

Original research article

## Prevalence of Anemia in Patients with type 2 Diabetes Mellitus at Tertiary Care Center, Karimnagar

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### Abstract

**Background:** Diabetes mellitus (DM) has a high prevalence worldwide. Anaemia is one of the most common conditions seen in diabetic patients which is the leading cause of morbidity in these patients. 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.

**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 the control group (10%). Diabetics had microcytic hypochromic anemia among 55%, 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

Anaemia is a common haematological finding in DM patients [1] It is an important global public health problem, affecting the lives of more than 2 billion people globally, accounting for about 30% of the world's population. Haematological changes in red blood cells (RBCs), white blood cells (WBCs), and the coagulation factors are shown to be directly associated with DM. 5, 6 Chronic hyperglycemia, hyperosmolarity, and increased levels of advanced glycation end-products affect the RBCs [2]. Diabetes mellitus (DM) has a high prevalence worldwide [3]. Anaemia is common but often overlooked in diabetes mellitus (DM) patients. 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 [4]. 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 [5]. 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 [6]. It is associated with increased perinatal mortality, immune incompetence, impaired mental development, and decreased performance at work [7]. It is a key indicator of chronic kidney disease and an important cardiovascular risk factor [8]. It is said to be highly prevalent affecting developing and developed countries, causing public health problem [9]. 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- $\alpha$ . Studies show that the longer the duration of the disease and/or loss of glycemic control, the higher inflammatory process [10]. 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 [11]. The inflammatory situation created by kidney disease also interferes with intestinal iron absorption and mobilization of inventories [12]. Therefore, diabetic patients with kidney disease have higher risk for developing anemia [13]. 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 B12-deficiency anemia [14]. 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 [15], anemia remains unidentified in most diabetic patients. Hence, it is important to identify anemia in diabetic patients.

### **Materials and Method :**

This Prospective study was carried out on 100 patients with type 2 DM attending Inpatient and outpatient department of General Medicine, CAIMS, Karimnagar, and 100 individuals as control group. This study was conducted over a period of 1 year after obtaining informed written consent from the patients approved by Institutional ethical committee.

### **Inclusion criteria :**

- Type 2 diabetics, good controlled DM [glycated hemoglobin (HbA1c)
- Patients on sulfonylureas and metformin were included.
- Anemic patients, with hemoglobin levels less than 13 g/dl for male and less than 12 g/dl for female,

### **Exclusion criteria\_:**

- Patients with type 1 diabetics,
- Gestational diabetics,
- patients on ACE inhibitors, hematinics, liver disease, and malignancy.

### **Method**

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
- (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  $[(140 - \text{age}) \times \text{weight (kg)} / \text{serum creatinine (mg/dl)}] \times 0.85$  (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 tests 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 25 and Microsoft Excel 2016 were used to analyze the data.

### Observation and Results

Our study showed following results

1.The prevalence of anaemia is significantly increased in patients with type 2 diabetes mellitus as compared to the control group.

2.Diabetic patients had microcytic hypochromic anemia among 55.4%, whereas 44.6% had normocytic normochromic anemia.

3. None of them had a macrocytic type of anemia.

4. 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.

5. As the level of albuminuria increased, the prevalence of anemia also increased.

6. There was a significant negative correlation between hemoglobin level and albuminuria and a significant positive correlation between hemoglobin level and creatinine clearance.

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

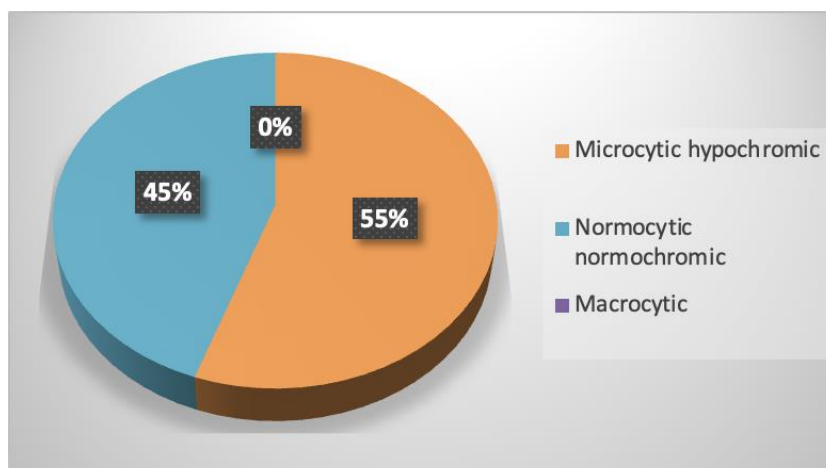
**Table 1 :Demographic and other parameter between cases and controls**

