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Evaluation of Complete Blood Count Parameters in Patients With Diabetes Mellitus: A Systematic Review

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ABSTRACT

Background and Aims: Several studies were performed to evaluate the relationship between CBC and patients with diabetes mellitus (DM). In this review, we discussed the prognostic value of CBC parameters in DM patients.

Methods: English literature was searched and retrieved from the Google Scholar search engine and PubMed database (1980–2024). "Diabetes mellitus," "Blood cell count," "Mean platelet volume," "Leukocytes," and "Inflammation" were used as keywords.

Results: DM increases vascular inflammation and oxidative stress, while vascular inflammation affects erythropoiesis and red blood cell deformation, thus increasing red cell distribution width (RDW). Mean platelet volume (MPV) is another useful prognostic biomarker for DM patients. Additionally, elevated neutrophil-lymphocyte ratio (NLR) levels are associated with poor glycemic control in T2DM patients, so it can be used as a screening tool in diabetic follow-up.

Conclusion: RDW can be used as a valuable independent biomarker to assess the prognosis of patients with DM. MPV can also be used as a noninvasive, widely available, and low-cost marker as a key factor as well as a Prognostic/diagnostic biomarker that could be used for DM patients. Total white blood cell count, NLR, Mean platelet volume lymphocyte ratio (MPVLR), and monocyte to high-density lipoprotein ratio (MHR) are valuable biomarkers in predicting DM.

1 | Introduction

Diabetes mellitus (DM) is a group of metabolic disorders characterized by chronic hyperglycemia, which results from defects in insulin secretion, insulin function, or insulin resistance (IR) [1–3]. The condition is most commonly classified into two main types: type 1 diabetes (T1DM) and type 2 diabetes (T2DM). T1DM, which is an autoimmune disorder, is characterized by the destruction of insulin-producing beta cells in the pancreas, resulting in an absolute deficiency of insulin [4–6]. In contrast, T2DM is primarily associated with insulin resistance and relative insulin deficiency, where the body's cells become less responsive to insulin, leading to increased blood glucose levels. T2DM is the most prevalent form of diabetes and is strongly associated with obesity, physical inactivity, and an unhealthy diet, and its incidence has been increasing globally, contributing to a significant public health burden [7–9]. Both types of diabetes, however, share a common complication—hyperglycemia—which is a primary contributor to the development of various diabetic complications [10]. The complications of DM can be broadly categorized into microvascular and macrovascular disorders. Microvascular complications include

diabetic retinopathy, nephropathy, and neuropathy, which can significantly impair the quality of life and lead to disability [11, 12]. Macrovascular complications, such as cardiovascular disease (CVD), stroke, and peripheral artery disease (PAD), are major contributors to the increased morbidity and mortality in diabetic patients. These complications are not only associated with prolonged hyperglycemia but also with a chronic inflammatory state that exacerbates disease progression [13–15]. In particular, Type 2 diabetes is known to be closely linked with systemic low-grade inflammation, which is thought to play a central role in the development of both microvascular and macrovascular complications. This inflammatory burden is often reflected by elevated levels of circulating inflammatory markers, such as C-reactive protein (CRP), interleukins, and tumor necrosis factor-alpha (TNF-α) and is considered a key mechanism in the pathophysiology of DM [16].

In addition to traditional biomarkers, several hemogram-derived markers have emerged as potential indicators of inflammation and disease progression in diabetes. These include mean platelet volume (MPV), red cell distribution width (RDW), and neutrophil-to-lymphocyte ratio (NLR). MPV is a marker of platelet activation and function, with increased levels often reflecting enhanced platelet reactivity and inflammation [17]. Elevated MPV levels have been observed in T2DM patients, as well as in those with diabetic kidney disease, and have been associated with an increased risk of cardiovascular events [18–21]. RDW, which reflects the variation in size of red blood cells, has been increasingly recognized as a marker of inflammation and oxidative stress. Elevated RDW levels have been reported in a wide range of inflammatory conditions, including autoimmune diseases, rheumatoid arthritis, malignancy, and CVD, as well as in DM patients, particularly those with poor blood sugar control and complications such as nephropathy [22–24]. RDW has also been identified as a predictor of adverse outcomes in various diseases, including mortality in diabetic patients [25–28]. Similarly, NLR, which represents the ratio of neutrophils to lymphocytes in the blood, is a robust marker of systemic inflammation. Increased NLR levels have been observed in conditions characterized by chronic inflammation, such as T2DM, thyroid disorders, CVD, and infections. In the context of DM, elevated NLR has been linked to insulin resistance and the development of diabetic complications, making it a potential prognostic marker for patients with T2DM [27, 29–32].

