% CI) | *P* value | OR (95% CI) |
| **Age (years)** | | | | |
| **<60** | **<0.001** | R | **<0.001** | R |
| **≥60** | | 4.17 (2.33 - 7.45) | | 3.18 (1.66 - 6.09) |
| **Sex** | | | | |
| **Male** | **0.015** | R | **<0.001** | R |
| **Female** | | 1.95 (1.14 - 3.36) | | 4.05 (2.12 - 7.74) |
| **Pulse pressure (mmHg)** | | | | |
| **<60** | **0.002** | R | **0.011** | R |
| **≥60** | | 2.40 (1.36 - 4.24) | | 2.31 (1.21 - 4.40) |
| **BMI grade** | 0.718 | 1.05 (0.82 - 1.34) | - | - |

## 4. Discussion

Prevalence of anemia in our study group was 36.3% as per the WHO diagnostic criteria of anemia [19].

In a study conducted by Shaheen *et al.*, type 2 diabetes Egyptian population had a prevalence of 65% compared with 10% in the control group. Of the 65% anemic patients, 55.4% had microcytic hypochromic anemia [36].

AlDallal *et al.* [37] also used the WHO criteria for diagnosis of anemia [19]. She found 29.7% prevalence of anemia in Kuwaiti patients with type 2 DM.

Mean HbA1c in her study was 7.5%. On the other hand the prevalence reported by Sharif *et al.* in the same population was 63%, a much higher level [38]. In Sherif's study, 71.5% of patients had poorly controlled diabetes. In AlDallal's study, 68% of the subjects had well controlled diabetes.

Studies of anemia in patients with diabetes were done in various places with different prevalence. In Taderegew's study [39], a prevalence of 20.1% was reported. In Iran it was 19.6% and 30.4% in two different studies [40] [41]. It was 12.3% in India [42], 63% in Pakistan [43], 31.7% and 39% in two different studies in Malaysia [44] [45] and 63% in Egypt [46].

Variability in the prevalence can be explained by differences in ethnicity, age of the study participants and duration of DM. The level of development of the country can also affect the quality of health care delivery. Health care may also differ from one place to another in the same country with reflection on patient health [25] [47] [48].

Similar to our study, AlDallal *et al.* [37] found that females with T2DM are at higher risk of anemia than males. This is consistent with findings of Alsayegh *et al.* which reported a prevalence of 35.8% in females versus 21.3% in males [49]. In our study, iron deficiency anemia was significantly more prevalent in females than males (47.9% vs. 19.6, respectively, $p < 0.001$). The prevalence was also higher in menopausal than premenopausal females but this did not reach a statistical significance (51.8% vs.30.8%, $p = 0.058$). We also found that female gender had 1.95 times higher odds to exhibit anemia than males (**Table 5**).

The higher prevalence of anemia in females may be explained by malnutrition, lack of empowerment and inadequate health awareness. Education, provision of iron rich food, prescription of vitamin and iron supplements and knowledge of the diabetes associated complications can help [50].

In the study conducted by Kaur [51], the prevalence of anemia was lowest in the younger age groups 45 - 55 years (78.8%) and highest in the oldest age groups 66 - 80 years (89.7%).

In our study, age of patients negatively correlated with Hb level ($p < 0.001$) and was a strong independent predictor of iron deficiency anemia. Participants with age ≥ 60 had 4.2 times higher odds to exhibit anemia. The age-related decrease in hemoglobin concentrations might be due to a lower erythropoietin secretion [52] or a reduced hematopoietic reserve [53]. Dietary deficiencies and diabetes associated comorbidities also increase with increasing age [54] [55].

Al Dallal [37] and others reported older age and less glycemic control in anemic patients in comparison with non-anemic patients [47] [56]. In our study, there was a trend towards higher HbA1c in anemic participants but it did not reach a statistical significance ($p = 0.072$).

In the study conducted by Taderegew *et al.* [39], age > 60 years was associated with greater odds for developing anemia. Increased odds ratio for developing anemia with increasing age has also been found in previous studies conducted in California [48], Australia [57], China [58], Nigeria [59] and Finote Selam hos-

pital [21].

