

# ANEMIA AND ASSOCIATED RISK FACTOR IN PATIENTS WITH TYPE 2 DIABETES MELLITUS: A CROSS-SECTIONAL ANALYTICAL STUDY

*Original Research*

Muhammad Asif Zeb<sup>1</sup>, Abdul Razaq<sup>2</sup>, Azhar Mehmood<sup>1</sup>, Tanzeel Saleem Gandapur<sup>3</sup>, Ahmad Raza<sup>4</sup>, Muhammad Alamgir Khan<sup>5</sup>, Ahmad Ullah<sup>6</sup>, Zakir Ahmad\*<sup>1</sup>

<sup>1</sup>Department of Medical Laboratory Technology, Khyber Medical University, Peshawar, Pakistan.

<sup>2</sup>Department of Medical Laboratory Technology, Khyber Medical University, Peshawar, Pakistan.

<sup>3</sup>Department of Dental Technology, Khyber Medical University, Peshawar, Pakistan.

<sup>4</sup>Department of Respiratory Therapy & Intensive Care, Khyber Medical University, Peshawar, Pakistan.

<sup>5</sup>Army Medical Corps school, Centre, and record wing, Abbottabad, Pakistan.

<sup>6</sup>Department of Anaesthesia Technology, Khyber Medical University, Peshawar, Pakistan.

**Corresponding Author:** Zakir Ahmad, Department of Medical Laboratory Technology, Khyber Medical University, Peshawar, Pakistan, [Zakirahmad@kmu.edu.pk](mailto:Zakirahmad@kmu.edu.pk)

**Acknowledgement:** The authors sincerely acknowledge the cooperation of all participants and the support of the participating healthcare facilities in Peshawar.

Conflict of Interest: None

Grant Support & Financial Support: None

## ABSTRACT

**Background:** Type 2 diabetes mellitus (DM2) is a chronic metabolic disorder increasingly associated with systemic complications beyond hyperglycemia. Among these, anemia remains under-recognized despite its potential to worsen morbidity, functional capacity, and cardiovascular risk. Limited regional evidence exists regarding the burden of anemia and its associated risk factors among diabetic populations in Pakistan, particularly in Khyber Pakhtunkhwa.

**Objective:** To determine the frequency of anemia and identify associated risk factors among patients with type 2 diabetes mellitus.

**Methods:** This cross-sectional analytical study included 150 patients with confirmed DM2 recruited from multiple healthcare facilities in Peshawar. Blood samples were collected under aseptic conditions. Hematological parameters were analyzed using the Sysmex 1000i automated hematology analyzer based on Coulter's principle. Biochemical parameters were measured using the COBAS-360 system operating on electrogenerated chemiluminescence. Anemia was classified according to WHO criteria. Data were analyzed using SPSS version 26. Chi-square test was applied to assess associations, with  $p < 0.05$  considered statistically significant.

**Results:** Among 150 participants, 89 (59.3%) were females and 61 (40.7%) were males. Anemia was identified in 93 (62.0%) patients. Of the anemic individuals, 71 (47.3%) had mild anemia, 19 (12.7%) had moderate anemia, and 3 (2.0%) had severe anemia. Normocytic normochromic anemia was the predominant morphological type. Significant associations were observed between anemia and educational qualification ( $p=0.03$ ), duration of diabetes ( $p=0.02$ ), frequent infections ( $p=0.006$ ), elevated creatinine ( $p=0.006$ ), raised blood urea ( $p=0.001$ ), increased alkaline phosphatase ( $p=0.011$ ), and thrombocytosis ( $p=0.001$ ). No significant association was found with sex ( $p=0.77$ ), diabetic meal plan adherence ( $p=0.94$ ), smoking ( $p=0.79$ ), exercise ( $p=0.50$ ), or other chronic complications.

**Conclusion:** Anemia was highly prevalent among patients with DM2 and was significantly associated with longer disease duration, lower educational status, recurrent infections, renal impairment markers, and thrombocytosis. Routine hematological screening should be integrated into diabetic care to facilitate early identification and comprehensive management of high-risk patients.

**Keywords:** Anemia, Diabetes Mellitus, Type 2, Infections, Renal Insufficiency, Risk Factors, Thrombocytosis, Urban Population.

