Section: General Medicine

Original Research Article

STUDY OF ANAEMIA IN PATIENTS WITH TYPE 2 DIABETES MELLITUS IN A TERTIARY CARE HOSPITAL

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ABSTRACT

Background: Diabetes mellitus (DM) is a metabolic disorder of great impact worldwide. The diabetes affects about 7% of the population worldwide. The prevalence of diabetes among adults in the southern states of India has been reported as being 18.6 % in urban populations and 10% in rural populations. Anemia in diabetic person has a significant adverse effect on quality of life and is associated with disease progression and the development of comorbidities, as obesity and dyslipidemia that are strongly associated with diabetic framework and significantly contribute to increasing the risk of cardiovascular diseases. Therefore, it is important to diagnose and treat anaemia in diabetic mellitus patients.

Materials and Methods: A prospective observational study was conducted at Basaveshwar Teaching and General Hospital, Kalaburagi, over 18 months (August 2022–January 2024). A total of 125 T2DM patients aged ≥18 years, meeting ADA diagnostic criteria and without renal dysfunction, were included. Detailed clinical evaluations, hematological and biochemical investigations including HbA1c and peripheral smear, were performed. Statistical analysis was done using IBM SPSS v20.0, with $p < 0.05$ considered significant.

Results: Of the 125 participants, 62.4% were females and 37.6% males, with a female preponderance (M:F = 0.65:1). The prevalence of anemia was 96%, with moderate anemia being most common (55.2%), followed by severe (20.8%) and mild (20%). Normocytic normochromic anemia (43.2%) was the predominant peripheral smear pattern. Statistically significant associations were found between severity of anemia and increasing age, female gender, poor glycemic control (HbA1c >10%, $p<0.001$), longer diabetes duration (>10 years, $p<0.01$), and presence of comorbidities such as CAD and HTN ($p<0.001$). Anemia severity was also significantly linked to OHA use and uncontrolled fasting blood glucose levels.

Conclusion: Anaemia is one of the most common preventable conditions especially in diabetes mellitus Patients with type 2 DM and anemia were more prone for hypertension, CAD and other comorbidities. Periodic hematological screening in all diabetics presenting to hospital and adequate cost-effective remedial measures in the form of supplementation of iron and vitamins will result in better outcome.

Keywords: Anemia, Type 2 Diabetes Mellitus, Glycemic Control, HbA1c, Comorbidities.

INTRODUCTION

Diabetes mellitus (DM) is a metabolic disorder of great impact worldwide. According to the 2021 report by the IDF, approximately 537 million individuals globally were affected with diabetes, constituting roughly 10.5% of the world's population. This condition incurred healthcare expenditures totalling to billions of dollars annually. Projections indicate a surge in diabetes cases to 783 million by

2045, with associated healthcare costs estimated to surpass $1054 billion. However, almost half of all people with diabetes are unaware of their medical condition, with the highest prevalence of undiagnosed diabetes Mellitus (DM) found in low and middle income countries (LMICs) of the regions of Africa, the Western Pacific, and Southeast Asia.[1] The diabetes affects about 7% of the population worldwide. The prevalence of diabetes among adults in the southern states of India has been reported as being 18.6 % in urban populations and 10% in rural populations .[2] The prevalence rate is increasing in the younger age groups.[3] The long term complications of diabetes is expected to occur during their productive years causing severe life burden in the form of economic and social burden.[4] The increasing prevalence of type 2 diabetes mellitus is emerging a major public health concern.[5]

Its worldwide prevalence is increasing fast among developing countries now. The type 2 diabetes affects people day to day activities leading to limitation of the activities. The increasing prevalence of type 2 diabetes mellitus (DM2) has become a major public health concern. The diabetic patients' number has been increasing due to growing population and growth of urbanization, increase in change in food habits and sedentary lifestyle, and the longer survival of patients with DM. [6]

Diabetes is a highly disabling disease, which can cause major complications in our body like loss of sight in the form of retinopathy, amputations of the fingers, renal disease, anemia, and cardiovascular and brain complications, among others, impairing the functional capacity and autonomy and day to day activities. Under these circumstances, anemia in patients with diabetes is of great concern and it must be treated once diagnosed, since it may contribute to the pathogenesis and progression of cardiovascular disease, hypertension and various other complications.[7] The regular screening for anemia along with other complications associated with diabetes, is of great importance since it can help slow the progression of major complications in these patients. Anemia in diabetic person has a significant adverse effect on quality of life and is associated with disease progression and the development of comorbidities, as obesity and dyslipidemia that are strongly associated with diabetic framework and significantly contribute to increasing the risk of cardiovascular diseases.[8]