The growing body of evidence linking these hemogram-derived markers to inflammatory processes in diabetes has prompted further exploration into their role in monitoring disease progression and predicting outcomes. These markers, which are routinely measured as part of the complete blood count (CBC), offer a noninvasive, cost-effective, and accessible means of assessing inflammation and disease status in diabetic patients. Given the chronic inflammatory nature of T2DM and its complications, incorporating CBC parameters into clinical practice could provide valuable insights into disease mechanisms, allowing for better risk stratification, early detection of complications, and personalized management strategies [33].

This review aims to provide a comprehensive examination of the relationship between CBC parameters and diabetes mellitus, focusing on markers such as MPV, RDW, and NLR. By synthesizing the available literature, we aim to highlight the potential of these biomarkers in understanding the pathophysiological mechanisms underlying diabetes and its complications, as well as their role in monitoring disease progression and prognosis. Ultimately, we hope to provide evidence supporting the integration of these markers into routine clinical practice as tools for improving the management and outcomes of diabetic patients.

2 | Methods

2.1 | Literature Search

This Systematic review was conducted following the PRISMA guidelines to systematically evaluate the relationship between CBC parameters and DM. We aimed to identify relevant studies that examined the prognostic value of various CBC indices in diabetic patients. The search terms included “Diabetes mellitus,” “Complete Blood Count,” “mean platelet volume,” “Red Cell Distribution Width,” “Leukocytes,” and “Inflammation.” We conducted searches across multiple databases, including PubMed, Scopus, and Google Scholar, from their inception up to October 2024. Additionally, we reviewed the reference lists of included studies to discover further relevant articles. This comprehensive search strategy yielded a total of 141 studies for initial review.

2.2 | Eligibility Criteria

Inclusion criteria for this study required that participants be diagnosed with diabetes mellitus, specifically type 1 or type 2, as defined by the American Diabetes Association. Studies included must have assessed CBC parameters such as RDW, MPV, and white blood cell (WBC) counts, focusing on their relationship with glycemic control and diabetes-related complications. Additionally, only studies published in English between 1980 and 2024 were considered, ensuring the accessibility and relevance of the literature. Exclusion criteria encompassed research that did not specifically examine CBC parameters in diabetic patients, studies focused on nondiabetic populations, and those lacking original data, such as reviews, commentaries, and conference abstracts. The exit qualities of the study aimed to ensure that the final selection of articles contributed valuable insights into the prognostic implications of CBC parameters in diabetes management, thereby enhancing clinical understanding and guiding future research directions.

2.3 | Data Extraction

To maintain rigor in our review process, two independent reviewers initially screened the titles and abstracts of the identified studies for relevance according to our inclusion and exclusion criteria. The selected articles underwent a full-text review by the same reviewers to confirm their suitability for inclusion. In cases of discrepancies or differing opinions between the reviewers, a third reviewer was involved to mediate

and reach a consensus. This systematic approach helped minimize selection bias, ensuring that only relevant and high-quality studies were included in our review.