## Anemia and Risk Factors in Type 2 Diabetes Mellitus

### Background

- Type 2 Diabetes Mellitus
- High prevalence of anemia

### Anemia

### Findings

62% of DM2 patients were anemic

Anemia more common in females in DM2

### Key Correlates

- Longer Duration
- Low Education
- Frequent Infections
- Renal Impairment
- Raised Alkaline Phosphatase

### Findings

Raised Alkaline Phosphatase

Renal Impairment

Thrombocytosis

### Conclusion

Routine hematologic screening should be incorporated into diabetic care

## INTRODUCTION

Diabetes mellitus type 2 (DM2) is a chronic, non-communicable metabolic disorder characterized by persistent hyperglycemia resulting from impaired insulin secretion, insulin resistance, or a diminished cellular response to insulin (1,2). It represents one of the most pressing global health challenges of the 21st century, not only because of its rapidly increasing prevalence but also due to its far-reaching systemic complications. Current estimates suggest that approximately 285 million individuals worldwide are living with diabetes, with nearly 80% residing in low- and middle-income countries. A substantial proportion of cases are concentrated in the Western Pacific region, particularly in East Asia, reflecting the shifting epidemiological burden toward developing regions (3). In Pakistan, DM2 has emerged as a major public health concern, with an overall prevalence of 11.80%, affecting 6.58% of males and 5.22% of females. The burden is comparatively higher in urban populations (14.77%) than in rural communities (11.80%), underscoring the influence of urbanization and lifestyle transitions on disease patterns (4,5). Beyond chronic hyperglycemia, DM2 exerts profound multisystem effects. Long-standing disease is associated with microvascular and macrovascular complications, including diabetic retinopathy, neuropathy, and nephropathy, all of which contribute significantly to morbidity and reduced quality of life. Persistent metabolic dysregulation and oxidative stress further promote tissue injury, endothelial dysfunction, and progressive organ damage (6,7). The development and progression of DM2 are influenced by a constellation of modifiable and non-modifiable risk factors. Advancing age, obesity—particularly central adiposity—sedentary lifestyle, excessive caloric and fat intake, family history, gestational diabetes, polycystic ovary syndrome, severe mental illness, hypertension, dyslipidemia, elevated triglycerides, reduced high-density lipoprotein (HDL) levels, and consumption of sugar-sweetened beverages are all well-established contributors to increased disease susceptibility and severity (8). These metabolic and behavioral determinants often coexist, creating a complex interplay that accelerates disease progression and complication risk.

Among the less frequently highlighted yet clinically significant comorbidities in DM2 is anemia. Anemia is functionally defined as a reduction in hemoglobin concentration below age- and sex-specific reference values, leading to a decreased oxygen-carrying capacity of red blood cells and subsequent tissue hypoxia. Its diagnostic thresholds may vary according to altitude, smoking status, and pregnancy, but it remains one of the most prevalent hematological disorders globally (9). In individuals with diabetes, anemia is particularly common, especially among those with albuminuria or impaired renal function, where reduced erythropoietin production and chronic inflammation contribute to its pathogenesis (10,11). Importantly, anemia in diabetic patients may exacerbate cardiovascular risk, accelerate nephropathy progression, impair functional capacity, and adversely affect overall prognosis. Despite its clinical implications, anemia often remains under-recognized in routine diabetic care. Existing literature indicates variability in the reported prevalence of anemia among individuals with DM2, likely reflecting geographical, nutritional, socioeconomic, and healthcare-related differences. Data specific to certain regions, particularly within Khyber Pakhtunkhwa, remain limited (12,13). This gap in evidence restricts the ability to develop targeted screening and management strategies tailored to local populations. Furthermore, the relationship between anemia and factors such as duration of diabetes, lifestyle patterns, chronic diabetic complications, family history, exercise habits, smoking, and dietary practices has not been sufficiently explored within this context. Given the growing burden of DM2 and its potential to coexist with anemia, there is a pressing need to better understand the magnitude and determinants of this association in regional populations. The present study was therefore designed to determine the frequency of anemia among patients with diabetes mellitus type 2 registered in healthcare facilities of Khyber Pakhtunkhwa and to examine its association with disease duration, lifestyle characteristics, chronic complications, family history, exercise, smoking status, and meal patterns. By addressing this gap, the study aims to contribute evidence that may inform early screening strategies and integrated management approaches for individuals living with DM2.

## METHODS

This cross-sectional analytical study was conducted in both urban and rural areas of Peshawar among patients with diagnosed type 2 diabetes mellitus (DM2) who were registered at Hayatabad Medical Complex (HMC), Lady Reading Hospital (LRH), Diabetes Hospital and Research Center (DH&RC), and selected affiliated healthcare facilities in Peshawar. The study was carried out over a six-month period from March 2019 to August 2019. Ethical approval was obtained from the Undergraduate Study Committee of KMU-IPMS prior to commencement of the research. Formal written permission was secured from the Heads of the concerned departments of the participating institutions. All participants were approached respectfully, and the objectives and procedures of the study were explained in their native language. Verbal informed consent was obtained from each participant before enrollment, ensuring voluntary participation and confidentiality of personal information in accordance with ethical research principles. The required sample size was initially