Now several studies suggest that anemia is twice as common in diabetics compared with non-diabetics. Despite these facts, anemia is unrecognized in 25% of the diabetic patients. Anemia also develops earlier and is more severe in patients with diabetes compared to non-diabetics leading to irreversible complications of DM. The role of diet in the etiology of T2DM was observed that the disease was almost confined to rich people who consumed oil, flour, and sugar in excessive amounts. Food intake has been strongly linked with obesity, not only related to the volume, composition and quality of diet. High intake of red meat, sweets and fried foods, contribute to the increased risk of insulin resistance and T2DM. An inverse correlation was observed between intake of vegetables and T2DM. Consumption of fruits and vegetables may protect the development of T2DM, as they are rich in nutrients, fibre and antioxidants which are considered as protective barrier against the diseases.[9]

The etiology of anemia in diabetes is multifactorial. Anemia in diabetic patients may lead to the development and progression of micro- and macrovascular complications of diabetes which affects the quality of life and gives an additional burden on the health of the patients.[10]

Therefore, it is important to diagnose and treat anaemia in diabetic mellitus patients. Thus, the present study is to evaluate the prevalence of anaemia in a sample of patients with type 2 diabetes mellitus and its prognostic significance in a tertiary care centre.

MATERIALS AND METHODS

This prospective observational study was conducted in the Department of General Medicine at Basaveshwar Teaching and General Hospital which is attached to Mahadevappa Rampure Medical College, Kalaburagi. The study duration was18 months extending from August 2022 to January 2024. A total of 125 patients were included in this study. Sample size was calculated using the formula $n=Z2\ p(1-p)/e2$. Where $p = 0.089$ (8.9% prevalence), $Z = 1.96$ at 95% confidence interval and $e = 0.05$ (margin of error). This yielded a sample size of approximately 124.5, which was rounded up to 125 participants. Patients were recruited consecutively from both outpatient and inpatient services on the basis of a predefined inclusion and exclusion criteria.

Eligible participants were individuals aged 18 years and above with a confirmed diagnosis of Type 2 Diabetes Mellitus as per American Diabetes Association (ADA) criteria. Data collection was carried out through a pre-structured proforma. A detailed clinical history was obtained and a detailed physical and systemic examination was done in all cases. Blood samples were collected for relevant laboratory investigations including complete blood count (CBC), fasting plasma glucose (FPG), 2-hour plasma glucose post-oral glucose tolerance test (OGTT), glycosylated hemoglobin (HbA1c), serum creatinine and urine albumin levels. These parameters were evaluated to assess the presence and type of anemia. Serum creatinine was done to rule out diabetic nephropathy as a potential confounding factor. Patients meeting inclusion criteria and without any exclusion conditions were enrolled after obtaining written and informed consent.

All data obtained were systematically recorded and tabulated. Identity and personal information of the participants was anonymised throughout the study. Patients were thoroughly evaluated to exclude those

with alternate aetiologies for anemia such as chronic blood loss, known pre-existing anemia or those on medications known to induce anemia. Additionally, patients with any stage of diabetic nephropathy, evidenced by microalbuminuria, macroalbuminuria or elevated serum creatinine were excluded to eliminate renal causes of anemia.

Statistical analysis was performed using IBM SPSS version 20.0. Descriptive statistics were used to summarize baseline demographic and clinical characteristics. Continuous variables were expressed as mean ± standard deviation (SD) and compared using Student's t-test or ANOVA as appropriate. Categorical variables were expressed as frequencies and percentages, and associations were assessed using the Chi-square test or Fisher's exact test. A p-value <0.05 was considered statistically significant.

Inclusion Criteria

- Patients aged 18 years and above.
- Diagnosed cases of Type 2 Diabetes Mellitus as per ADA criteria:
  - Fasting plasma glucose >126 mg/dL (7.0 mmol/L)
  - 2-hour plasma glucose >200 mg/dL (11.1 mmol/L) during OGTT
  - HbA1C >6.5% (48 mmol/mol)
  - Random plasma glucose >200 mg/dL (11.1 mmol/L) in symptomatic patients

Exclusion Criteria

- Patients below 18 years of age
- Patients with anemia due to chronic blood loss or pre-existing anemia
- Patients with known haemoglobinopathies such as sickle cell disease or thalassemia trait.
- Patients on medications known to cause anemia
- Diabetic patients with evidence of renal dysfunction (microalbuminuria, macroalbuminuria, or elevated serum creatinine).