3 | RDW as an Independent Prognostic Biomarker in DMs

RDW is a parameter of the change in size (anisocytosis) of circulating erythrocytes, which is usually obtained by a standard complete red blood cell count [34]. High RDW indicates anisocytosis and it is associated with impaired erythropoiesis and erythrocyte degradation, which reflects chronic inflammation and increased oxidative stress, which are obvious symptoms of T2DM and may significantly lead to atherosclerotic disease [35, 36]. Studies have shown an association between high RDW and adverse health outcomes such as increased mortality [37], increased incidence of atrial fibrillation and heart failure [38, 39] and poor prognosis in patients with heart failure or coronary artery disease [40, 41]. Increasing the rate of RDW changes is associated with increasing the incidence of DM [42]. In several studies on DM patients, higher mortality has been reported in primary coronary interventions (PCI) in individuals with high RDW [43]. Recent studies suggested that RDW may be helpful in assessing the risk of patients at risk for T2DM. Veeranna et al. reported RDW has gradually increased among HBA1Cs group in 15,343 nondiabetic adults free of CVD based on using the National Health and Nutrition Examination Survey (NHANES) database [44]. Similarly, in a large population-based cohort study, 26,709 nondiabetic Swedes patients reported that RDW is positively associated with HBA1C so that every 1 SD increase in RDW results in a 0.10% increase in HBA1C [45]. DM increases vascular inflammation and oxidative stress, while vascular inflammation affects erythropoiesis and erythrocyte deformation, thus increase RDW [37, 40, 41, 46] (Figure 1). RDW is strongly associated with chronic inflammation and is a strong indicator of mortality risk in CVD, DM as well as in the general population. Inflammatory conditions, such as DM, cause red blood cells to deform due to multiple pathophysiological mechanisms [47]. It has recently been reported that hyperglycemia affects human RBCs by altering the content and dispersion of the three isotypes of tubulin, thereby reducing RBC deformation and osmotic resistance. Although tubulin is not the major protein in RBC base on volume, it plays an important structural role and regulates enzymatic activity such as Na+/K+ ATPase and PMCA (Plasma membrane ca2+ ATPase) [48]. Several studies and their almost identical results confirm the association between RDW and DM compared to other CBC parameters (Table 1). As a result, RDW can be considered as a valuable independent biomarker for DM prognosis.