calculated using the standard formula  $S = (Z^2 \times p(1-p)) / (M.E)^2$ , assuming a prevalence (p) of 50%, a margin of error of 5%, and a 95% confidence interval. This yielded a calculated sample size of 384 participants. However, due to time constraints and limited resources, the final sample size was reduced to 150 participants after formal approval from the Undergraduate Study Committee of KMU-IPMS. A non-probability consecutive sampling technique was employed to recruit eligible participants during the study period. The study included adult patients diagnosed with type 2 diabetes mellitus who were registered in the selected healthcare facilities and willing to participate. Patients were excluded if they had any known hematological conditions that could independently interfere with red blood cell production or hemoglobin levels, including lymphoproliferative or myeloproliferative disorders. Individuals with congenital kidney anomalies or other known conditions directly affecting hemoglobin measurements were also excluded to minimize confounding effects. Data were collected using a predesigned structured proforma through face-to-face interviews and review of relevant medical records. Sociodemographic characteristics, clinical history, lifestyle factors, and family history were documented. The dependent variable was anemia. Anemia was defined and classified according to the World Health Organization (WHO) reference criteria (14). Participants were considered anemic if hemoglobin levels were <12.5 g/dL in females and <13.5 g/dL in males. Independent variables included age, gender, duration of diabetes, smoking status, exercise habits, family history of diabetes, and presence of chronic diabetic complications. Participants who self-reported smoking at the time of evaluation were categorized as smokers. Individuals were considered physically inactive if they did not perform regular exercise at least four times per week.

Each participant was given a scheduled appointment for blood sample collection. Blood samples were collected under aseptic conditions by trained laboratory personnel. EDTA tubes were used for complete blood count (CBC), fluoride tubes for blood glucose estimation, and lithium heparin tubes for other biochemical parameters. Hematological parameters were analyzed using automated hematology analyzers, including Sysmex 1000i and Mindray BC-5000. Biochemical analyses, including blood glucose and other parameters, were performed using Micro-lab 300 and Roche Cobas 360 analyzers. Complete blood count, renal function tests (RFTs), liver function tests (LFTs), and blood glucose levels were measured according to standardized laboratory protocols (15). Hematological parameters were specifically processed using the automated Sysmex 1000i system to ensure accuracy and reproducibility (16). Renal function was assessed using serum creatinine, serum urea, and serum uric acid levels. Glomerular filtration rate (GFR) was estimated using the Cockcroft–Gault formula: Creatinine clearance (CrCl) =  $[(140 - \text{age}) \times \text{weight in kg}] / (\text{serum creatinine} \times 72)$  (17). Serum creatinine values above 1.2 mg/dL and GFR values less than 60 mL/min/1.73 m<sup>2</sup> calculated through the Cockcroft–Gault equation were considered indicative of impaired renal function, representing approximately a 50% reduction in normal kidney function (18,19). Data were entered and analyzed using the Statistical Package for Social Sciences (SPSS) version 26.0. Qualitative variables were presented as frequencies and percentages, whereas quantitative variables were expressed as mean  $\pm$  standard deviation, median (minimum–maximum), and mean values as appropriate. The chi-square test and Pearson's exact test were applied to compare categorical variables and to assess differences between patients with and without anemia. Spearman's rank correlation coefficient was used to determine associations between hemoglobin levels and biochemical or clinical parameters. A p-value of <0.05 was considered statistically significant, and all analyses were conducted with a 95% confidence interval.

## RESULTS

A total of 150 patients with type 2 diabetes mellitus (DM2) were included in the analysis. Of these, 89 (59.3%) were females and 61 (40.7%) were males. The age distribution showed that the majority of participants were aged 60 years and above (24.0%), followed by those aged 51–55 years (20.0%) and 56–60 years (16.0%). Younger age groups constituted a smaller proportion, with only 2.0% below 30 years of age. The overall distribution demonstrated that most participants were middle-aged to elderly individuals. Regarding lifestyle characteristics, 14 (9.33%) participants were active smokers at the time of assessment, 117 (78.0%) were non-smokers, and 19 (12.66%) had recently quit smoking. The mean body weight was 64 kg (SD  $\pm$ 2.194), with values ranging from less than 50 kg to 109 kg. The largest proportion of participants weighed between 50–55 kg (23.3%), followed by 61–65 kg (16.7%) and 66–70 kg (15.3%). A total of 111 (74.0%) participants reported adherence to a prescribed diabetic meal plan, whereas 39 (26.0%) did not follow dietary recommendations regularly. Regular physical activity was reported by 95 (63.33%) individuals. Family history of diabetes was present in 64% of participants. Chronic complications were frequently observed. Ophthalmic problems were reported in 108 (72.0%) participants. Cardiovascular conditions, including hypertension, coronary artery disease, stent placement, angiography, or bypass surgery, were present in 77 (51.33%) individuals. Dental and gum problems were identified in 45 (30.0%) participants. Diabetic foot complications, including amputations involving toes or lower limbs, were found in 68 (45.33%). Skin disorders were present in 37 (24.66%). Gastrointestinal complaints were reported by 74 (49.33%) participants. Renal impairment, based on renal function test



