Elite Journal of Haematology. Volume 2 issue 1(2024), Pp. 19-25
https://epjournals.com/journals/EJPH

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

Dahir Farax Fartuun and Emmanuel Ifeanyi Obeagu

Department of Medical Laboratory Science, Kampala International University, Uganda

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.1[4]

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

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.

References

1. Hameed I, Masoodi SR, Mir SA, Nabi M, Ghazanfar K, Ganai BA. Type 2 diabetes mellitus: From a metabolic disorder to an inflammatory condition. *World Journal of Diabetes*, 2015; *6*(4), 598. https://doi.org/10.4239/wjd.v6.i4.598
2. Ifediora AC, Obeagu EI, Akahara IC, Eguzouwa UP. Prevalence of urinary tract infection in diabetic patients attending Umuahia health care facilities. J Bio Innov. 2016;5(1):68-82. links/5ae45fdfaca272ba507eb3c3/PREVALENCE-OF-URINARY-TRACT-INFECTION-IN-DIABETIC-PATIENTS-ATTENDING-UMUAHIA-HEALTH-CARE-FACILITIES.pdf.
3. Ugwu OP, Alum EU, Okon MB, Aja PM, Obeagu EI, Onyeneke EC. Ethanol root extract and fractions of Sphenocentrum jollyanum abrogate hyperglycaemia and low body weight in streptozotocin-induced diabetic Wistar albino rats. RPS Pharmacy and Pharmacology Reports. 2023;2(2):rqad010.
4. Obeagu EI, Obeagu GU. Utilization of Antioxidants in the management of diabetes mellitus patients. J Diabetes Clin Prac. 2018;1(102):2. links/5b6c2dec92851ca65053b74e/Utilization-of-Antioxidants-in-the-Management-of-Diabetes-Mellitus.pdf.
5. Obeagu EI, Okoroiwu IL, Obeagu GU. Some haematological variables in insulin dependent diabetes mellitus patients in Imo state Nigeria. Int. J. Curr. Res. Chem. Pharm. Sci. 2016;3(4):110-117. links/5ae4abee458515760ac07a13/Some-haematological-variables-in-insulin-dependent-diabetes-mellitus-patients-in-Imo-state-Nigeria.pdf.
6. Nwakuilite A, Nwanjo HU, Nwosu DC, Obeagu EI. Evaluation of some trace elements in streptozocin induced diabetic rats treated with Moringa oleifera leaf powder. WJPMR. 2020;6(12):15-18. links/5fcb587092851c00f8516430/EVALUATION-OF-SOME-TRACE-ELEMENTS-IN-STREPTOZOCIN-INDUCED-DIABETIC-RATS-TREATED-WITH-MORINGA-OLEIFERA-LEAF-POWDER.pdf.
7. Anyiam AF, Obeagu EI, Obi E, Omosigho PO, Irondi EA, Arinze-Anyiam OC, Asiyah MK. ABO blood groups and gestational diabetes among pregnant women attending University of Ilorin Teaching Hospital, Kwara State, Nigeria. International Journal of Research and Reports in Hematology. 2022;5(2):113-121.

8. Okafor CJ, Yusuf SA, Mahmoud SA, Salum SS, Vargas SC, Mathew AE, Obeagu EI, Shaib HK, Iddi HA, Moh'd MS, Abdulrahman WS. Effect of Gender and Risk Factors in Complications of Type 2 Diabetic Mellitus among Patients Attending Diabetic Clinic in Mnazi Mmoja Hospital, Zanzibar. Journal of Pharmaceutical Research International. 2021;33(29B):67-78.
9. Galano ES, Yusuf SA, Ogbonnia SO, Ogundahunsi OA, Obeagu EI, Chukwuani U, Okafor CJ, Obianagha NF. Effect of Extracts of Kigelia Africana Fruit and Sorghum Bicolor Stalk on the Biochemical Parameters of Alloxan-Induced Diabetic Rats. Journal of Pharmaceutical Research International. 2021;33(25B):86-97.
10. Kama SC, Obeagu EI, Alo MN, Ochei KC, Ezugwu UM, Odo M, Ikpeme M, Ukeekwe CO, Amaeze AA. Incidence of Urinary Tract Infection among Diabetic Patients in Abakaliki Metropolis. Journal of Pharmaceutical Research International. 2020 Nov 17;32(28):117-121.
11. Nwakulite A, Obeagu EI, Eze R, Vincent CC, Chukwurah EF, Okafor CJ, Ibekwe AM, Adike CN, Chukwuani U, Ifionu BI. Evaluation of Catalase and Manganese in Type 2 Diabetic Patients in University of Port Harcourt Teaching Hospital. Journal of Pharmaceutical Research International. 2021:40-45.
12. Kharroubi AT. Diabetes mellitus: The epidemic of the century. *World Journal of Diabetes*,2015; *6*(6), 850. https://doi.org/10.4239/wjd.v6.i6.850
13. Rahman MS, Hossain KS, Das S, Kundu S, Adegoke EO, Rahman MA, Hannan MA, Uddin MJ, Pang MG. Role of insulin in health and disease: An update. *International Journal of Molecular Sciences*, 2021; *22*(12), 1–19. https://doi.org/10.3390/ijms22126403
14. Wang Y, Yang P, Yan Z, Liu Z, Ma Q, Zhang Z, Wang Y, Su Y.The Relationship between Erythrocytes and Diabetes Mellitus. *Journal of Diabetes Research*, 2021; *2021*. https://doi.org/10.1155/2021/6656062
15. Buys AV, Van Rooy MJ, Soma P, Van Papendorp D, Lipinski B, Pretorius E. Changes in red blood cell membrane structure in type 2 diabetes: A scanning electron and atomic force microscopy study. *Cardiovascular Diabetology*, 2013; *12*(1). https://doi.org/10.1186/1475-2840-12-25
16. Alareeqi OAA, Obady YHA, Al-Khulaidi MQ, Al-Mureish K. Some Studies on Red Blood Cells Morphology of Healthy and Diabetic Patients in Taiz, Yemen. *Electronic Journal of University of Aden for Basic and Applied Sciences*, 2021; *2*(3), 109–123. https://doi.org/10.47372/ejua-ba.2021.3.105
17. Nwakulite A, Obeagu EI, Nwanjo HU, Nwosu DC, Nnatuanya IN, Vincent CC, Amaechi CO, Ochiabu O, Barbara MT, Ibekwe AM, Okafor CJ. Studies on Pancreatic Gene Expression in Diabetic Rats Treated with Moringa oleifera Leaf. Journal of Pharmaceutical Research International. 2021 May 4;33(28A):78-86.
18. Nwosu DC, Nwanjo HU, Obeagu EI, Ugwu GU, Ofor IB, Okeke A, Ochei KC, Kanu SN, Okpara KE. Evaluation of Lipoprotein A and Lipid Tetrad Index Pattern in Diabetic Patients Attending Metabolic Clinic in The Federal Medical Centre, Owerri, Imo State. World Journal of Pharmacy and Pharmaceutical Sciences, 2015; 4 (3):126-140
19. Ezema GO, Omeh NY, Egbachukwu S, Agbo EC, Ikeyi AP, Obeagu EI. Evaluation of Biochemical Parameters of Patients with Type 2 Diabetes Mellitus Based on Age and