In the study conducted by Maninder *et al.* [50], postmenopausal females experienced higher prevalence of anemia. Hemoglobin concentration showed negative correlation with age of the patients. Women with anemia had lower intake of nutrients essential for erythropoiesis such as calcium, protein and iron. Maninder considered age as a possible predictor of anemia with an odds ratio of 1.04.

Higher prevalence of anemia in post menopausal women in our study can be explained by the fact that menopausal women are older than premenopausal women. Similar to our study, several authors mentioned increasing prevalence of anemia in women with increasing age [52] [60] [61] [62].

Previous studies indicated nutrition as an important factor for controlling anemia. Intake of protein, vegetables, fruits, calcium and iron are protective. Thomson *et al.* [63] described inadequate nutrient intake as a significant risk factor for anemia in older women. They further elaborated that among anemic postmenopausal women enhanced access to nutrient-rich foods particularly iron and vitamin intake may be required to correct nutritional anemia.

In Merlin's study [64], at all levels of eGFR, patients with diabetes were more likely to have anemia. In agreement with Shaheen's study, we found a significant positive correlation between hemoglobin level and e GFR in our study population ($p < 0.001$) [36] (**Table 4**).

Also in agreement with Shaheen's report [36], in our study, Hb was significantly and positively associated with body weight ($p = 0.011$) but no association with the duration of diabetes was found ($p = 0.386$). Merlin did not find an association between Hb and age, BMI or duration of diabetes [64].

Alap *et al.* [65], similar to our study, did not find a significant correlation between HbA1c and hemoglobin ($p = 0.064$) (**Table 4**).

According to the explanation provided by Sluiter *et al.*, glycation of Hb is an irreversible process. Hence, HbA1 levels in the red blood cell increases with cell age. The average age of circulating red cells is increased in iron deficiency anemia due to decreased production of young cells. HbA1c can spuriously increase in patients with iron deficiency or low hemoglobin. So, iron studies are highly recommended in patients of diabetes mellitus with unexplained high HbA1c before changing their medication [66].

Contrary to our study, Barbieri *et al.* found a higher prevalence of obesity and higher mean BMI and waist circumference in anemic patients when compared with nonanemic ones [34]. In our study, BMI was higher in non anemic patients who were overweight, grade I and II obese. However, grade III obesity was more in anemic persons.

Barbieri *et al.* [34] did not find correlation between Hb and creatinine or statistical differences in creatinine values or eGFR between anemic and non anemic individuals. In our study eGFR was significantly lower in anemic persons ($p < 0.001$).

Normal pulse pressure is 30 - 40 mmHg. Cardiovascular death has been shown to be closely associated with high pulse pressure. After the age of 60 years, a pulse pressure > 60 mmHg can be a predictor of cardiovascular and heart attacks [67]. An increase of pulse pressure by 10 mmHg or more is associated with 20% increased risk of CVD [68].

Iron deficiency anemia is associated with hyperdynamic circulation which is characterized by wide pulse pressure [69]. In our study, wide pulse pressure was a significant independent predictor of iron deficiency anemia. An adult with type 2 diabetes with pulse pressure ≥ 60 mmHg has 2.4 higher odds to have iron deficiency anemia (**Table 5**).

Limitation of our study includes the retrospective nature and absence of a placebo group. We recommend an extended prospective study which should include a placebo group with further analysis of the effect of iron replacement on the different study variables in patients with iron deficiency anemia.

## 5. Conclusion

In conclusion, iron deficiency anemia is common in patients with type 2 diabetes. Age ≥ 60 years, female gender and wide pulse pressure ≥ 60 mmHg are significant independent predictors of iron deficiency anemia in type 2 diabetic patients. Diabetic patients with these predictors should be investigated thoroughly for iron deficiency anemia.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

## References

[1] MacCiò, A. and Madeddu, C. (2012) Management of Anemia of Inflammation in the Elderly. *Anemia*, **2012**, Article ID: 563251. https://doi.org/10.1155/2012/563251

[2] Angelousi, A. and Larger, E. (2015) Anaemia, a Common but Often Recognized Risk in Diabetic Patients: A Review. *Diabetes & Metabolism*, **41**, 18-27. https://doi.org/10.1016/j.diabet.2014.06.001

[3] Singh, D.K., Winocour, P. and Farrington, K. (2009) Erythropoietic Stress and Anemia in Diabetes Mellitus. *Nature Reviews Endocrinology*, **5**, 204-210. https://doi.org/10.1038/nrendo.2009.17