parameters, was observed in 44 (29.33%), while 108 (70.66%) had normal renal function. Elevated alkaline phosphatase (ALP) levels were detected in 22 (14.66%) participants, whereas 128 (85.33%) had normal ALP activity. Among female participants, 4 (4.08%) reported a history of miscarriage. Recurrent infections were documented in 49 (55.05%) of females.

Hematological analysis revealed that 93 (62.0%) participants were anemic according to WHO criteria (22). Among anemic patients, 71 (47.30% of total participants) had mild anemia, 19 (12.7%) had moderate anemia, and 3 (2.0%) had severe anemia. Mean corpuscular volume (MCV) ranged from 58 to 100 fL. Normocytic normochromic anemia was identified in 61 (40.7%) participants, microcytic hypochromic anemia in 32 (21.3%), and macrocytic patterns were observed in a smaller subset. Mean corpuscular hemoglobin (MCH) ranged from 20.5 to 37.0 pg, with a mean of 26.02 (SD  $\pm$ 3.20). Mean corpuscular hemoglobin concentration (MCHC) ranged from 18.9 to 38.30 g/dL, with a mean of 32.77 (SD  $\pm$ 5.6). Thrombocytosis (platelet count  $>450,000/\mu\text{L}$ ) was observed in 47 (31.3%) participants. Associational analysis demonstrated statistically significant relationships between anemia and educational qualification ( $p=0.03$ ), duration of diabetes ( $p=0.02$ ), frequent infections ( $p=0.006$ ), elevated creatinine levels ( $p=0.006$ ), blood urea ( $p=0.001$ ), alkaline phosphatase ( $p=0.011$ ), and thrombocytosis ( $p=0.001$ ). Anemia prevalence increased with longer duration of diabetes, particularly among those with more than 15 years of disease (27.95% in anemic vs 10.52% in non-anemic). Frequent infections were more common among anemic patients (40.86%) compared to non-anemic individuals (19.29%). Elevated blood urea and creatinine levels were also more frequently observed in anemic participants. No statistically significant association was found between anemia and sex ( $p=0.77$ ), diabetic meal plan adherence ( $p=0.94$ ), eye problems ( $p=0.71$ ), heart problems ( $p=0.15$ ), diabetic foot ( $p=0.10$ ), dental problems ( $p=0.13$ ), gastrointestinal problems ( $p=0.96$ ), kidney problems ( $p=0.96$ ), smoking status ( $p=0.79$ ), or exercise ( $p=0.50$ ), as all  $p$ -values exceeded 0.05.

**Table 1: Age wise distribution of the participant**

		Frequency	Percent
Valid	less than 30	3	2.0
	30 to 35	10	6.7
	36 to 40	14	9.3
	41 to 45	18	12.0
	46 to 50	15	10.0
	51 to 55	30	20.0
	56 to 60	24	16.0
	60+	36	24.0
	Total	150	100.0

**Table 2: Weight wise distribution of the participants**

		Frequency	Percent
Valid	less than 50 kg	4	2.7
	50 to 55 kg	35	23.3
	56 o 60 kg	22	14.7
	61 to 65 kg	25	16.7
	66 to 70 kg	23	15.3

	Frequency	Percent
71 to 75 kg	14	9.3
76 to 80 kg	10	6.7
81 to 85 kg	6	4.0
more than 85	11	7.3
Total	150	100.0

**Table 3: Association of Anemia with Sociodemographic, Clinical, and Biochemical Factors in Patients with Type 2 Diabetes Mellitus**

Variables	Anemia (Yes) n (%)	Anemia (No) n (%)	P-value
Educational qualification			0.03
Illiterate	69 (74.19%)	37 (64.91%)	
Literate	24 (25.80%)	20 (35.08%)	
Duration of diagnosis			0.02
< 4 years	15 (16.12%)	20 (35.08%)	
4 to 8 years	16 (17.20%)	15 (26.31%)	
9 to 12 years	16 (17.20%)	7 (12.28%)	
13 to 15 years	20 (21.50%)	9 (15.78%)	
> 15 years	26 (27.95%)	6 (10.52%)	
Frequent infection	38 (40.86%)	11 (19.29%)	0.006
Creatinine level	69 (74.19%)	54 (94.73%)	0.006
Blood Urea	62 (66.66%)	31 (54.38%)	0.001
Alkaline phosphatase	74 (79.56%)	54 (94.73%)	0.011
Thrombocytosis	38 (40.86%)	9 (15.78%)	0.001