RESULTS

Amongst the 125 cases of T2DM included in this study there were 78 (62.40%) females and 47 (37.60%) males. There was an overall female preponderance in the studied cases with a M:F ratio of 0.65:1 [Figure 1].

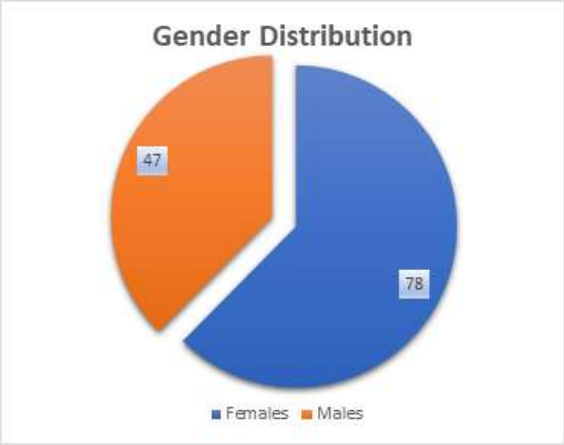

Figure 1: Gender Distribution of Studied Cases.

Table 1: demographic and clinical characteristics of the studied cases.

Parameter	Category	Frequency (n)	Percentage (%)
Age (years)	< 40	28	22.4
	41–50	31	24.8
	51–60	44	35.2
	> 60	22	17.6
	Total	125	100
Duration of Diabetes (years)	< 5	27	21.6
	5–10	57	45.6
	> 10	41	32.8
	Total	125	100
HbA1c (%)	< 7	29	23.2
	7–10	66	52.8
	> 10	30	24.0
	Total	125	100
Hemoglobin Category	Severe	26	20.8
	Moderate	69	55.2
	Mild	25	20.0
	Normal	5	4.0
	Total	125	100
History of CAD	Absent	54	43.2
	Present	71	56.8
	Total	125	100
History of HTN	Absent	44	35.2
	Present	81	64.8
	Total	125	100
OHA Use	No	56	44.8
	Yes	69	55.2
	Total	125	100
Insulin Use	No	92	73.6
	Yes	33	26.4
	Total	125	100
Combined OHA + Insulin Use	No	106	84.8
	Yes	19	15.2

	Total	125	100
FBS (mg/dL)	< 125	23	18.4
	> 125	102	81.6
	Total	125	100
PPBS (mg/dL)	< 200	52	41.6
	> 200	73	58.4
	Total	125	100

The analysis of the demographic and clinical characteristics of the studied cases showed that the majority of patients were between 51–60 years of age (35.2%), followed by those aged 41–50 years (24.8%). Most participants had diabetes for 5–10 years (45.6%), while 32.8% had it for more than 10 years. Glycemic control was poor in the majority, with 52.8% having HbA1c between 7–10% and 24% having values over 10%. Anemia was predominantly moderate in severity (55.2%), followed by severe (20.8%) and mild (20%), while only 4% had normal hemoglobin levels. A history of coronary artery disease was present in 56.8% and hypertension in 64.8% of the patients. Regarding treatment, 55.2% were on oral hypoglycaemic agents alone, 26.4% used insulin, and only 15.2% were on a combination of insulin and OHAs. Most patients had uncontrolled fasting blood sugar levels, with 81.6% recording FBS >125 mg/dL, and 58.4% had postprandial blood sugar levels >200 mg/dL [Table 1].

The analysis of the peripheral smear pattern of the studied cases showed that the most common finding was a normocytic normochromic pattern seen in 54 patients (43.2%), followed by microcytic hypochromic smears in 33 cases (26.4%). Dimorphic patterns were noted in 22 cases (17.6%), while megaloblastic changes were the least common, observed in 16 patients (12.8%) [Figure 2].

The analysis of the correlation between severity of anemia and gender and age among the studied cases showed that moderate anemia was the most frequent overall, especially among females (59.0%) and males (48.9%). Severe anemia was slightly more common in males (21.3%) than females (20.5%), while normal hemoglobin levels were observed only in males (10.6%) and not in any females. The difference in anemia severity between males and females was statistically significant ($p = 0.031$). Age-wise, a strong association was observed: all patients above 60 years had severe anemia (100%), while those in the 51–60 and 41–50 age groups predominantly had moderate anemia (90.9% and 93.5%, respectively). In contrast, patients below 40 years mostly had mild anemia (82.1%) or normal hemoglobin levels (17.9%). This age-related difference in anemia severity was statistically highly significant ($p < 0.001$) [Table 2].