[4] Bosman, D.R., Winkler, A.S., Marsden, J.T., Macdougall, I.C. and Watkins, P.J. (2001) Anemia with Erythropoietin Deficiency Occurs Early in Diabetic Nephropathy. *Diabetes Care*, **24**, 495-499. https://doi.org/10.2337/diacare.24.3.495

[5] Keane, W.F. and Lyle, P.A. (2003) Recent Advances in Management of Type 2 Diabetes and Nephropathy: Lessons from the RENAAL Study. *American Journal of Kidney Diseases*, **41**, S22-S25. https://doi.org/10.1053/ajkd.2003.50078

[6] Eckardt, K.U. (1999) Cardiovascular Consequences of Renal Anemia and Erythropoietin Therapy. *Nephrology Dialysis Transplantation*, **14**, 1317-1323. https://doi.org/10.1093/ndt/14.5.1317

[7] Nils, M. (2011) Anemia—Still a Major Health Problem in Many Parts of the World.

*Annals of Hematology*, **90**, 369-377. https://doi.org/10.1007/s00277-010-1144-5

[8] Clark, S.F. (2009) Iron Deficiency Anemia: Diagnosis and Management. *Current Opinion in Gastroenterology*, **25**, 122-128. https://doi.org/10.1097/MOG.0b013e32831ef1cd

[9] Jeffery, L.M. (2013) Iron Deficiency Anemia: A Common and Curable Disease. *Cold Spring Harbor Perspectives in Medicine*, **3**, Article ID: a011866. https://doi.org/10.1101/cshperspect.a011866

[10] Gnana-Prakasam, J.P., Martin, P.M., Smith, S.B. and Ganapathy, V. (2010) Expression and Function of Iron-Regulatory Proteins in Retina. *IUBMB Life*, **62**, 363-370. https://doi.org/10.1002/iub.326

[11] Iqbal, M.S., Ahmed, M.S., Ogras, T.T., Ullah, S., Asif, J. and Keshavarzi, F. (2012) Diagnosis & Management of Iron Deficiency Anemia via Parental Iron. *International Journal of Natural Sciences*, **2**, 88-90. https://doi.org/10.3329/ijns.v2i3.12138

[12] Wang, J. and Pantopoulos, K. (2011) Regulation of Cellular Iron Metabolism. *Biochemical Journal*, **434**, 365-381. https://doi.org/10.1042/BJ20101825

[13] Bermejo, F. and García-López, S. (2009) A Guide to Diagnosis of Iron Deficiency and Iron Deficiency Anemia in Digestive Diseases. *World Journal of Gastroenterology*, **15**, 4638-4643. https://doi.org/10.3748/wjg.15.4638

[14] Balarajan, Y., Ramakrishnan, U., Ozaltin, E., Shankar, A.H. and Subramanian, S.V. (2012) Anaemia in Low-Income and Middle-Income Countries. *Lancet*, **378**, 2123-2135. https://doi.org/10.1016/S0140-6736(10)62304-5

[15] Pasricha, S.R., Drakesmith, H., Black, J., Hipgrave, D. and Biggs, B.-A. (2013) Control of Iron Deficiency Anemia in Low-and Middle-Income Countries. *Blood*, **121**, 2607-2617. https://doi.org/10.1182/blood-2012-09-453522

[16] Dolai, T.K., Nataraj, K.S., Sinha, N., Mishra, S., Bhattacharya, M. and Kumar Ghosh, M. (2012) Prevalence of Iron Deficiency in Thalassemia Minor: A Study from Tertiary Hospital. *Indian Journal of Hematology and Blood Transfusion*, **28**, 7-9. https://doi.org/10.1007/s12288-011-0088-9

[17] Lynch, S.R. (2011) Why Nutritional Iron Deficiency Persists as a Worldwide Problem. *Journal of Nutrition*, **141**, 763S-768S. https://doi.org/10.3945/jn.110.130609

[18] Shrivastava, S.R., Shrivastava, P.S. and Ramasamy, J. (2013) Nutritional Anemia: Analysis of the Existing Gaps and Proposed Public Health Measures. *Health Care*, **1**, 43-46.

