

Molecular Basis of Diabetes: A Focus on Red Blood Cells Morphology

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Abstract

Diabetes mellitus, a chronic metabolic disorder characterized by elevated blood glucose levels, poses a significant global health challenge. While much research has centered on the impact of diabetes on major organs such as the pancreas, liver, and kidneys, the intricate relationship between diabetes and red blood cells (RBCs) morphology has gained recognition as a crucial aspect of the disease's pathophysiology. This review aims to elucidate the molecular mechanisms underlying the alterations in RBC morphology associated with diabetes. In diabetes, hyperglycemia induces a cascade of events that lead to oxidative stress, inflammation, and glycation, collectively contributing to changes in RBC structure and function. These alterations manifest as variations in cell size, shape, and membrane flexibility, ultimately impacting the rheological properties of blood. The compromised deformability of diabetic RBCs has implications for microcirculation and tissue perfusion, exacerbating complications such as diabetic retinopathy, nephropathy, and neuropathy.

Keywords: *Diabetes mellitus, Red blood cells (RBCs), Morphology, Hyperglycemia, Oxidative stress, Advanced glycation end products (AGEs), Complications*

Introduction

Diabetes mellitus is a complex metabolic disorder characterized by chronic hyperglycemia resulting from impaired insulin secretion, insulin action, or both. It is a major global health concern with a rising incidence and prevalence worldwide. The pathogenesis of diabetes involves a multitude of factors, including genetic predisposition, environmental influences, and molecular abnormalities. While much research has been dedicated to understanding the role of pancreatic beta cells, adipose tissue, and liver in diabetes, the impact of this disease on other cell types and tissues is also of great interest.¹⁻¹¹

Red blood cells (RBCs), also known as erythrocytes, are the most abundant cells in the bloodstream and play a crucial role in oxygen transport. Traditionally, the investigation of RBCs in diabetes has primarily focused on their association with microvascular complications such as retinopathy, nephropathy, and neuropathy. However, recent studies have highlighted the potential involvement of RBCs in the pathogenesis and progression of diabetes.¹³ One intriguing aspect of RBCs in diabetes is their morphology. Normal RBCs are biconcave discs with a characteristic shape that facilitates flexibility and efficient oxygen delivery. Alterations in RBC morphology, such as changes in size, shape, and deformability, have been observed in diabetic patients. These

Citation: Fartuun DF, Obeagu EI. Molecular Basis of Diabetes: A Focus on Red Blood Cells Morphology. *Elite Journal of Haematology*, 2024; 2 (1):19-25

alterations, commonly referred to as RBC morphological abnormalities, may have significant implications for the microcirculation, oxygen supply, and overall vascular health in individuals with diabetes.¹³ Understanding the molecular basis of RBC morphological changes in diabetes could provide valuable insights into the pathophysiology of the disease. Several mechanisms have been proposed to explain the observed alterations in RBC morphology, including hyperglycemia-induced oxidative stress, advanced glycation end products (AGEs) formation, impaired antioxidant defense systems, and altered membrane lipid composition. These factors can disrupt the delicate balance between RBC structure and function, potentially leading to impaired oxygen transport, increased hemolysis, and enhanced procoagulant activity.¹⁴

Furthermore, RBCs themselves may contribute to the development of insulin resistance and glucose homeostasis dysregulation through their interactions with other cell types. RBCs have been shown to adhere to vascular endothelial cells, release vasoactive substances, and interact with platelets and leukocytes, all of which can influence vascular function and contribute to the pathogenesis of diabetes. Overall, investigating the molecular basis of RBC morphological changes in diabetes represents an important avenue of research that has the potential to uncover new insights into the pathophysiology of the disease. By elucidating the intricate interplay between RBCs and diabetes, we may advance our understanding of the disease mechanisms and identify novel therapeutic targets for more effective management of diabetes and its complications.¹⁵

Diabetes mellitus

Diabetes mellitus is a complex metabolic disorder characterized by chronic hyperglycemia resulting from impaired insulin secretion, insulin action, or both. While the understanding of diabetes pathogenesis has traditionally focused on pancreatic beta cells, adipose tissue, and liver, recent research has shed light on the involvement of red blood cells (RBCs) in the molecular basis of the disease. This literature review aims to explore the molecular basis of diabetes, with a specific focus on RBC morphology and its potential implications in the pathophysiology of diabetes.¹⁶⁻²⁶

Alterations in RBC Morphology in Diabetes

Several studies have reported significant alterations in RBC morphology in individuals with diabetes. These alterations include changes in RBC size, shape, and deformability. For instance, diabetic patients often exhibit an increase in mean corpuscular volume (MCV), indicating larger RBCs compared to non-diabetic individuals. Moreover, RBCs from diabetic patients may show abnormal shapes, such as the presence of spherocytes or echinocytes. These morphological changes can impact RBC function, leading to impaired oxygen delivery and increased susceptibility to hemolysis.²⁷

Molecular Mechanisms of RBC Morphological Changes

The molecular mechanisms underlying RBC morphological changes in diabetes are multifactorial. One prominent factor is hyperglycemia-induced oxidative stress, which can lead to the production of reactive oxygen species (ROS). Excessive ROS generation can damage RBC membranes and cytoskeletal proteins, altering RBC morphology. Additionally, the formation of advanced glycation end products (AGEs) in diabetes can modify RBC membrane proteins, impairing their function and contributing to morphological abnormalities.²⁸

Implications of RBC Morphological Abnormalities

RBC morphological abnormalities in diabetes have important implications for microvascular complications. Alterations in RBC shape and deformability can affect blood flow and increase the risk of microvascular occlusions. These occlusions, coupled with impaired oxygen delivery, may contribute to the development of diabetic retinopathy, nephropathy, and neuropathy. Furthermore, abnormal RBC morphology can influence the rheological properties of blood, leading to increased blood viscosity and thrombotic events.²⁹

Interactions between RBCs and Other Cell Types

RBCs in diabetes not only undergo morphological changes but also interact with other cell types, contributing to the pathogenesis of the disease. RBCs have been shown to adhere to vascular endothelial cells, promoting endothelial dysfunction and inflammation. Additionally, RBCs can release vasoactive substances, such as nitric oxide and endothelin-1, which can further disrupt vascular homeostasis. These interactions between RBCs and endothelial cells, platelets, and leukocytes may exacerbate insulin resistance and contribute to the development of cardiovascular complications in diabetes.³⁰

Potential Therapeutic Strategies

Understanding the molecular basis of RBC morphological changes in diabetes opens avenues for potential therapeutic strategies. Targeting oxidative stress and AGE formation through antioxidant therapies or agents that inhibit AGE formation could potentially mitigate RBC morphological abnormalities. Additionally, interventions aimed at improving RBC deformability, such as

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pharmacological agents or physical exercise, may enhance microcirculation and alleviate complications associated with abnormal RBC morphology.³¹

Conclusion

Exploring the molecular basis of diabetes with a specific focus on RBC morphology provides valuable insights into the pathophysiology of the disease. The alterations in RBC size, shape, and deformability observed in diabetes have implications for microvascular complications and cardiovascular health. Understanding the molecular mechanisms underlying these morphological changes and the interactions between RBCs and other cell types can pave the way for novel therapeutic strategies to improve the management and outcomes of diabetes. Further research is warranted to unravel the intricate molecular pathways involved in RBC morphological changes and their impact on diabetes progression.

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