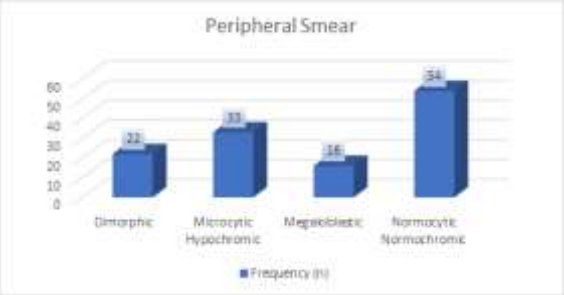

Figure 2: Peripheral Smear Findings in studied cases.

Table 2: correlation between severity of anemia and gender and age.

Parameter	Category	Severe n (%)	Moderate n (%)	Mild n (%)	Normal n (%)	Total n (%)	p-value
Sex	Female	16 (20.5%)	46 (59.0%)	16 (20.5%)	0 (0.0%)	78 (100%)	0.031
	Male	10 (21.3%)	23 (48.9%)	9 (19.1%)	5 (10.6%)	47 (100%)	
	Total	26 (20.8%)	69 (55.2%)	25 (20.0%)	5 (4.0%)	125 (100%)	
Age group (years)	< 40	0 (0.0%)	0 (0.0%)	23 (82.1%)	5 (17.9%)	28 (100%)	< 0.001
	41–50	0 (0.0%)	29 (93.5%)	2 (6.5%)	0 (0.0%)	31 (100%)	
	51–60	4 (9.1%)	40 (90.9%)	0 (0.0%)	0 (0.0%)	44 (100%)	
	> 60	22 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	22 (100%)	
	Total	26 (20.8%)	69 (55.2%)	25 (20.0%)	5 (4.0%)	125 (100%)	

The analysis of the correlation between anemia severity and various clinical parameters showed several statistically significant associations. Poor glycemic control strongly correlated with increasing anemia severity: all patients with HbA1c >10% had severe anemia (86.7%), while those with HbA1c <7% predominantly had mild anemia (82.8%) or normal hemoglobin (17.2%), with a highly significant p-value (<0.001). A similar trend was seen with diabetes duration; patients with diabetes >10 years had the highest rate of severe anemia (63.4%), whereas those with less than 5 years duration mostly had mild anemia or normal levels (81.5% and 18.5%, respectively), also statistically significant ($p < 0.01$). Presence of coronary artery disease (CAD) and hypertension (HTN) were both significantly associated with more severe anemia; none of the patients without CAD or HTN had severe anemia, while all patients with these comorbidities had either moderate or severe anemia ($p < 0.001$ for both). Likewise, patients on oral hypoglycaemic agents (OHAs) had a higher proportion of severe anemia (34.8%) compared to those not on OHAs, who mostly had mild anemia or normal hemoglobin levels ($p < 0.001$). The association between anemia severity and gender was also statistically significant ($p = 0.031$),

with normal hemoglobin found only in males (10.6%). Age was another important factor; severe anemia was exclusively seen in those above 60 years, while younger age groups mainly had mild or moderate anemia ($p < 0.001$). These findings highlight that poor glycemic control, longer diabetes duration, presence of CAD or HTN, and use of OHAs are all significantly associated with more severe forms of anemia [Table 3].

Table 3: Correlation between anemia severity and various clinical parameters.