[19] World Health Organization (1968) Nutritional Anemia: Report of a WHO Scientific Group. World Health Organization, Geneva.

[20] Wright, J.A., Oddy, M.J. and Richards, T. (2014) Presence and Characterization of Anaemia in Diabetic Foot Ulceration. *Anemia*, **2014**, Article ID: 104214. https://doi.org/10.1155/2014/104214

[21] Abate1, A., Birhan, W. and Alemu, A. (2013) Association of Anemia and Renal Function Test among Diabetes Mellitus Patients Attending Fenote Selam Hospital, West Gojam, Northwest Ethiopia: A Cross Sectional Study. *BMC Blood Disorders*, **13**, Article No. 6. https://doi.org/10.1186/2052-1839-13-6

[22] Thomas, M.C., MacIsaac, R.J., Tsalamandris, C., Molyneaux, L., Goubina, I., Fulcher, G., *et al.* (2004) The Burden of Anaemia in Type 2 Diabetes and the Role of Nephropathy: A Cross-Sectional Audit. *Nephrology Dialysis Transplantation*, **19**, 1792-1797. https://doi.org/10.1093/ndt/gfh248

[23] Dikow, R., Schwenger, V., Schomig, M. and Ritz, E. (2002) How Should We Manage Anaemia in Patients with Diabetes? *Nephrology Dialysis Transplantation*, **17**, 67-72.

https://doi.org/10.1093/ndt/17.suppl_1.67

[24] Ishimura, E., Nishizawa, Y., Okuno, S., Matsumoto, N., Emoto, M., Inaba, M., *et al.* (1998) Diabetes Mellitus Increases the Severity of Anemia in Non-Dialyzed Patients with Renal Failure. *Journal of Nephrology*, **11**, 83-86.

[25] El-Achkar, T.M., Ohmit, S.E., McCullough, P.A., Crook, E.D., Brown, W.W., Grimm, R., *et al.* (2005) Higher Prevalence of Anemia with Diabetes Mellitus in Moderate Kidney Insufficiency: The Kidney Early Evaluation Program. *Kidney International*, **67**, 1483-1488. https://doi.org/10.1111/j.1523-1755.2005.00226.x

[26] National Kidney Foundation (2007) KDOQITM Clinical Practice Guidelines and Clinical Practice Recommendations for Diabetes and Chronic Kidney Disease. *American Journal of Kidney Diseases*, **49**, S12-S154. https://doi.org/10.1053/j.ajkd.2006.12.005

[27] Trinder, P. (1969) Determination of Glucose in Blood Using Glucose Oxidase with an Alternative Oxygen Acceptor. *Annals of Clinical Biochemistry*, **6**, 24-27. https://doi.org/10.1177/000456326900600108

[28] Genc, S., Omer, B., Gurdol, F., Ince, N., Bal, F. and Gurdol, F. (2012) Evaluation of Turbidimetric Inhibition Immunoassay (TINIA) and HPLC Methods for Glycated Haemoglobin Determination. *Journal of Clinical Laboratory Analysis*, **26**, 481-485. https://doi.org/10.1002/jcla.21550

[29] Levey, A.S., Bosch, J.P., Lewis, J.B., Greene, T., Rogers, N. and Roth, D. (1999) A More Accurate Method To Estimate Glomerular Filtration Rate from Serum Creatinine: A New Prediction Equation. *Annals of Internal Medicine*, **130**, 461-470. https://doi.org/10.7326/0003-4819-130-6-199903160-00002

[30] Levey, A.S., Coresh, J., Greene, T., Stevens, L.A., Zhang, Y., Hendriksen, S., *et al.* (2006) Using Standardized Serum Creatinine Values in the Modification of Diet in Renal Disease Study Equation for Estimating Glomerular Filtration Rate. *Annals of Internal Medicine*, **145**, 247-254. https://doi.org/10.7326/0003-4819-145-4-200608150-00004

[31] Bain, B. (2006) Blood Cells: A Practical Guide. 4th Edition, Blackwell, Oxford. https://doi.org/10.1002/9780470987551

[32] Goddard, A.F., James, M.W., McIntyre, A.S. and Scott, B.B. (2011) Guidelines for the Management of Iron Deficiency Anaemia. *Gut*, **60**, 1309-1316. https://doi.org/10.1136/gut.2010.228874