**Table 4: Association of Anemia with Demographic Characteristics, Lifestyle Factors, and Diabetic Complications in Patients with Type 2 Diabetes Mellitus**

Variables	Anemia (Yes) n (%)	Anemia (No) n (%)	P-value
Sex			0.77
Male	37 (39.78%)	24 (42.10%)	
Female	52 (60.21%)	33 (57.89%)	
Diabetic Meal Plan			0.94
Regular	69 (74.19%)	42 (73.68%)	
Irregular	24 (25.80%)	15 (26.31%)	

Variables	Anemia (Yes) n (%)	Anemia (No) n (%)	P-value
Eye Problem	66 (70.96%)	42 (73.68%)	0.71
Heart Problem	25 (25.88%)	52 (91.22%)	0.15
Diabetic Foot	47 (50.53%)	21 (36.84%)	0.10
Teeth Problems	32 (34.40%)	13 (22.80%)	0.13
GI Problems	46 (49.46%)	28 (49.12%)	0.96
Kidney Problems	27 (29.03%)	17 (29.82%)	0.96
Smoking	9 (9.67%)	5 (8.77%)	0.79
Exercise	57 (61.29%)	38 (66.66%)	0.50

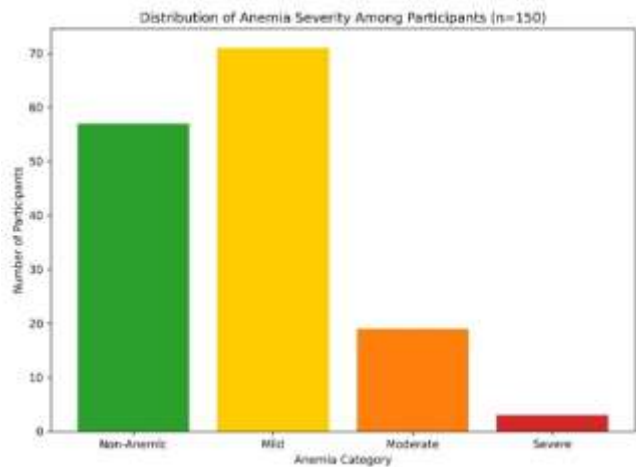


Figure 2 Distribution of Anemia Severity Among Participants (n=150)

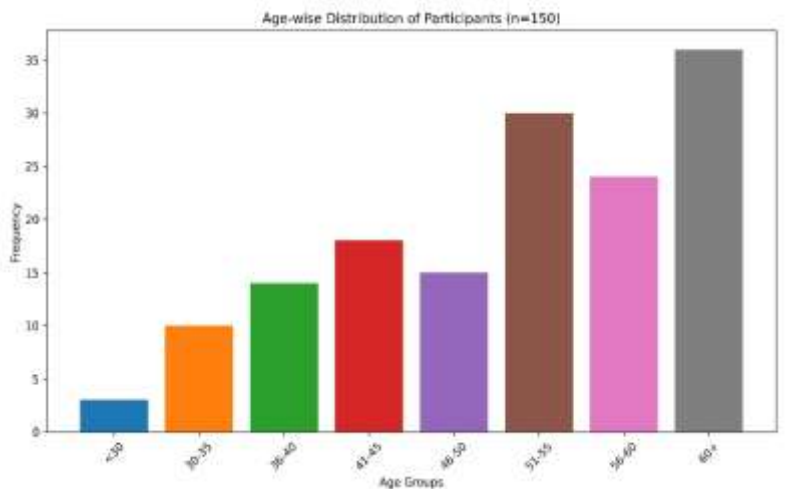


Figure 2 Age-wise Distribution of Participants (n=150)