Parameter	Category	Severe n (%)	Moderate n (%)	Mild n (%)	Normal n (%)	Total n (%)	p-value
HbA1c (%)	< 7	0 (0.0%)	0 (0.0%)	24 (82.8%)	5 (17.2%)	29 (100%)	< 0.001
	7–10	0 (0.0%)	65 (98.5%)	1 (1.5%)	0 (0.0%)	66 (100%)	
	>10	26 (86.7%)	4 (13.3%)	0 (0.0%)	0 (0.0%)	30 (100%)	
	Total	26 (20.8%)	69 (55.2%)	25 (20.0%)	5 (4.0%)	125 (100%)	
History of CAD	Absent	0 (0.0%)	24 (44.4%)	25 (46.3%)	5 (9.3%)	54 (100%)	< 0.001
	Present	26 (36.6%)	45 (63.4%)	0 (0.0%)	0 (0.0%)	71 (100%)	
	Total	26 (20.8%)	69 (55.2%)	25 (20.0%)	5 (4.0%)	125 (100%)	
History of HTN	Absent	0 (0.0%)	14 (31.8%)	25 (56.8%)	5 (11.4%)	44 (100%)	< 0.001
	Present	26 (32.1%)	55 (67.9%)	0 (0.0%)	0 (0.0%)	81 (100%)	
	Total	26 (20.8%)	69 (55.2%)	25 (20.0%)	5 (4.0%)	125 (100%)	
OHA Use	No	2 (3.6%)	24 (42.9%)	25 (44.6%)	5 (8.9%)	56 (100%)	< 0.001
	Yes	24 (34.8%)	45 (65.2%)	0 (0.0%)	0 (0.0%)	69 (100%)	
	Total	26 (20.8%)	69 (55.2%)	25 (20.0%)	5 (4.0%)	125 (100%)	
Sex	Female	16 (20.5%)	46 (59.0%)	16 (20.5%)	0 (0.0%)	78 (100%)	0.031
	Male	10 (21.3%)	23 (48.9%)	9 (19.1%)	5 (10.6%)	47 (100%)	
	Total	26 (20.8%)	69 (55.2%)	25 (20.0%)	5 (4.0%)	125 (100%)	
Age (years)	<40	0 (0.0%)	0 (0.0%)	23 (82.1%)	5 (17.9%)	28 (100%)	< 0.001
	41–50	0 (0.0%)	29 (93.5%)	2 (6.5%)	0 (0.0%)	31 (100%)	
	51–60	4 (9.1%)	40 (90.9%)	0 (0.0%)	0 (0.0%)	44 (100%)	
	>60	22 (100.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	22 (100%)	
	Total	26 (20.8%)	69 (55.2%)	25 (20.0%)	5 (4.0%)	125 (100%)	
DM Duration (years)	<5	0 (0.0%)	0 (0.0%)	22 (81.5%)	5 (18.5%)	27 (100%)	< 0.01
	5–10	0 (0.0%)	54 (94.7%)	3 (5.3%)	0 (0.0%)	57 (100%)	
	>10	26 (63.4%)	15 (36.6%)	0 (0.0%)	0 (0.0%)	41 (100%)	
	Total	26 (20.8%)	69 (55.2%)	25 (20.0%)	5 (4.0%)	125 (100%)	

The analysis of factors associated with HbA1c levels among the studied cases revealed several statistically significant associations. Patients without a history of coronary artery disease (CAD) or hypertension (HTN) were more likely to have better glycemic control, with 53.7% and 65.9% of them respectively having HbA1c <7%, whereas none of the patients with CAD or HTN had HbA1c <7%. Among those with CAD, 42.3% had HbA1c >10%, and similarly, 37% of hypertensive patients had HbA1c >10%, with both associations being highly significant ($p < 0.001$) [Table 4].

Table 4: Factors associated with HbA1c levels among the studied cases

Parameter	Category	HbA1C < 7%	HbA1C 7–10%	HbA1C > 10%	Total n (%)	p-value
History of CAD	Absent	29 (53.7%)	25 (46.3%)	0 (0.0%)	54 (100%)	< 0.001
	Present	0 (0.0%)	41 (57.7%)	30 (42.3%)	71 (100%)	
	Total	29 (23.2%)	66 (52.8%)	30 (24.0%)	125 (100%)	
History of HTN	Absent	29 (65.9%)	15 (34.1%)	0 (0.0%)	44 (100%)	< 0.001
	Present	0 (0.0%)	51 (63.0%)	30 (37.0%)	81 (100%)	
	Total	29 (23.2%)	66 (52.8%)	30 (24.0%)	125 (100%)	

DISCUSSION

In the present study there was a striking relationship between worsening glycemic control (as reflected by rising HbA1c) and increasing severity of hemoglobin (Hb) abnormalities among individuals with type 2 diabetes mellitus (T2DM). In a cross-sectional study by Mitku Mammo Taderegew et al conducted among 249 T2DM patients, poor glycemic control was significantly associated with anemia, along with other factors such as longer duration of diabetes and age over 60 years.[11] Similarly, a more recent investigation by H Agarwal et al. demonstrated that anemia is common among diabetic patients and is correlated with poor glycemic control.[12]

The gender-based differences observed in our cohort with females (62.4%) having a higher proportion of anemia is also consistent with gender related susceptibility to anemia reported in prior literature. Fathi AE et al identified female gender as a strong determinant of anemia along with hypertension, elevated BMI, impaired renal function and higher BUN levels.[13] The gender effect may reflect underlying differences in nutritional status, iron stores, or comorbidities that predispose women to anemia. Taken together this data suggest that female diabetic patients may warrant more vigilant hematologic monitoring particularly in the setting of poor glycemic control.