Gender in Umuahia. Asian Journal of Dental and Health Sciences. 2023;3(2):32-6. http://ajdhs.com/index.php/journal/article/view/43.

20. Adu ME, Chukwuani U, Ezeoru V, Okafor CJ, Amaechi CO, Vincent CC, Obeagu GU, Eze R, Nnatuanya IN, Nwosu DC, Nwanjo HU. Studies on molecular docking of moringa oleifera leaf phytochemical constituents on alpha glucosidase, alpha amylase and dipeptidyl peptidase. Journal of Pharmaceutical Research International. 2021;33(28A):239-245.
21. Ezugwu UM, Onyenekwe CC, Ukibe NR, Ahaneku JE, Obeagu EI. Plasma Level of Macromolecules and Mathematical Calculation of Potential Energy in Type 2 Diabetic Individuals at NAUTH, Nnewi, Nigeria. Journal of Pharmaceutical Research International. 2021 Nov 2;33(47B):242-248.
22. Nwakulite A, Obeagu EI, Eze R, Ugochi VE, Vincent CC, Okafor CJ, Chukwurah EF, Unaeze BC, Amaechi CO, Okwuanaso CB, Chukwuani U. Estimation of Serum Glutathione Peroxidase in Streptozotocin Induced Diabetic Rat Treated with Bitter Leaf Extract. Journal of Pharmaceutical Research International. 2021;33(30B):200-206.
23. Okoroiwu IL, Obeagu EI, San Miguel HG, Bote SA, Obeagu GU. Characterisation of HLA-DR antigen in patients type 1 diabetes mellitus in patient attending a tertairy hospital in Enugu, south-east Nigeria. ACADEMIC JOURNAL. 2023.
24. Okoroiwu IL, Obeagu EI, Obeagu GU, Chikezie CC, Ezema GO. The prevalence of selected autoimmune diseases. Int. J. Adv. Multidiscip. Res. 2016;3(3):9-14.
25. Nwakuilite A, Nwanjo HU, Nwosu DC, Obeagu EI. Evaluation Of Enzyme Antioxidants In Streptozocin Induced Diabetic Rats Treated with Moringa Oleifera Leaf Powder. European Journal of Biomedical. 2020;7(11):285-288.
26. Nwosu DC, Nwanjo HU, Opara AU, Ofor IB, Obeagu EI, Ugwu GU, Ojiegbe GC, Nnorom RM, Nwokike GI, Okpara KE, Ochei KC. EVALUATION OF C-REACTIVE PROTEIN, SELENIUM AND GLYCOSYLATED HAEMOGLOBIN LEVELS IN DIABETIC PATIENTS ATTENDING METABOLIC CLINIC IN THE FEDERAL MEDICAL CENTRE, OWERRI, IMO STATE. World Journal of Pharmacy and Pharmaceutical Sciences, 2015; 4 (3):141-152. https://www.academia.edu/download/38320132/NWOSU_EMMA_9.pdf.
27. 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; *30*(3), 327–345. https://doi.org/10.3390/pathophysiology30030026
28. Pretorius, E. (2013). The adaptability of red blood cells. *Cardiovascular Diabetology*, *12*(1). https://doi.org/10.1186/1475-2840-12-63
29. Cho YI, Mooney MP, Cho DJ. Hemorheological disorders in diabetes mellitus. *Journal of Diabetes Science and Technology*, 2008; *2*(6), 1130–1138. https://doi.org/10.1177/193229680800200622
30. Passos A. The effect of red blood cell deformability on microscale blood flows. 2020.
31. Pan LJ. *https://theses.gla.ac.uk/ Theses Digitisation:* 284. 1999.