## SHORT REVIEW

# ANAEMIA IN DIABETES MELLITUS

UMMEY  MAIMUNA

**Abstract:**

*Anaemia in Diabetes Mellitus should be addressed properly. Because, anaemia in this immunocompromised state may deteriorate the physical status of this group of patients. Multiple factors have been found to be associated with anemia in Diabetes mellitus. This review article contains basic and updated concepts as well as recent studies regarding anaemia with diabetes mellitus.*

**Keywords**: *Anaemia; Diabetes Mellitus; nephropathy*

## Introduction:

Anaemia is a common hematological disorder among the diabetic patients.Globally, above 400 million adults live with Diabetes mellitus (DM).[1] According to International Diabetes Federation (IDF) the number is 473 million.[1] Mortality rates remain unacceptably high in Africa, with over 70% of all-cause mortality occurring in people living with DM under the age of 60 years.[2]

## Importance of anaemia in diabetic patients:

Anaemia may occur invariably in chronic diseases. DM itself is an immunocompromised state. Therefore, superimposed anaemia may worsen the physical status of the patient.

Anaemia is associated with an increased risk of microvascular and macrovascular disease. Anaemia may also be significant in determining the outcome of heart failure and hypoxia-induced organ damage in diabetes.[3-5]

Factors associated with anemia among diabetic patients:

*   Prevalence of anaemia in diabetic patients is linked with some factors like ethnicity ,age, sex, other microvascular complications, associated comorbities etc.[1,2]

*   Obesity, duration of time, albuminuria, hypertriglyceridemia have been reported as associated factors. [4]

*   In CKD, both absolute and relative iron deficiency are common. Absolute iron deficiency is defined as a depletion of tissue iron stores evidenced by a serum ferritin level <100 ng/ml or a transferrin saturation of <20%.[5] The most powerful predictors are transferrin saturation and GFR, acounting for 22% and 10% of the variance in Hb, respectively.[5]

## Pathophysiology:

The chronic hyperglycemia of diabetes, especially when poorly controlled, causes long-term damage, dysfunction, and failure of different organs. [6-9] Hyperglycemia causes the development of an inflammatory condition showed by the increased expression of proinflammatory cytokines such as IL-6, TNF-á, and NFêB.(9) IL-6 causes antierythropoietic effect [9] This cytokine changes the sensitivity of progenitors to erythropoietin (erythroid growth factor) and also promotes apoptosis of immature erythrocytes.[9] In chronic hyperglycemia, RBCs display morphological, enzymatic, and biophysical change.[10]

**Correspondence:** Dr. Ummey Maimuna, Chittagong Medical College Hospital, Email:  maimunab-intemohsin@gmail.com

**Studies relevant to anaemia with DM:**

**Table I**
*Studies relevant to DM with anaemia*
*Summary from these studies:*

| Year of publication | Place of the study | Mode of the study | Sample size | Important findings |
|---|---|---|---|---|
| 2021(1) | Ethopia | Systematic Review and Meta-analysis | 1978 | The pooled prevalence of anemia among diabetic patients was 24.81%.Age, glomerular filtration rate, and duration of being diabetic are factors significantly associated with the occurrence of anemia in diabetic patients. |
| 2023 (6) | Iran | Cross-sectional | 416 | 21.5% were anemic |
| 2014(7) | Iran | Cross-sectional | 305 | total of 93 patients (30.4%) had anemia including 46 (15.1%) with normochromic normocytic, 44 (14.4%) with hyperchromic microcytic, and 3 (1%) with hyperchromic macrocytic |
| 2021(3) | Ethopia | Systematic Review and Meta-analysis | 2889 | prevalence of anaemia in type I and type II DM patients was 16.78% [95% CI: 11.53-22.04] and 31.12% [95% CI; 9.66-52.58] respectively |
| 2022 (8) | Ethopia | Cross sectional | 261 | Total WBC, neutrophils, Monocyte, were significantly higher in poor glycemic and complicated T2DM |
| 2021(2) | Africa | Systematic Review and Meta-analysis | 5913 | The pooled prevalence of anemia was 35%,whereas the pooled prevalence was 56% in the patients with diabetic foot.The prevalence of anemia was higher in patients with type II DM than type I DM (35% vs 26%). |
| 2023(13) | Global survey | Systematic Review and Meta-analysis | 19,118 | higher prevalence of anemia was observed in Africa region |
| 2019(11) | Ethopia | Cross-sectional | 249 | One out of five T2DM patients had anemia. Poor glycemic control, decreased eGFR, presence of DM complications, duration of DM >10 years, and age >60 years were significantly associated with the occurrence of anemia among T2DM. |
| 2023(4) | South Asia | Systematic Review and Meta-analysis. | 14,194 | This studyfound variation in pooled prevalence estimates of anemia considering the type of DM, such as type 1 reported 2% (95% CI: 0.00–4.00), type-2 reported 48% (95% CI: 40.0–56.0, I2 = 98.94%) |