Beyond glycemic control and gender our study also found significant associations between severity of anemia and several clinical parameters such as presence of hypertension (HTN), history of coronary artery disease (CAD), duration of diabetes, age, and use of oral hypoglycaemic agents (OHA) or insulin. Patients with HTN or CAD had Severe or Moderate anemia. Similarly, a longer duration of diabetes (>10 years) and older age (>60 years) correlated with more severe Hb abnormalities. These findings mirror results from prior studies. Taderegew et al noted older age, longer duration of DM (>10 years), and presence of diabetic complications (including cardiovascular disease) as significant predictors of anemia in T2DM.[11] Moreover, J Barbieri et al in a cohort of 146 T2DM patients reported that hypertension and hematological variables had significant associations with anemia of chronic disease among diabetic patients. This suggested that comorbidities and diabetic complications contribute substantially to anemia prevalence in T2DM.[14] Thus, our study's pattern of increasing severity of anemia with accumulating comorbidities, longer disease duration and advancing age aligns with established observations.

An important implication of our findings concerns the possible bidirectional relationship between anemia and glycemic control. While our results suggest that poor glycemic control may lead to hemoglobin derangements there is also evidence from other studies that anemia—particularly iron deficiency anemia (IDA) can itself affect the interpretation of HbA1c. For example, B Aydın et al. demonstrated that IDA is associated with increased HbA1c concentrations and that HbA1c decreased significantly following iron supplementation.[15] Similarly, KM Srinath et al. found elevated HbA1c levels in diabetics with IDA compared to non anemic controls, and noted negative correlations between HbA1c and serum iron/ferritin, and a positive correlation with total iron binding capacity (TIBC) indicating that iron deficiency may spuriously raise HbA1c independently of glycemia.[16] These observations raise the possibility that in some of our study participants, low Hb (or anemia) might have influenced HbA1c measurements, potentially overestimating glycemic control in anemic patients or exaggerating glycemic derangement in iron deficient individuals. Therefore, while our data support a link between high HbA1c and severe Hb abnormalities, we must also consider that underlying anemia or iron status may confound HbA1c-based assessments.

Nevertheless, our data substantiate the clinical need for routine hematological evaluation in T2DM patients, not just for the detection of anemia but also for informed interpretation of HbA1c values. As shown by A Al-Dwairi et al. in a recent cross sectional study from Jordan, anemia was common among T2DM patients and strongly associated with poor glycemic control, especially in females, underscoring the importance of including anemia screening in standard diabetes care protocols.[17] Likewise, SK Subramaniam et al. reported that uncontrolled diabetics had significantly lower hemoglobin and hematocrit levels compared to controlled diabetics, with anemia prevalence particularly high in older age groups.[18] Given our findings, we support a similar approach: T2DM management should integrate periodic hemoglobin and iron studies — especially in patients with long-standing diabetes, comorbid HTN or CAD, or suboptimal glycemic control — to detect and treat anemia early and avoid misinterpretation of HbA1c.

Finally, our study adds to the growing body of evidence that T2DM is not just a disorder of glucose metabolism but frequently coexists with hematologic abnormalities that may influence both patient morbidity and the accuracy of routine biomarkers. However, we acknowledge certain limitations: we did not systematically assess iron status (serum ferritin, TIBC, transferrin saturation), renal function (e.g., eGFR), or other potential causes of anemia (nutritional deficiencies, hemoglobinopathies, chronic inflammation). These factors have been shown by prior studies to significantly affect hemoglobin levels in diabetics.[19] Future studies should incorporate a comprehensive panel — including iron studies, renal profile, inflammatory markers — to better delineate the etiology of anemia in diabetic populations. Furthermore, given possible confounding of HbA1c by anemia or iron deficiency, alternative measures of glycemic control (e.g., fructosamine, glycated albumin) might be considered in anemic diabetic patients. Similar hematological abnormalities in cases of diabetes were also reported by the authors such as Getawa S et al.[20]

CONCLUSION

Anaemia is common in patient with diabetes mellitus and is associated with an increased risk of hypertension, coronary artery disease and other comorbidities. Anemia is known to adversely affects quality of life and contribute to the progression of both microvascular and macrovascular complications in cases of diabetes. Periodic hematological screening of all diabetic patients is important along with cost-effective treatment through iron and vitamin supplementation to improve outcomes and prevent major complications.

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