DISCUSSION

The present study examined the frequency of anemia and its associated risk factors among patients with type 2 diabetes mellitus (DM2) in Peshawar, addressing an evidence gap that remains particularly pronounced in Pakistan and, more specifically, in Khyber Pakhtunkhwa (KPK). Although anemia has been increasingly recognized as a relevant comorbidity in DM2, it is still frequently under-screened and under-treated in routine diabetic care. In chronic inflammatory conditions, including diabetes, mild to moderate anemia is commonly observed and is often described as anemia of chronic disease or anemia of inflammation/infection, reflecting the role of persistent low-grade inflammation, altered iron handling, and impaired erythropoiesis (13). A notably high anemia prevalence was observed in this cohort, with 93 (62%) of participants classified as anemic, spanning mild, moderate, and severe categories. This frequency exceeded estimates reported in several studies conducted in other settings where anemia prevalence in DM2 ranged approximately between 19.6% and 23.3% after excluding iron-deficiency anemia and other systemic causes (14,15). Another large cohort-based study similarly reported anemia in roughly one-fifth of type 2 diabetic patients (16). The magnitude of anemia observed in this study may reflect population-specific and context-related factors. The sampled group included a substantial proportion of females, many participants were older, a considerable segment belonged to rural backgrounds, and a large number were recruited through hospital-associated services where comorbidities and complications were more likely to be present. In addition, frequent infections, high illiteracy, and longer duration of diabetes were prominent characteristics, each of which plausibly contributed to the observed burden of anemia by increasing inflammatory load, worsening nutritional and healthcare access pathways, and amplifying chronic disease impact

(17). The predominance of normocytic normochromic anemia in this population was clinically consistent with an inflammation-driven or chronic disease pattern. This observation aligned with the biological rationale that long-standing diabetes can produce chronic inflammatory states, repeated infections, and renal impairment, which collectively suppress erythropoietin response and reduce red blood cell survival. In line with prior literature, renal dysfunction appeared to be an important correlate of anemia, as anemia showed significant associations with creatinine and urea levels in this cohort. Previous evidence has emphasized albuminuria and impaired kidney function as key determinants of anemia in type 2 diabetes (18,19). Although albuminuria data were not reported in the current results, the observed associations with renal biochemical markers supported the broader concept that declining kidney function contributes meaningfully to anemia risk in DM2 through reduced erythropoietin production, uremic inflammation, and impaired iron utilization.

Disease duration also demonstrated a statistically significant relationship with anemia. This finding supported the plausible progression model in which prolonged hyperglycemia and cumulative metabolic stress increase the likelihood of microvascular injury, recurrent infection, chronic inflammation, and renal functional decline, all of which can contribute to reduced hemoglobin levels over time. Educational status also showed a significant association with anemia, suggesting that social determinants may have played an important role in shaping risk. Lower education levels can be linked to delayed healthcare seeking, reduced awareness of dietary planning, limited adherence to long-term disease monitoring, and poorer access to preventive care, collectively increasing vulnerability to complications including anemia. Frequent infections likewise showed a significant association with anemia, reinforcing the clinical relevance of inflammation and recurrent illness in influencing hemoglobin levels in diabetic populations (20). Thrombocytosis was present in 47 (31.3%) participants and was significantly associated with anemia. This pattern was clinically important because thrombocytosis may emerge as a reactive response to inflammation, infection, iron dysregulation, or chronic tissue injury. In diabetic populations, the coexistence of anemia and thrombocytosis may reflect persistent inflammatory activation and may carry potential implications for vascular risk, particularly in patients who also exhibit renal impairment or cardiovascular disease markers. Raised alkaline phosphatase activity was also associated with anemia, and this finding could reflect overlapping metabolic and organ-related disturbances, including hepatobiliary involvement, bone turnover abnormalities, or chronic kidney disease-related mineral and bone disorder, particularly in individuals with higher body mass index (21). The coexistence of anemia with renal biochemical derangements and inflammatory markers of clinical history suggested a multi-factorial pathway rather than a single isolated mechanism. In contrast, no statistically significant associations were observed between anemia and smoking status, exercise, or adherence to a diabetic meal plan. This lack of association did not necessarily indicate absence of effect; rather, it may have reflected measurement limitations. Smoking, exercise, and dietary adherence were recorded through self-report, which is prone to recall bias and social desirability bias, particularly in clinical environments where participants may underreport unhealthy behaviors or overreport positive routines. Additionally, the operational definition used for physical activity may not have aligned with standardized physical activity guidelines, potentially reducing discriminatory ability. Similarly, categorizing meal plan adherence as regular versus irregular without a validated dietary assessment tool may have limited precision and weakened the ability to detect meaningful associations (22).