[33] Lam, A.P., Gundabolu, K., Sridharan, A., Jain, R., Msaouel, P., Chrysofakis, G., *et al.* (2013) Multiplicative Interaction between Mean Corpuscular Volume and Red Cell Distribution width in Predicting Mortality of Elderly Patients with and without Anemia. *American Journal of Hematology*, **88**, E245-E249. https://doi.org/10.1002/ajh.23529

[34] Barbieri, J., Fontela, P.C., Winkelmann, E.R., Zimmermann, C.E.P., Sandri, Y.P., Mallet, E.K.V., *et al.* (2015) Anemia in Patients with Type 2 Diabetes Mellitus. *Anemia*, **2015**, Article ID: 354737. https://doi.org/10.1155/2015/354737

[35] Peduzzi, P., Concato, J., Kemper, E., Holford, T.R. and Feinstein, A.R. (1996) A Simulation Study of the Number of Events Per Variable in Logistic Regression Analysis. *Journal of Clinical Epidemiology*, **49**, 1373-1379. https://doi.org/10.1016/S0895-4356(96)00236-3

[36] Shaheen, E.S. (2019) Prevalence of Anemia in Patients with Type 2 Diabetes. *Journal of Research in Medical Sciences*, **2**, 114-117. https://doi.org/10.4103/JMISR.JMISR_29_19

[37] AlDallal, S.M. and Jena, N. (2018) Prevalence of Anemia in Type 2 Diabetic Pa-

tients. *Journal of Hematology & Oncology*, **7**, 57-61. https://doi.org/10.14740/jh411w

[38] Sharif, A., Younus, S., Baig, K. and Ali, N. (2014) Prevalence and Risk of Anemia in Type-2 Diabetic Patients. *Health*, **6**, 1415-1419. https://doi.org/10.4236/health.2014.612173

[39] Taderegew, M.M., Gebremariam, T., Tareke, A.A. and Woldeamanuel, G.G. (2020) Anemia and Its Associated Factors among Type 2Diabetes Mellitus Patients Attending DebreBerhan Referral Hospital, North-East Ethiopia: A Cross-Sectional Study. *Journal of Blood Medicine*, **11**, 47-58. https://doi.org/10.2147/JBM.S243234

[40] Bonakdaran, S., Gharebaghi, M. and Vahedian, M. (2011) Prevalence of Anemia in Type 2 Diabetes and Role of Renal Involvement. *Saudi Journal of Kidney Diseases and Transplantation*, **22**, 286-290.

[41] Hosseini, M.S., Rostami, Z., Saadat, A., Saadatmand, S.M. and Naeimi, E. (2014) Anemia and Microvascular Complications in Patients with Type 2 Diabetes Mellitus. *Nephro-Urology Monthly*, **6**, Article No. e19976. https://doi.org/10.5812/numonthly.19976

[42] Ranil, P.K., Raman, R., Rachepalli, S.R., Pal, S.S., Kulothungan, V., Lakshmipathy, P., *et al.* (2010) Anemia and Diabetic Retinopathy in Type 2 Diabetes Mellitus. *Journal of the Association of Physicians of India*, **58**, 91-94.

[43] Shams, N. and Osmani, M.H. (2015) Newly Diagnosed Anemia in Admitted Diabetics, Frequency, Etiology and Associated Factors. *Journal of College of Physicians and Surgeons Pakistan*, **25**, 242-246.

[44] Idris, I., Tohid, H., Muhammad, N.A., Radzniwan A Rashid, M., Mohd Ahad, A., Ali, N., *et al.* (2018) Anaemia among Primary Care Patients with Type 2 Diabetes Mellitus (T2DM) and Chronic Kidney Disease (CKD): A Multicentred Cross-Sectional Study. *BMJ Open*, **8**, e025125. https://doi.org/10.1136/bmjopen-2018-025125

[45] Thambiah, S.C., Samsudin, I.N., George, E., Kaur, L., Saat, N.S., Zanariah, H., *et al.* (2015) Anaemia in Type 2 Diabetes Mellitus (T2DM) Patients in Hospital Putrajaya. *Malaysian Journal of Medicine and Health Sciences*, **11**, 49-62.