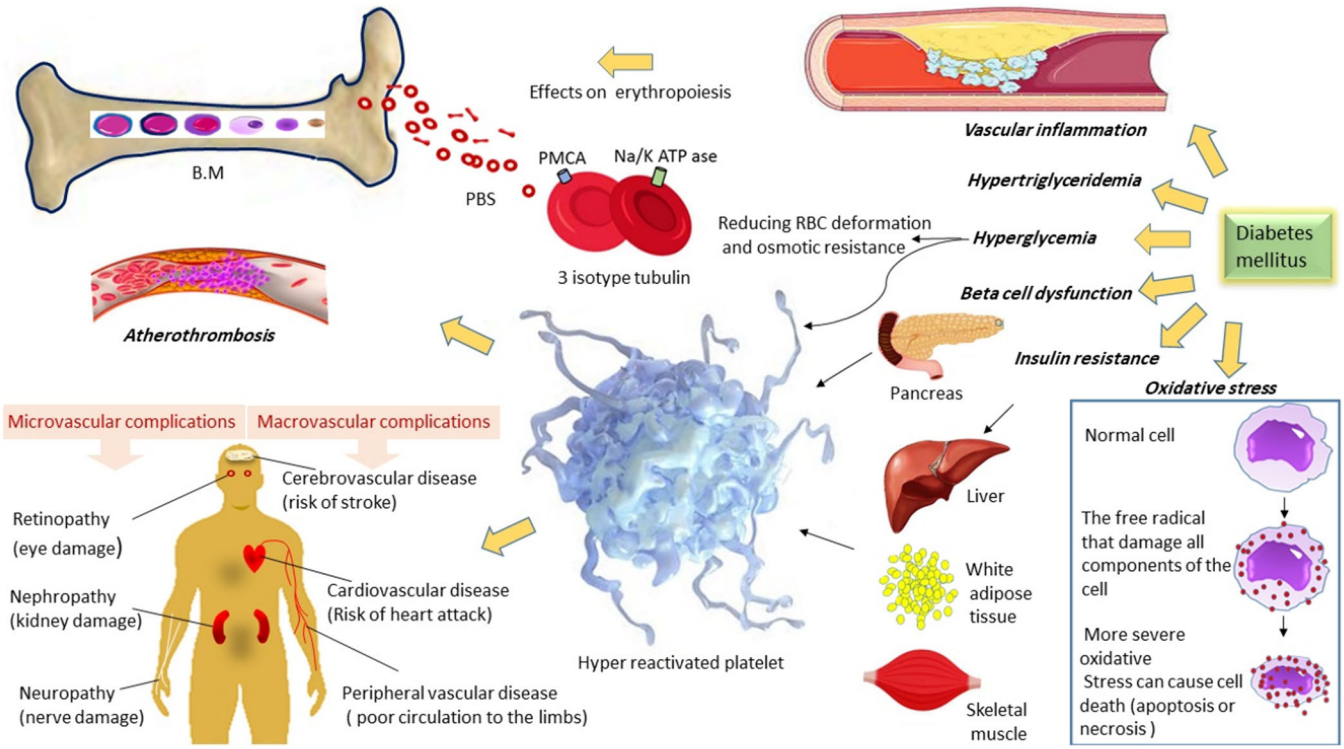

FIGURE 1 | Diabetes mellitus and its complications. Diabetes mellitus can be classified into two classes, type 1 (absence of insulin secretion due to the destruction of beta cells) and type 2 (insulin resistance). Inadequate blood sugar control in diabetic people is associated with complications such as vascular inflammation, hypertriglyceridemia, hyperglycemia, and increased oxidative stress so that vascular inflammation affects the process of erythropoiesis in the bone marrow and changes the shape of RBCs, and ultimately causes anisocytosis. Hyperglycemia also leads to a decrease in deformation and osmotic resistance of RBCs through changes in the content and distribution of three isotypes of tubulin, which is a protein that regulates the activity of plasma membrane Ca2+ ATPase and Na+/K+ ATPase. On the other hand, hyperglycemia, insulin resistance, or destruction of beta cells through increasing thromboxane biosynthesis and calcium mobilization lead to an increase in MPV and subsequently to an increase in the reactivity of platelets that these cells have a greater tendency to thrombotic events and lead to complications such as atherothrombosis and micro and macrovascular complications. B.M, Bone marrow; PBS, Peripheral blood smear; PMCA, Plasma membrane ca2+ ATPase.

TABLE 1 | Summary of CBC parameters in the patients with diabetes mellitus.

Parameters	Index	M/F (%)	Median/ mean age	Number of participants	Clinical findings	Level of CBC parametr	*p* value	Ref.
WBC	Neu	64/56	30–90	DM:120 Control:120	Neutrophil count was statistically positively correlated with FBG, BMI and SBP	3.96 (2.27)	0.226	[49]
	Baso	64/56	30–90	DM:120 Control:120	Basophil count was statistically positively correlated with FBG, BMI and SBP	0.04 (0.03)	0.000	[49]
	Total WBC	48/52	66 [59–72]	DM:301 Control:359	Total WBC count was positively associated with HbA1c and higher in T2DM	7.29 (6.11–8.99)	< 0.001	[50]
	Mono	60/40	60.71 ± 9.07	DM:494 Control:1848	Increased monocyte count is associated with T2DM patients	0.47 ± 0.14	0.254	[51]
	Eos	46/54	57.7 ± 9.8	DM:37 Conrtol:34	There was no statistically significant between eosinophil count and DM	0.25 (0.2)	0.51	[52]
	Lymph	45/55	61 ± 9.8	DM:689 Control:NA	Low lymphocytes count were predictors of macrovascular complication and mortality in individuals with T2DM	1.8 ± 0.5	NA	[53]
RBC	MCV	46/54	50 [40–60]	DM:105 Control:NA	Red blood cell indices such as MCV, MCH and MCHC were decreased in diabetic patients	87.52 ± 6	0.016	[54]
	MCH					27.27 ± 2.71	0.054	
	MCHC					31.09 ± 1.68	0.829	
	Hgb	58/42	NA	DM:164 Control:82	The mean values of Hgb among DM patients were significantly lower than those of nondiabetic	13.8 ± 1.8	< 0.001	[55]
	HCT	48/52	56.34	DM:100 Control:100	There was no significant association	41.376	0.736	[56]
	RDW	63/37	73 (11.2)	DM:71 Control:147	RDW was associated with higher event rate both in HF patients with and without DM	15.2 (1.5)	0.744	[57]
PLT	Plt	70/30	69.3 (±9.8)	DM:1272 Control:2210	Mean MPV values were significantly higher in diabetics than in non-diabetics	215.6 (±66.4)	0.72	[58]
	MPV					11 (±0.99)	< 0.001	