The study offered several strengths. It generated region-specific data from multiple healthcare facilities and incorporated both hematological and biochemical assessments, allowing evaluation of anemia alongside renal and metabolic parameters. The inclusion of a broad set of potential correlates, including educational status, disease duration, recurrent infection history, and laboratory markers, strengthened the clinical interpretability of associations. The emphasis on identifying local patterns in KPK was also valuable given the relative scarcity of published evidence from this setting. However, important limitations constrained inference. The reduced sample size, decreased from the initially calculated 384 to 150, likely lowered statistical power and may have increased the risk of both type I and type II errors. The cross-sectional design prevented temporal inference, meaning causality between DM2-related factors and anemia could not be established. The results did not report multivariable modeling, which limited the ability to determine whether observed associations remained significant after adjustment for confounding factors such as age, sex distribution, disease duration, renal impairment, and comorbidities. Additionally, key etiological evaluations for anemia were not presented, including iron indices, vitamin B12/folate levels, inflammatory markers, or measures of albuminuria, each of which would have helped differentiate anemia of chronic inflammation from nutritional anemia, occult blood loss, or renal erythropoietin deficiency. The study also reported conditions such as miscarriage history, diabetic foot complications, and thrombocytosis, yet further diagnostic exploration was not available to clarify their underlying mechanisms, limiting clinical specificity. The large proportion of female participants may also have influenced anemia prevalence estimates, particularly if sex-specific contributors such as menstrual blood loss, nutritional factors, or reproductive health histories were unevenly distributed but not fully assessed (23). Future work would benefit from larger, adequately powered sampling with balanced representation by sex and residence, and the use of standardized instruments for dietary adherence and physical activity.



Prospective designs would help clarify temporal links between renal decline, inflammation, and hemoglobin reduction. Multivariable regression models should be incorporated to identify independent predictors of anemia in DM2. Diagnostic expansion to include ferritin, transferrin saturation, C-reactive protein, vitamin B12/folate levels, stool occult blood testing when appropriate, and albuminuria assessment would allow clearer classification of anemia subtypes and guide targeted interventions. Further investigation into thrombocytosis, diabetic foot ulcer pathways, and reproductive outcomes in diabetic females would also strengthen understanding of the broader clinical burden and refine screening priorities. Overall, the findings supported the need for routine anemia screening in DM2 care pathways in this region, particularly among individuals with longer disease duration, renal biochemical abnormalities, recurrent infections, and socioeconomically vulnerable backgrounds.

## CONCLUSION

Anemia was found to be a frequent and clinically relevant comorbidity among patients with type 2 diabetes mellitus, particularly in those with longer disease duration, lower educational status, recurrent infections, and biochemical evidence of renal and metabolic disturbance. The observed associations highlighted anemia as a manifestation of chronic disease burden that may further compromise quality of life and potentially aggravate diabetic progression and cardiovascular risk. These findings underscore the importance of incorporating routine hematological evaluation into standard diabetic care, especially for patients with prolonged illness and emerging complications. Strengthening early detection strategies and integrating laboratory markers such as renal parameters, platelet indices, and long-term glycemic indicators into clinical monitoring frameworks may enhance individualized management and improve overall outcomes in this population.

## AUTHOR CONTRIBUTIONS

Author	Contribution
Muhammad Asif Zeb	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Abdul Razaq	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Azhar Mehmood	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Tanzeel Saleem Gandapur	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Ahmad Raza	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Muhammad Alamgir Khan	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published
Ahmad Ullah	Contributed to study concept and Data collection Has given Final Approval of the version to be published
Zakir Ahmad*	Writing - Review & Editing, Assistance with Data Curation

