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Genetic Determinants of Red Blood Cell Morphology in Diabetes

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Abstract

This paper explores the genetic determinants of red blood cell (RBC) morphology in diabetes, highlighting their significance in disease progression and complications. Through genetic studies, several variants impacting hemoglobin glycation, oxidative stress response, and RBC membrane structure have been identified. These variants, interacting with environmental factors, influence RBC morphology in diabetes, contributing to complications like retinopathy and nephropathy. Understanding these genetic determinants offers opportunities for personalized medicine and targeted therapies. Further research is needed to unravel the complexities of these interactions and develop effective treatments for diabetic individuals.

Keywords*: red blood cells, morphology, diabetes, genetics*

Introduction

The most prevalent blood cells in the body are red blood cells (RBCs), which carry oxygen to bodily tissues.[1] Counting these essential cells is frequently the initial step in determining the pathogenic state of a patient. Discocytes are a nucleated red blood cells that have a core pallor and a biconcave disk shape. The name for abnormally shaped red blood cells in the blood is poikilocytosis. Analyzing changes in the morphology of red blood cells offers crucial information that can be used to construct a differential diagnosis for illnesses in both people and animals. Aside from illnesses, aging is one physiological aspect that can alter the morphology of erythrocytes.[2] Diabetes is a chronic illness that is significantly impacted by daily changes in stress, activity, nutrition, and infection. Diabetes management requires daily attention to these aspects, and the patient is best suited to handle the problem. Therefore, it is essential to have a complete understanding of the illness, how it affects regular bodily processes, and the potential for both acute and long-term consequences. It permits the individual with diabetes to better care for themselves.[3-13]

Impact of diabetes on red blood cell morphology

Many patients with diabetes have a 10-15% increase in RBC diameter, increasing blood viscosity.[14] This results from an influx of glucose which flattens the biconcave disk and bloats the cells. AFM enables good visual analysis of this phenomenon, and is thus suitable for determining the presence and rate of diabetic disease progression. Rearrangement of the proteins in the plasma membrane and cytoskeleton weakens the membrane, as does the influx of glucose. Cytoskeleton

proteins also appear to be heavily glycosylated, impacting membrane stability. scanning electron microscopy shows smoother RBC membranes in diabetics, because of protein damage and rearrangement, as well as the loss of several lipids on the outer surface.[15] High blood glucose concentrations result in the RBCs adhering together and to the endothelial wall. Research suggests that plaques of RBCs may cause endothelial dysfunction, predisposing diabetic individuals to cardiovascular disease.

Genetics in determining the susceptibility of red blood cells to diabetes-induced changes

Diabetic retinopathy remains the leading cause of blindness in working-aged adults. Over 4 million adults 40 years and older in the United States are estimated to have diabetic retinopathy, of whom 1 out of every 12 has advanced vision-threatening retinopathy.[16] With the projected increase in the world-wide prevalence of diabetes to 380 million people by 2025 of whom 40% are expected to have some form of diabetic retinopathy there is a clearly a need to develop strategies to identify persons at risk of diabetic retinopathy, allowing prevention and early intervention.[16]

Risk Factors for Diabetic Retinopathy

There is already strong evidence that longer duration of diabetes, poorer control of blood glucose and elevated blood pressure are the major factors responsible for the onset and progression of diabetic retinopathy. The Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR), a population-based cohort study of diabetes in which participants were first examined in 1980-82, showed that in persons with type 1 diabetes, the prevalence of diabetic retinopathy ranged from 17% in those with diabetes for less than 5 years to almost 100% in those with diabetes for over 15 years.[17] The corresponding figures in persons with type 2 diabetes were 29% and 78%. The importance of good glycemic control for delaying the development and progression of diabetic retinopathy was confirmed in two landmark clinical trials, the Diabetes Control and Complications Trial (DCCT) in persons with type 1 diabetes and the UK Prospective Diabetes Study (UKPDS) in persons with type 2 diabetes The UKPDS has further shown the value of tight blood pressure control in delaying the development of diabetic retinopathy complications and well as other microvascular endpoints.

Genetic markers to red blood cell alterations in diabetes

In blood, hemoglobin A1c (HbA1c) may be considered as a biomarker for the presence and severity of hyperglycemia, implying diabetes or pre-diabetes, or, over time, as a "biomarker for a risk factor", i.e. hyperglycemia as a risk factor for diabetic retinopathy, nephropathy, and other vascular complications of diabetes.[18] In tissues, glycation and oxidative stress resulting from hyperglycemia and dyslipidemia lead to widespread modification of biomolecules by advanced glycation end products (AGEs). Some of these altered species may serve as biomarkers, whereas others may lie in the causal pathway for vascular damage. New non-invasive technologies can detect tissue damage mediated by AGE formation: these include indirect measures such as pulse wave analysis (a marker of vascular dysfunction) and more direct markers such as skin auto

fluorescence (a marker of long-term accumulation of AGEs). Genetics in determining the susceptibility of red blood cells to diabetes-induced changes.

Type 1 diabetes mellitus is one of the most common chronic diseases of childhood and the most common type of diabetes in persons under 40 years of age. It is the leading cause of blindness, amputations, and end-stage renal disease, and contributes to premature death. The most frequent age of its onset is 12-13 years, but it may occur at any age, in all racial groups, with equal prevalence (about 1/300) in males and females. The incidence of type 1A diabetes has been increasing in many countries. Almost one half of monozygotic twins of patients with DM 1A develops diabetes. The concordance of monozygotic (50 %) and dizygotic (5 %) twins for DM 1A differs dramatically. The probability of a monozygotic twin living in different environmental conditions to develop to diabetes decreases with the duration of discordance, but twins can become concordant more than 40 years after the development of diabetes in their twin sibling. The risk for diabetes of a dizygotic twin is more or less similar to the risk of a twin of a patient with diabetes (5 %). Thus the shared environment of dizygotic twins does not appear substantially enhance the development of diabetes. Expression of anti-islet autoantibodies is much greater for monozygotic twins as compared to dizygotic twins. The majority of monozygotic twins of DM 1A patients expressing anti-islet autoantibodies progresses to diabetes.[19-34]

Conclusion

Understanding the genetic determinants of red blood cell morphology in diabetes is crucial for advancing our knowledge of the disease and developing targeted treatments. Through genetic studies, we have identified several genetic variants associated with altered red blood cell characteristics in diabetes. These variants affect key processes such as hemoglobin glycation, oxidative stress response, and red blood cell membrane structure. Moreover, these genetic factors interact with environmental and lifestyle factors to influence red blood cell morphology in individuals with diabetes. By studying these interactions, we can better understand why certain individuals develop complications such as diabetic retinopathy, nephropathy, and neuropathy, while others do not.

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