Abbreviations: BMI, body mass index; DM, diabetes mellitus; FBG, fasting blood glucose; HF, Heart failure; IR, insulin resistance; M/F, Male to Female ratio; MCH, Mean corpascular hemoglobin; MCHC, Mean corpascular hemoglobin concentration; MCV, Mean corpascular volume; MPV, mean platelet volume; RDW, Red cell distribution width; SBP, systolic blood pressure.

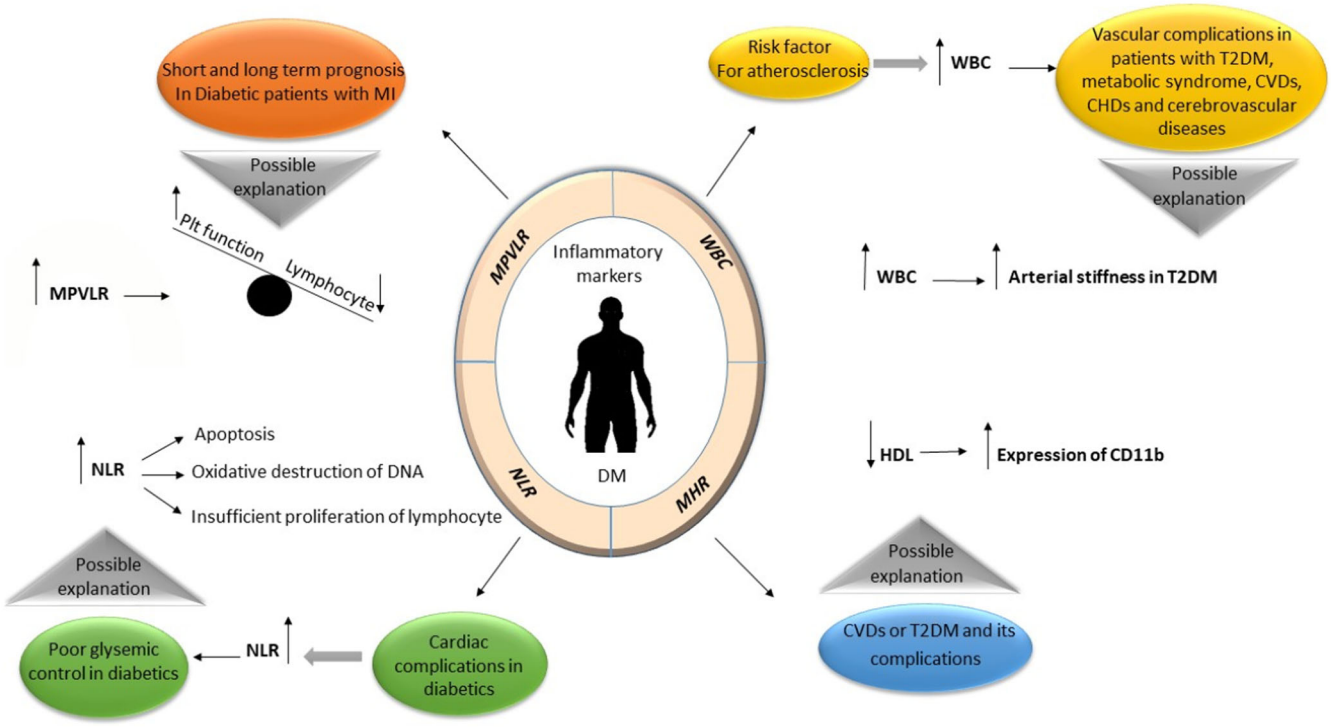

FIGURE 2 | Inflammatory markers derived from CBC can predict DM events. WBC is an inflammatory marker in diabetes mellitus, which can be used as a risk factor for atherosclerosis, and its increase is associated with vascular complications in T2DM patients, metabolic syndrome, CVDs, CHDs, and cerebrovascular diseases, and it can be the possible cause of increased stiffness in T2DM patients. The increase of MHR is also a prognostic marker in CVDs and T2DM patients and it can be attributed to the reduction of HDL as an inflammatory lipid and the subsequent increase in CD11b expression. NLR is an important predictor of cardiac complications in diabetic patients, and its increase is related to poor blood sugar control in these patients. Factors such as apoptosis, oxidative DNA damage, and insufficient proliferation of lymphocytes lead to an increase in NLR. MPVLR is also known as an independent predictor of short-term and long-term prognosis in diabetic patients with myocardial infarction (MI), whose increase can be attributed to increased platelet activity and decreased lymphocytes. CHD, coronary heart disease; CVD, cardiovascular disease; HDL, High-density lipoprotein; MHR, monocyte to high-density lipoprotein ratio; MI, myocardial infarction; MPVLR, mean platelet volume lymphocyte ratio; NLR, neutrophil-lymphocyte ratio; T2DM, Type 2 diabetes mellitus; WBC, white blood cell.

4 | MPV as a Key Factor for DMs

Platelets are abundant cells in the bloodstream, which play a classic role in thrombosis and homeostasis [59]. Increased platelet activity plays an important role in the development of vascular complications in DM [60]. Although there are several measurements for platelet activity such as (platelet aggregometry, platelet surface p-selectin, platelet-activated glycoprotein GPIIb/IIIa, serum troboxane B2, and urinary 