## REFERENCES

1. Hu JC, Shao SC, Tsai DH, Chuang AT, Liu KH, Lai EC. Use of SGLT2 Inhibitors vs GLP-1 RAs and Anemia in Patients With Diabetes and CKD. *JAMA Netw Open*. 2024;7(3):e240946.
2. Scott L, Truong LL, Houlden RL, Wijeratne DT. Screening and Management Recommendations for Type 2 Diabetes in Women With Breast Cancer. *Can J Diabetes*. 2024;48(1):66-72.
3. Chang YL, Nfor ON, Chou YH, Hsiao CH, Zhong JH, Huang CN, et al. Risk of diabetes mellitus based on the interactive association between G6PD rs72554664 polymorphism and sex in Taiwan Biobank individuals. *Sci Rep*. 2024;14(1):12802.
4. Choi BG, Kim JB, Rha SW, Kim SW, Lee MW, Lee MS, et al. A relationship between unrecognized anaemia and the development of type 2 diabetes mellitus in patient with cardiovascular risks. *Clin Exp Pharmacol Physiol*. 2021;48(4):455-62.
5. Zhang J, Chen Y, Zou L, Gong R. Prognostic nutritional index as a risk factor for diabetic kidney disease and mortality in patients with type 2 diabetes mellitus. *Acta Diabetol*. 2023;60(2):235-45.
6. Zhang J, Xiao X, Wu Y, Yang J, Zou Y, Zhao Y, et al. Prognostic Nutritional Index as a Predictor of Diabetic Nephropathy Progression. *Nutrients*. 2022;14(17).
7. Hizomi Arani R, Fakhri F, Naeimi Tabiee M, Talebi F, Talebi Z, Rashidi N, et al. Prevalence of anemia and its associated factors among patients with type 2 diabetes mellitus in a referral diabetic clinic in the north of Iran. *BMC Endocr Disord*. 2023;23(1):58.
8. Rupasinghe S, Jayasinghe IK. Prevalence and associated factors of anaemia in patients with type 2 diabetes mellitus: a cross-sectional study in a tertiary care medical unit, Sri Lanka. *BMC Endocr Disord*. 2024;24(1):156.
9. Triposkiadis F, Xanthopoulos A, Parissis J, Butler J, Farmakis D. Pathogenesis of chronic heart failure: cardiovascular aging, risk factors, comorbidities, and disease modifiers. *Heart Fail Rev*. 2022;27(1):337-44.
10. Wu CT, Tsai YT, Jung HK, Fu SL, Hsiung CA, Liu HY, et al. Metformin and the Risk of Anemia of Advanced Chronic Kidney Disease in Patients With Type 2 Diabetes Mellitus. *J Clin Pharmacol*. 2022;62(2):276-84.
11. Siddiqui R, Obi Y, Dossabhoy NR, Shafi T. Is There a Role for SGLT2 Inhibitors in Patients with End-Stage Kidney Disease? *Curr Hypertens Rep*. 2024;26(12):463-74.
12. Huang B, Wen W, Ye S. Iron-Deficiency Anemia Elevates Risk of Diabetic Kidney Disease in Type 2 Diabetes Mellitus. *J Diabetes*. 2025;17(2):e70060.
13. Patel S, Ahsanuddin S, Cadwell JB, Lambert WC. The impact of diabetes mellitus on medical complication and mortality rates among inpatients with bullous pemphigoid. *Ir J Med Sci*. 2022;191(4):1669-75.
14. Stanigut AM, Pana C, Enciu M, Deacu M, Cimpineanu B, Tuta LA. Hypoxia-Inducible Factors and Diabetic Kidney Disease-How Deep Can We Go? *Int J Mol Sci*. 2022;23(18).
15. Valdez Ortiz R, Escorza-Valdivia S, Benitez-Renteria S, Lopez-Alvarenga JC, Pérez-Navarro LM. Factors of Poor Prognosis Associated with Chronic Kidney Disease by Stage in Ambulatory Patients: A Cross-sectional Study. *Arch Med Res*. 2022;53(5):524-32.
16. Koshino A, Neuen BL, Jongs N, Pollock C, Greasley PJ, Andersson EM, et al. Effects of dapagliflozin and dapagliflozin-saxagliptin on erythropoiesis, iron and inflammation markers in patients with type 2 diabetes and chronic kidney disease: data from the DELIGHT trial. *Cardiovasc Diabetol*. 2023;22(1):330.
17. Cases A, Cigarrán S, Luis Górriz J, Nuñez J. Effect of SGLT2 inhibitors on anemia and their possible clinical implications. *Nefrologia (Engl Ed)*. 2024;44(2):165-72.
18. Al-Dwairi A, Al-Shboul O, Al-U'datt D GF, Saadeh R, AlQudah M, Khassawneh A, et al. Effect of poor glycemic control on the prevalence and determinants of anemia and chronic kidney disease among type 2 diabetes mellitus patients in Jordan: An observational cross-sectional study. *PLoS One*. 2024;19(11):e0313627.

19. Zou Y, Zhao L, Zhang J, Wang Y, Wu Y, Ren H, et al. Development and internal validation of machine learning algorithms for end-stage renal disease risk prediction model of people with type 2 diabetes mellitus and diabetic kidney disease. *Ren Fail.* 2022;44(1):562-70.
20. Koshino A, Schechter M, Chertow GM, Vart P, Jongs N, Toto RD, et al. Dapagliflozin and Anemia in Patients with Chronic Kidney Disease. *NEJM Evid.* 2023;2(6):EVIDoa2300049.
21. Larsson SC, Wang L, Li X, Jiang F, Chen X, Mantzoros CS. Circulating lipoprotein(a) levels and health outcomes: Phenome-wide Mendelian randomization and disease-trajectory analyses. *Metabolism.* 2022;137:155347.
22. Xie L, Shao X, Yu Y, Gong W, Sun F, Wang M, et al. Anemia is a risk factor for rapid eGFR decline in type 2 diabetes. *Front Endocrinol (Lausanne).* 2023;14:1052227.
23. Zhao L, Han Q, Zhou L, Bai L, Wang Y, Wu Y, et al. Addition of glomerular lesion severity improves the value of anemia status for the prediction of renal outcomes in Chinese patients with type 2 diabetes. *Ren Fail.* 2022;44(1):346-57.