[46] Fayed, H.M., Elsaied, A.R., Alsenbesy, M.A. and Moubark, I.A. (2013) Proportion of Anemia in Type 2 Diabetic Patients in Qena Governorate Case-Control Study: Clinical Correlates And prognostic Significance. *International Journal of Diabetes Research*, **2**, 64-75.

[47] Antwi-Bafour, S., Hammond, S., Adjei, J.K., Kyeremeh, R., Martin-Odoom, A. and Ekem, I. (2016) A Case-Control Study of Prevalence of Anemia among Patients with Type 2 Diabetes. *Journal of Medical Case Reports*, **10**, Article No. 110. https://doi.org/10.1186/s13256-016-0889-4

[48] Ahmed, A.T., Go, A.S., Warton, E.M., Parker, M.M. and Karter, A.J. (2010) Ethnic Differences in Anemia among Patients with Diabetes Mellitus: The Diabetes Study of Northern California (DISTANCE). *American Journal of Hematology*, **85**, 57-61. https://doi.org/10.1002/ajh.21577

[49] Alsayegh, F., Waheedi, M., Bayoud, T., Al Hubail, A., Al-Refaei, F. and Sharma, P. (2017) Anemia in Diabetes: Experience of a Single Treatment Center in Kuwait. *Primary Care Diabetes*, **11**, 383-388. https://doi.org/10.1016/j.pcd.2017.04.002

[50] Maninder, K. (2018) Dietary Intake, Prevalence, and the Effect of Anemia on Various Morphophysiological Variables of Postmenopausal Women of North India. *Journal of Mid-Life Health*, **9**, 72-78. https://doi.org/10.4103/jmh.JMH_20_18

[51] Kaur, R., Kaur, M. and Singh, J. (2018) Endothelial Dysfunction and Platelet Hyperactivity in Type 2 Diabetes Mellitus: Molecular Insights and Therapeutic Strategies.

*Cardiovascular Diabetology*, **17**, Article No. 121. https://doi.org/10.1186/s12933-018-0763-3

[52] Choi, C.W., Lee, J., Park, K.H., Yoon, S.Y., Choi, I.K., Oh, S.C., *et al.* (2004) Prevalence and Characteristics of Anemia in the Elderly: Cross-Sectional Study of Three Urban Korean Population Samples. *American Journal of Hematology*, **77**, 26-30. https://doi.org/10.1002/ajh.20140

[53] Salive, M.E., Cornoni-Huntley, J., Guralnik, J.M., Phillips, C.L., Wallace, R.B., Ostfeld, A.M., *et al.* (1992) Anemia and Hemoglobin Levels in Older Persons: Relationship with Age, Gender, and Health Status. *Journal of the American Geriatrics Society*, **40**, 489-496. https://doi.org/10.1111/j.1532-5415.1992.tb02017.x

[54] Gaskell, H., Derry, S., Moore, R.A. and McQuay, H.J. (2008) Prevalence of Anaemia in Older Persons: Systematic Review. *BMC Geriatrics*, **8**, Article No. 1. https://doi.org/10.1186/1471-2318-8-1

[55] Samuel, T.R., Tejaswi, N., Kumar, P., Prudhvi, K., Sravani, N.S., Govardhini, B., *et al.* (2018) Clinical Significance of Screening for Anaemia in Diabetic Patients. *International Journal of Pharmaceutical Sciences Research*, **48**, 20-24.

[56] Mounika, V., Sarumathy, S., Ebens, J.A. and Shanmugarajan, T.S. (2017) A Prospective Study on Incidence of Anaemia in Type 2 Diabetes Mellitus Patients. *Research Journal of Pharmacy and Technology*, **10**, 11-14. https://doi.org/10.5958/0974-360X.2017.00003.8

[57] Thomas, M., Tsalamandris, C., MacIsaac, R. and Jerums, G. (2005) Anaemia in Diabetes: An Emerging Complication of Microvascular Disease. *Current Diabetes Reviews*, **1**, 107-126. https://doi.org/10.2174/1573399052952587

[58] Chen, C.X.R., Li, Y.C., Chan, S.L. and Chan, K.H. (2013) Anaemia and Type 2 Diabetes: Implications from a Retrospectively Studied Primary Care Case Series. *Hong Kong Medical Journal*, **19**, 214-221. https://doi.org/10.12809/hkmj133814