11 dehydro thromboxane B2), almost all of these BIOMARKERS are time-consuming, expensive or require special training [61, 62]. Mean platelet volume (MPV) is an alternative marker for platelet activity that can be determined by conventional autologous hemograms as part of a relatively low-cost CBC test [63, 64]. Normal MPV values in a simple CBC test are between 7.2 and 11.7 fl, and higher MPV values indicate larger platelets that are more active metabolically and enzymatically and have greater anticoagulant potential [64–66]. In addition to being a risk factor for CVD, elevated MPV is also known as a risk factor for DM [8], impaired fasting glucose [67], hyperlipidemia [68], and metabolic syndrome [69]. Most published studies have been conducted to investigate the relationship between MPV, prevalence, severity of diabetes and its complications [70, 71]. Several studies reported that MPV was significantly increased in DM cases and in patients with poor glycemic control, and the duration of diabetes was longer. In addition, both groups of diabetic patients have higher MPV values compared to the nondiabetic group [72–75]. Diabetics, especially patients with T2DM, are prone to increased platelet reactivity due to factors such as metabolic disorders (hyperglycemia, hypertriglyceridemia), systemic disorders (such as oxidative stress, inflammation), and insulin resistance [76–78]. Atherothrombosis is a common complication in DM patients. Therefore, patients with T2DM are 2–4 times more likely to develop coronary artery disease and stroke [79]. Possible mechanisms include hyperglycemia or insulin resistance, which increases thromboxane biosynthesis and calcium mobilization and subsequently leads to increased platelet reactivity [80, 81]. Due to metabolic disorders, DM patients have overactive platelets that release more granules and are more prone to thrombotic events, which in turn leads to micro- and macrovascular complications in these patients, which in turn increases the risk of diabetes And increases mortality in these patients [82, 83]. Given the above, it can be concluded that MPV as a noninvasive marker, widely available and low cost can be used as a key prognostic and diagnostic biomarker in DM patients.

