

Hematological Indices as Early Biomarkers of Diabetic Nephropathy

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Abstract

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Diabetic nephropathy (DN) is one of the most dangerous microvascular conditions that is linked to diabetes mellitus and is one of the major causes of end-stage renal disease on the international level. Recent reviews have emphasized the possible importance of the several hematological indices, such as red blood cell counts, hemoglobin levels, red cell distribution width (RDW), and mean platelet volume (MPV), as easily accessible biomarkers of the early identification of DN and its further monitoring. There is evidence that patients with diabetes who are found to have developed renal complications are often characterized by a low level of hemoglobin, low red blood cell counts and low hematocrit values, which are accompanied by elevated values of RDW and MPV. Such blood-related deviations could indicate underlying pathology infection processes, including chronic inflammation, oxidative stress, endothelial impairment, and erythropoiesis impairment due to chronic hyperglycemia and progressive renal disease. Since the parameters in question come as a result of regular complete blood count tests, they constitute relatively cheap and easily accessible resources that could help clinicians find diabetic patients at the risk of nephropathy. This review is a synthesis of modern evidence on the nature of hematological changes in diabetes mellitus and its future application in the detection and management of diabetic nephropathy at an early stage.

1. Introduction

Diabetes mellitus (DM) is one of the main chronic metabolic diseases in the world with a characteristic of stable hyperglycemia with the insulin secretion,

insulin resistance, or both pathophysiologic processes. There has been a keen increase in the global burden of DM in the past decades which has been majorly premised

by unhealthy behavioral traits in the form of sedentary practices and the antagonistic dietary patterns, as well as the ongoing skyrocketing obesity prevalence [1]. Type 2 diabetes mellitus (T2DM) is the most common of the heterogeneous phenotypes of the disease, with the proportion of all clinically diagnosed cases estimated as 90-95-percent, and with long-term morbidities intricately associated with the disease [2]. The case of diabetic nephropathy (DN) is the leading etiological determinant of chronic kidney disease (CKD) and resultant end-stage renal disease (ESRD) in various geographical locations [3]. The pathological consequences of DN develop gradually, with the continued hyperglycemia causing damage to the renal microvasculature, which triggers structural and functional disorganizations in the glomerular architecture [4]. Accumulatively, these changes stimulate a gradual but irresistible deterioration of the renal performance.

The most important thing is early diagnosis of DN since timely therapeutic intervention can significantly slow down the spread of the disease and reduce the risk of kidney failure. On the other hand, traditional diagnostic biomarkers often are only pathologically aberrant only after significant nephron damage, hence the urgent need to implement more sensitive,

pre-clinical detection methods. For this reason, considerable research attention has been directed toward identifying simple and cost-effective biomarkers that may help detect diabetic complications at an earlier stage [5]. Hematologic parameters as a result of a routine complete blood count (CBC) assays have received significant interest as future biomarkers in disease progression. The fact that erythrocyte indices, platelet measurements and inflammatory mediators are altered in individuals with diabetes is hypothesized to reflect systemic inflammation, oxidative stress and endothelial dysfunction that results due to chronic hyperglycemia.

According to the latest epidemiologic estimates, more than 537 million adults of the world are currently infected with diabetes; this number is expected to reach about 783 million by 2045, unless the current trends are reversed. Among diabetic individuals, approximately 30–40% eventually develop diabetic nephropathy, highlighting the urgent need for early detection strategies [6].

2. Hematological Alterations in Diabetes Mellitus

Diabetes mellitus can influence several hematological parameters due to persistent

metabolic disturbances and chronic inflammatory processes [7]. Specifically, the effect of diabetes mellitus on a variety of hematological parameters is due to the combined effect of persistent metabolic imbalances and chronic inflammation. Chronic hyperglycaemia has been proved to alter the morphology and functional properties of erythrocytes hence, altering deformability, lifespan, and oxygen-carrying capacity [8]. Empirical studies have reported that there is a reduction in the red blood cell quantities, the haemoglobin levels and haematocrit levels among patients with poorly controlled diabetes [9]. Such changes can be a result of a multiplicity of processes including impaired erythropoiesis, oxidative damage to erythrocytes, and hypo-production of erythropoietin [10].