[59] Adejumo, B.I., Dimkpa, U., Ewenighi, C.O., Onifade, A., Mokogwu, A., Erhabor, T., *et al.* (2012) Incidence and Risk of Anemia in Type-2 Diabetic Patients in the Absence of Renal Impairment. *Health*, **4**, 304-308. https://doi.org/10.4236/health.2012.46050

[60] Chaves, P.H.M., Ashar, B., Guralnik, J.M. and Fried, L.P. (2002) Looking at the Relationship between Hemoglobin Concentration and Prevalent Mobility Difficulty in Older Women. Should the Criteria Currently Used to Define Anemia in Older People Be Reevaluated? *Journal of the American Geriatrics Society*, **50**, 1257-1264. https://doi.org/10.1046/j.1532-5415.2002.50313.x

[61] Chaves, P.H.M., Semba, R.D., Leng, S.X., Woodman, R.C., Ferrucci, L., Guralnik, J.M., *et al.* (2005) Impact of Anemia and Cardiovascular Disease on Frailty Status of Community-Dwelling Older Women: The Women's Health and Aging Studies I and II. *Journals of Gerontology*: *Series A*, **60**, 729-735. https://doi.org/10.1093/gerona/60.6.729

[62] Beard, C.M., Kokmen, E., O'Brien, P.C., Anía, B.J. and Joseph Melton III, L. (1997) Risk of Alzheimer's Disease among Elderly Patients with Anemia: Population-Based Investigations in Olmsted County, Minnesota. *Annals of Epidemiology*, **7**, 219-224. https://doi.org/10.1016/S1047-2797(97)00015-X

[63] Thomson, C.A., Stanaway, J.D., Neuhouser, M.L., Snetselaar, L.G., Stefanick, M.L., Arendell, L., *et al.* (2011) Nutrient Intake and Anemia Risk in the Women's Health Initiative Observational Study. *Journal of the American Dietetic Association*, **111**, 532-541. https://doi.org/10.1016/j.jada.2011.01.017

[64] Merlin, C.T., Richard, J.M., Tsalamandris, C., Power, D. and Jerums, G. (2003) Un-

recognized Anemia in Patients with Diabetes: A Cross-Sectional Survey. *Diabetes Care*, **26**, 1164-1169. https://doi.org/10.2337/diacare.26.4.1164

[65] Christy, A.L., Manjrekar, P.A., Babu, R.P., Hegde, A. and Rukmini, M.S. (2014) Influence of Iron Deficiency Anemia on Hemoglobin A1C Levels in Diabetic Individuals with Controlled Plasma Glucose Levels. *Iranian Biomedical Journal*, **18**, 88-93.

[66] Sluiter, W.J., van Essen, L.H., Reitsma, W.D. and Doorenbos, H. (1980) Glycosylated Haemoglobin and Iron Deficiency. *Lancet*, **316**, 531-532. https://doi.org/10.1016/S0140-6736(80)91853-X

[67] Domanski, M.J., Sutton-Tyrrell, K., Mitchell, G.F., Faxon, D.P., Pitt, B. and Sopko, G. (2001) Determinants and Prognostic Information Provided by Pulse Pressure in Patients with Coronary Artery Disease Undergoing Revascularization. The Balloon Angioplasty Revascularization Investigation (BARI). *American Journal of Cardiology*, **87**, 675-679. https://doi.org/10.1016/S0002-9149(00)01482-X

[68] Kostis, J.B., Lawrence-Nelson, J., Ranjan, R., Wilson, A.C., Kostis, W.J. and Lacy, C.R. (2001) Association of Increased Pulse Pressure with the Development of Heart Failure in SHEP. Systolic Hypertension in the Elderly (SHEP) Cooperative Research Group. *American Journal of Hypertension*, **14**, 798-803. https://doi.org/10.1016/S0895-7061(01)02044-1

[69] Blacher, J., Staessen, J.A., Girerd, X., Gasowski, J., Thijs, L., Liu, L., *et al.* (2000) Pulse Pressure Not Mean Pressure Determines Cardiovascular Risk in Older Hypertensive Patients. *Archives of Internal Medicine*, **160**, 1085-1089. https://doi.org/10.1001/archinte.160.8.1085