This article included mostly recent studies on diabetes mellitus with anaemia. According to the literature, 20%-25% diabetic patients are anaemic.Most of this population have diabetic nephropathy. Duration of DM,age and obesity are proportionaly related to anaemia. Interestingly, most of the studies conductrd in Africa. The underlying cause of geographical variation of prevelance of DM with anaemia is unknown. Microcytic, normocytic, macrocytic- all the morphology of anaemia has been reported. Studies mainly emphasized on type 2 DM.

**Anaemia & HbA1c:**
An increase in circulating RBC age can contribute to high HbA1c levels, Among patients with T2DM, iron deficiency anemia may misrepresent the glycemic status of patients due to elevated HbA1c levels [10,11]

**Treatment of anaemia:**
Treatment should be individual pattient-centered.It can vary with serum creatinine,age,level of hemoglobin, patient's adherence to therapy. Oral and injectable form of iron are available as primary options.Partial

anaemia correction became the standard of care. Because, trials showed near-normal haemoglobin levels impose a higher risk of adverse cardiovascular events.[12,13]

Controlled clinical trials of anemia treatment with erythropoietin stimulating agents (ESAs) demonstrated improved quality of life (QOL).[5]

**New update:**

•   Hypoxia-inducible factor prolyl hydroxylase inhibitors (HIF-PHIs) are small molecules than can be formulated into orally active pills. They simulate reduced tissue oxygen pressure, thus stimulating the production of endogenous erythropoietin (Epo) by the kidneys and liver. [14]

•   According to a recent study in 2020,Treatment with dapagliflozin can correct anaemia in T2D . A gradual increase in hemoglobin beyond week 4 may indicate an erythropoiesis-stimulatpatientsing effect of sodium-glucose cotransporter 2 inhibition.[12]

**Conclusion:**

Anaemia in diabetic patients should be addressed appropriately with consideration of microvascular and macrovascular complications. Further multinational studies can add valuable evidence.

**References:**

1.   Atlaw D, Tariku Z. Magnitude and factors associated with anemia among diabetic patients in Ethiopia: A systematic review and meta-analysis. SAGE Open Med. 2021 Jul 9;9:20503121211031126. doi: 10.1177/ 20503121211031126. PMID: 34290867; PMCID: PMC8274127. https://doi.org/10.1177/2050312 1211031126. PMid:34290867 PMCid:PMC 8274127

2.   Olum R, Bongomin F, Kaggwa MM, Andia-Biraro I, Baluku JB. Anemia in diabetes mellitus in Africa: A systematic review and meta-analysis. Diabetes Metab Syndr. 2021 Sep-Oct;15(5):102260. doi: 10.1016/ j.dsx.2021.102260. Epub 2021 Aug 28. PMID: 34479102. https://doi.org/10.1016/ j.dsx.2021.102260. PMid:34479102

3.   Adane T, Getawa S. Anaemia and its associated factors among diabetes mellitus patients in Ethiopia: A systematic review and meta-analysis. Endocrinol Diabetes Metab. 2021 May 14;4(3):e00260. doi: 10.1002/edm2.260. PMID: 34277984; PMCID: PMC8279623. https://doi.org/10.1002/edm2.260. PMid:34277984 PMCid:PMC8279623

4.   Mazumder H, Islam KF, Rahman F, Gain EP, Saha N, Eva IS, Shimul MMH, Das J, Hossain MM. Prevalence of anemia in diabetes mellitus in South Asia: A systematic review and meta-analysis. PLoS One. 2023 May 10;18(5):e0285336. doi: 10.1371/

journal.pone.0285336. Erratum in: PLoS One. 2023 Dec 7;18(12):e0295777. PMID: 37163539; PMCID: PMC10171606. https://doi.org/10.1371/ journal.pone.0295777. PMid:38060548 PMCid:PMC 10703192

5.   Uzma Mehdi, Robert D. Toto; Anemia, Diabetes, and Chronic Kidney Disease. Diabetes Care 1 July 2009; 32 (7): 1320-1326. https://doi.org/10.2337/dc08-0779 https://doi.org/10.2337/dc08-0779. PMid:19564475 PMCid:PMC2699743