Additionally, anaemia could particularly be worsened by chronic inflammation that is inherent to diabetes. Erythrocytic morphology and related indices could also be altered, such as mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), and mean corpuscular haemoglobin concentration (MCHC) [11]. The change in these parameters can be indicators of metabolic distress, membrane damage and reduced erythrocyte viability due to increased oxidative stress [12].

Moreover, inflammatory mediators that are generated during the condition of chronic metabolic disorders can disrupt the normal haematopoietic activity in the bone marrow; the disruption can disrupt the production of healthy erythrocytes, which also plays a role in the haematological abnormalities frequently found in diabetic patients [13]. There is an emerging body of evidence suggesting the haematological parameters may provide useful information regarding systemic metabolic maladjustments and inflammatory conditions in diabetes mellitus [14]. Seeing that these parameters are regularly measured in clinical practice, they might be used as convenient biomarkers to track the development of the disease and define those patients who are at high risk of developing complications [8].

This is further confirmed by recent clinical studies that indicate that persistent hyperglycaemia causes oxidative stress and inflammation that undermine erythrocyte membrane integrity and reduce the lifespan of red blood cells. These changes are also associated with the haematological abnormalities which are ubiquitous in diabetic patients [15].

3. Role of Red Cell Distribution Width in Diabetic Nephropathy

Red cell distribution width (RDW) is a hematological parameter used to measure the variability in the size of erythrocytes, which is also known as anisocytosis [16]. Rarely used historically, RDW was mostly utilized in the process of differentiating various anemic conditions in the field of diagnostic evaluation [17]. However, emerging empirical evidence indicates that RDW could be used as an adjunctive biomarker in a continuum of chronic diseases, such as cardiovascular disease, chronic kidney disease, and diabetes mellitus [18]. High levels of RDW in patients with diabetes have been associated with the inefficient glycemic control and the development of microvascular complications, including diabetic nephropathy and diabetic retinopathy [19]. It is hypothesized that the augmentation of RDW is the result of long-term chronologically inflammatory conditions, oxidative stress, and erythropoiesis disturbance due to chronic hyperglycemia [20].

Many studies have found significantly increased RDW values in patients with diabetic nephropathy in comparison with so-called healthy controls [21]. In addition, RDW has demonstrated a positive relationship with glycosylated hemoglobin (HbA1c) levels and urinary albumin-creatinine ratio suggesting its ability to

reflect metabolic regulation as well as kidney dysfunction [22]. Modern literature also hints that the higher the RDW the higher the diabetic renal disease can progress.

The high RDW levels are explained as signs of the inflammatory processes and endothelial dysfunction that are all known to cause renal damage in diabetics. One group of scientists has postulated that RDW might be a prognostic tool in diabetic microvascular complications in the early stages with the help of complementary inflammatory indices like neutrophil to lymphocyte ratio [23]. Together, they are likely to provide a more comprehensive assessment of patient systemic inflammation and the severity of the disease in the diabetic group.

4. Platelet Indices and Mean Platelet Volume

Platelets play a crucial role in maintaining vascular integrity and regulating thrombosis. In patients with diabetes mellitus, platelet function is frequently altered due to chronic hyperglycemia and metabolic stress. These alterations can promote platelet activation and aggregation, thereby contributing to endothelial dysfunction and the

development of microvascular complications [24].

Mean platelet volume (MPV) is a platelet size and functional activity biomarker. Platelets which are larger in diameter are more metabolically active and show an augmented pro-thrombotic ability [25]. Empirical studies have recorded high values of MPV in the subjects with type 2 diabetes mellitus, especially those with no optimal glycemic regulation and subsequent vascular complications [26].

High MPV has also been associated with progression of renal disease among diabetic populations. Activation of platelets in an augmented manner can contribute to vascular injury in the renal microcirculation, accelerating diabetic nephropathy development [27].

The inflammatory cytokine, especially interleukin-6, can activate the megakaryocyte in the bone marrow leading to the formation of bigger and more active platelets [28]. This is a possible pathophysiological mechanism that can explain the relationship that is found between elevated MPV and chronic inflammatory conditions including diabetes mellitus and chronic renal disease.

