ANAEMIA IN DIABETES MELLITUS

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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 anaemia 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). According to International Diabetes Federation (IDF) the number is 473 million. 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.

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.

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 comorbidities etc.
- Obesity, duration of time, albuminuria, hypertriglyceridemia have been reported as associated factors.
- 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%. The most powerful predictors are transferrin saturation and GFR, accounting for 22% and 10% of the variance in Hb, respectively.

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

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Studies relevant to anaemia with DM:

<table>
<thead>
<tr>
<th>Year of publication</th>
<th>Place of the study</th>
<th>Mode of the study</th>
<th>Sample size</th>
<th>Important findings</th>
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</thead>
<tbody>
<tr>
<td>2021(1) Ethiopia</td>
<td>Systematic Review and Meta-analysis</td>
<td>1978</td>
<td>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.</td>
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<tr>
<td>2023 (6) Iran</td>
<td>Cross-sectional</td>
<td>416</td>
<td>21.5% were anemic</td>
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<td>2014(7) Iran</td>
<td>Cross-sectional</td>
<td>305</td>
<td>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</td>
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<td>2021(3) Ethiopia</td>
<td>Systematic Review and Meta-analysis</td>
<td>2889</td>
<td>prevlance of anemia 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</td>
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<tr>
<td>2022 (8) Ethiopia</td>
<td>Cross sectional</td>
<td>261</td>
<td>Total WBC, neutrophils, Monocyte, were significantly higher in poor glycemic and complicated T2DM</td>
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<td>2021(2) Africa</td>
<td>Systematic Review and Meta-analysis</td>
<td>5913</td>
<td>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%).</td>
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<tr>
<td>2023(13) Global survey</td>
<td>Systematic Review and Meta-analysis</td>
<td>19,118</td>
<td>higher prevalence of anemia was observed in Africa region</td>
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<tr>
<td>2019(11) Ethiopia</td>
<td>Cross-sectional</td>
<td>249</td>
<td>One out of five T2DM patients had anemia. Poor glycemic control, decreased eGFR, presence of DM complications, duration of DM &gt;10 years, and age &gt;60 years were significantly associated with the occurrence of anemia among T2DM.</td>
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<tr>
<td>2023(4) South Asia</td>
<td>Systematic Review and Meta-analysis</td>
<td>14,194</td>
<td>This study found 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%)</td>
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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 proportionally related to anaemia. Interestingly, most of the studies conducted in Africa. The underlying cause of geographical variation of prevalence 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 anaemia may misrepresent the glycemic status of patients due to elevated HbA1c levels.10,11

Treatment of anaemia:
Treatment should be individual patient-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.\textsuperscript{12,13}

Controlled clinical trials of anemia treatment with erythropoietin stimulating agents (ESAs) demonstrated improved quality of life (QOL).\textsuperscript{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.\textsuperscript{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-stimulating effect of sodium-glucose cotransporter 2 inhibition.\textsuperscript{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:**