6.   Hizomi Arani R, Fakhri F, Naeimi Tabiee M, Talebi F, Talebi Z, Rashidi N, Zahedi M. 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 Mar 9;23(1):58. doi: 10.1186/s12902-023-01306-5. PMID: 36894956; PMCID: PMC9997001. https://doi.org/10.1186/ s12902-023-01306-5 PMid:36894956 PMCid:PMC 9997001

7.   Hosseini MS, Rostami Z, Saadat A, Saadatmand SM, Naeimi E. Anemia and microvascular complications in patients with type 2 diabetes mellitus. Nephrourol Mon. 2014 Jul 5;6(4):e19976. doi: 10.5812/ numonthly.19976. PMID: 25695026; PMCID: PMC4317715. https://doi.org/10.5812/numonthly.1 9976

8.   Regassa DA, Kiya GT, Kebede RA, Beyene W. Assessment of Hematological Profiles and Prognostic Role of Hemogram-Derived Novel Markers for Diabetes Mellitus and Its Complications Among Type 2 Diabetes Mellitus Adult Patients Attending Bishoftu General Hospital, Central, Ethiopia: A Comparative Cross-Sectional Study. J Blood Med. 2023 Dec 28;14:681-699. doi: 10.2147/JBM.S435452. PMID: 38164459; PMCID: PMC10758194. https://doi.org/10.2147/ JBM.S435452. PMid:38164459 PMCid:PMC10758194

9.   Barbieri J, Fontela PC, Winkelmann ER, Zimmermann CE, Sandri YP, Mallet EK, Frizzo MN. Anemia in Patients with Type 2 Diabetes Mellitus. Anemia. 2015;2015:354737. doi: 10.1155/2015/354737. Epub 2015 Nov 11. PMID: 26640706; PMCID: PMC4658398. https://doi.org/10.1155/2015/354737. PMid:26640706 PMCid:PMC4658398

10.   Williams A, Bissinger R, Shamaa H, Patel S, Bourne L, Artunc F, Qadri SM. Pathophysiology of Red Blood Cell Dysfunction in Diabetes and Its Complications. Pathophysiology. 2023 Aug 2;30(3):327-345. doi: 10.3390/pathophysiology30030026. PMID: 37606388; PMCID: PMC10443300. https://doi.org/10.3390/ pathophysiology30030026. PMid:37606388 PMCid:PMC10443300

11.   Taderegew MM, Gebremariam T, Tareke AA, Woldeamanuel GG. Anemia and Its Associated Factors Among Type 2 Diabetes Mellitus Patients Attending Debre Berhan Referral Hospital, North-East Ethiopia: A Cross-Sectional Study. J Blood Med. 2020 Feb

11;11:47-58. doi: 10.2147/JBM.S243234. PMID: 32104127; PMCID: PMC7023873. https://doi.org/ 10.2147/JBM.S243234. PMid:32104127 PMCid:PMC 7023873

12. Thomas MC, Cooper ME, Rossing K, Parving HH. Anaemia in diabetes: Is there a rationale to TREAT? Diabetologia. 2006 Jun;49(6):1151-7. doi: 10.1007/ s00125-006-0215-6. Epub 2006 Apr 4. PMID: 16586069. https://doi.org/10.1007/s00125-006-0215-6. PMid:16586069

13. Arkew M, Asmerom H, Gemechu K, Tesfa T. Global Prevalence of Anemia Among Type 2 Diabetic Adult Patients: A Systematic Review and Meta-Analysis. Diabetes Metab Syndr Obes. 2023 Jul 31;16:2243-2254. doi: 10.2147/DMSO.S421851. PMID: 37545742; PMCID: PMC10402722. https://doi.org/10.2147/ DMSO.S421851. PMid:37545742 PMCid:PMC 10402722

14. Locatelli F, Del Vecchio L, Elliott S. The anaemia treatment journey of CKD patients: from epoetins to hypoxia-inducible factor-prolyl hydroxylase inhibitors. Clin Kidney J. 2023 Aug 17;16(10):1563-1579. doi: 10.1093/ckj/sfad105. PMID: 37779852; PMCID: PMC10539216. https://doi.org/10.1093/ckj/sfad105. PMid:37779852 PMCid:PMC10539216

15. Stefánsson BV, Heerspink HJL, Wheeler DC, Sjöström CD, Greasley PJ, Sartipy P, Cain V, Correa-Rotter R. Correction of anemia by dapagliflozin in patients with type 2 diabetes. J Diabetes Complications. 2020 Dec;34(12): 107729. doi: 10.1016/j.jdiacomp.2020. 107729. Epub 2020 Sep 5. PMID: 32948397. https:// doi.org/10.1016/j.jdiacomp.2020.107729. PMid:32948397.