Other platelet indices such as platelet distribution width (PDW) and platelet count are also investigated as putative biomarkers

of the complications of diabetes in addition to MPV [29]. Some studies show that these platelet parameters are associated with albuminuria and lower glomerular filtration rate, thus opening up to their future application as predictors of diabetic nephropathy development [30,31].

5. Clinical Significance of Hematological Biomarkers

Diagnosis of diabetic nephropathy at early stage is still a significant problem in clinical practice[32]. Despite the fact that renal biopsy can be regarded as a gold standard in diagnosing kidney pathology, it is an invasive method, expensive, and is also linked to possible complications [33]. As a result, there is an increasing demand to find non-invasive and easily available biomarkers that could be used to help in facilitating early diagnosis and risk evaluation [34]. Potential biomarkers are hematology parameters based on standard complete blood count tests, which have a number of viable benefits. The tests are cheap, easily accessible and common in the clinical practice.

The changes in such parameters as red cell distribution width (RDW), the level of hemoglobin and the mean platelet volume (MPV) can be useful indicators of systemic inflammation, oxidative stress, and

endothelial dysfunction in diabetic patients [35]. The major hematological parameters associated with diabetic nephropathy and their potential clinical significance are summarized in Table 1. Recent researches indicate the potential of hematological indices integrated with conventional biochemical ones, in addition to HbA1c, serum creatinine, and urinary albumin levels, to improve the early diagnosis of diabetic nephropathy [36].

This combined strategy can help clinicians to more efficiently detect high-risk patients and have an opportunity to initiate the required therapeutic intervention at earlier stages. Although these were encouraging results, larger, prospective studies are necessary in order to prove the diagnostic and prognostic value of hematological parameters in diabetic nephropathy and to identify how to apply them in clinical practice [37].

Table 1. Hematological Biomarkers Associated with Diabetic Nephropathy

Hematological Parameter	Change Observed in Diabetic Nephropathy	Possible Pathophysiological Mechanism	Clinical Significance
Hemoglobin (Hb)	Decreased	Reduced erythropoietin production, chronic inflammation, and oxidative stress	May indicate early anemia associated with declining kidney function
Red Blood Cell Count (RBC)	Decreased	Impaired erythropoiesis and shortened erythrocyte lifespan due to hyperglycemia	Reflects metabolic imbalance and renal impairment
Hematocrit (HCT)	Decreased	Reduced RBC production and increased destruction of erythrocytes	Suggests progression of renal dysfunction in diabetic patients
Red Cell Distribution Width (RDW)	Increased	Chronic inflammation, oxidative stress, and ineffective erythropoiesis	Potential marker for early detection and progression of diabetic nephropathy
Mean Platelet Volume (MPV)	Increased	Platelet activation and endothelial	Associated with vascular

		dysfunction caused by persistent hyperglycemia	complications and renal microvascular damage
Platelet Distribution Width (PDW)	Increased	Increased platelet activation and variability in platelet size	May correlate with inflammatory state and nephropathy severity
Platelet Count	Variable	Altered platelet production and activation due to metabolic disturbances	Can reflect pro-thrombotic state in diabetic complications

Conclusion

Diabetic nephropathy is one of the worst complications that come with diabetes mellitus and is a leading cause of chronic kidney disease burden in the world. The new findings show that significant changes in different hematological parameters are noticed in diabetic patients particularly those who develop renal complications. Diabetic nephropathy patients often have lower hemoglobin levels, a decrease in the number of red blood cells, higher red cell distribution width (RDW) and mean platelet volume (MPV) values. These hematologic perturbations are believed to reflect pathogenic mechanisms underlying, such as chronic inflammation, oxidative stress, endothelial dysfunction and disrupted erythropoiesis due to sustained hyperglycemia. Considering the fact that the hematologic indices are cheap and can be regularly acquired via regular laboratory

tests, they have potential of becoming convenient supplements towards early detection and monitoring of diabetic complications. However, more strictly constructed clinical studies are needed to assess their reliability and also come up with standardized guidelines to govern their use in the diagnosis and treatment of diabetic nephropathy.

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