Variables	Case (n=100)	Control (n=100)	p value
Age	50.33±5.5	50.21±6.3	>0.05
Gender (male/female)	64/36	63/37	>0.05
Number of anemics	65	10	<0.05
HbA1c	6.5±0.43	5.4±0.79	<0.05
Hemoglobin (g/dl)	9.84±1.8	13.1±1.4	<0.05
Serum creatinine (mg%)	0.96±0.032	0.9±0.55	>0.05

**Table 2 : Distribution of anaemia in the study population**

Anaemia	Males(%)	Females(%)	Total(%)
Present	44(67.74%)	21(32.3%)	65(100%)
Absent	23(65.7%)	12(34.3%)	35(100%)
Total	67(67%)	33(33%)	100(100%)

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.



**Figure 1: Percentage of Morphological Types of anaemia in type 2 diabetes mellitus**

Figure 1 shows classification of anemia in patients with type 2 DM. Diabetic patients had microcytic hypochromic anemia among 55%, whereas 45% had normocytic normochromic anemia. None of them had a macrocytic type of anemia.

**Table 3 : Creatinine clearance in patients with type 2 diabetes mellitus**

Creatinine clearance (ml/min)	≤30 (%)	31-60	61-90	>90	P value
Anaemic (n=65)	8(100%)	33(91.7%)	22(53.7%)	2(13.3%)	<0.05
Non-Anaemic (n=35)	0	3(8.3%)	19(46.3%)	13(86.7%)	<0.05
Total (n=200)	8(8%)	36(36%)	41(41%)	15(15%)	<0.05

Table 3 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 4 : Relation of number of anemic patients with albuminuria**

Albuminuria (mg/day)	Anemic patients(%)	Nonanemic patients(%)	P- value
<30 (n=18)	4(22.4%)	16(88.9%)	<0.05
30-300 (n=37)	16(43.2%)	21(56.8%)	<0.05
>300 (n=45)	45(100%)	0	<0.05

Table 4 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 5 : Relation of albuminuria with creatinine clearance and hemoglobin level**

Albuminuria (mg)	Creatinine clearance (ml/min)	Hemoglobin level (mg/dl)	P-value
<30 (n=18)	105±11.4	12.5±3.4	<0.05
30-300 (n=37)	75.45±11.5	11.9±2.7	
>300 (n=45)	50.61±13.0	9.08±3.1	

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 individuals in the control group. In contrast, a study conducted by Kaushik et al. [16] showed 63% were anemic and 37% were nonanemic. In another study conducted by Ezenwaka et al. [17], 46.45% were anemic and 53.54% were nonanemic. Andrews and Arredondo [26] determined the presence of anemia in type 2 diabetic patients as well as evaluating the expression of genes related to inflammation and immune response. Chronic disease, such as DM, is accompanied by mild- to- moderate anemia, often called anemia of inflammation or infection or anemia of chronic disease (ACD) [18]. The results in few studies found that diabetic patients with anemia exhibit increased expression of proinflammatory cytokines as compared with patients with only diabetes. In an anemic patient, an increase in IL- 6 production, as well as B cell activity was confirmed which reinforced the association between IL- 6 production and anti erythropoietic action [19]. 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 processes present in diabetes [20].

In this study, of anemic patients 45 % had normocytic normochromic anemia, characterized as ACD [21]. ACD is a mild- to- moderate anemia shortening the survival of red blood cells (~80 days instead of 120 days normal) [22]. 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 [23]. 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 [24]. In our study, 55% 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 [16]. 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%. These findings were supported by Kaushik et al. [16], 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 the 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. [16] reported that as the level of albuminuria increased, the prevalence of anemia increased. Often, chronic diseases, such as DM, are accompanied by mild-to-moderate anemia, often called anemia of inflammation or infection or anemia of chronic disease [25].

**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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**Conflict of Interest : None**

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