5 | Inflammatory Markers Derived From CBC Can Predict DM Events

Generally, the immune system response to inflammation is associated with an increase in WBC and neutrophil as well as a relative decrease in lymphocyte count [49, 50, 84]. Many epidemiological studies have shown an association between chronic inflammation and various inflammatory markers in DM pathogenesis so that chronic inflammation plays an important role in the acceleration and development of micro- and macroangiopathy complications [85–87] (Figure 2). Neutrophil lymphocyte ratio (NLR), is an important marker in systemic inflammation and an indicator of increased risk for cardiovascular events in patients with metabolic syndrome [88, 89] additionally, two other studies showed that NLR is an independent predictor, which is important for cardiac complications in diabetic patients [90, 91]. Elevated NLR levels are associated with poor glycemic control in T2DM patients. Therefore, it can be used as a screening tool in the follow-up of diabetic patients [92, 93]. Also, NLR is superior to other leukocyte parameters due to its stability to various physiological, pathological and physical factors [94, 95]. NLR is a combination of two major components of chronic inflammation (neutrophil increase and lymphocyte depletion). High neutrophil counts indicate a process of nonspecific and persistent destructive inflammation and lymphocyte depletion indicates relatively inadequate immune control as well as an inactive immune pathway [96]. Decrease in lymphocytes is attributed to the increased oxidative damage of DNA and apoptosis of peripheral blood lymphocytes as well as insufficient proliferation of lymphocytes due to low IL2 receptor expression [84, 97, 98]. In addition, NF-kB (Nuclear factor kappa-light-chain-enhancer of activated B cells) can be induced by stimuli such as hyperglycemia and oxidative stress, and the inflammatory response by increasing the expression of adhesion molecules such as ICAM 1 (Intercellular adhesion molecule 1) stimulates pro-inflammatory cytokines and chemokines, and this inflammatory response cascade will eventually lead to an increase in neutrophils [99, 100]. Simultaneously, WBC count is an essential marker in inflammation that elevated levels are associated with vascular complications in patients with T2DM and metabolic syndrome [50, 101–104], as well as increased WBC in atherosclerotic pathogenesis in patients with T2DM, CVD and mortality from coronary heart disease and cerebrovascular disease [105–108]. Additionally, increased arterial stiffness is associated with increased WBC in T2DM patients [109]. Mean platelet volume lymphocyte ratio (MPVLR) is also a new inflammatory marker in diabetic patients that has been recognized in recent studies as an independent predictor of short-term and long-term prognosis in diabetic patients with myocardial infarction (MI) [110, 111]. Increase in MPVLR is followed by decreasing lymphocyte count due to induction of apoptosis, systemic inflammation, oxidative stress, calcium metabolism deficiency, decrease in nitric oxide, increase in phosphorylation and glycosylation of cellular proteins lead to increased platelet activation and subsequent increase in MPV and proinflammation in diabetic patients [112–115]. Like NLR, and MPVLR, monocyte to high-density lipoprotein ratio (MHR) is also known as a new marker associated with increased inflammation and oxidative stress as well as adverse cardiovascular outcomes [116]. Numerous studies have shown that increased monocytes are associated with insulin resistance (IR), T2DM, coronary artery disease, and micro- and macrovascular complications of diabetes [104, 117–119]. On the other hand, reduction of HDL as an anti-inflammatory lipid and antioxidant that has an antithrombotic effect in inflammatory conditions by inhibiting CD11b integrin activation that is involved in adhesion, migration, and regulation of monocyte/macrophage inflammatory activity leads to accelerated atherosclerosis in diabetic patients [120–122]. Therefore, increasing MHR can be used as a new marker of cardiovascular prognosis or inflammation in T2DM patients and its complications [51, 123]. See (Table 2).

6 | Evaluating Confounding Factors in CBC Parameters Related to Diabetes Mellitus

In the exploration of CBC parameters and their associations with DM, it is essential to recognize and evaluate various confounding factors that may influence these parameters. This section aims to provide a detailed analysis of how co-existing medical conditions and medication use can impact CBC results and subsequently affect the interpretation of their relationship with diabetes.

6.1 | Co-Existing Conditions

Co-existing medical conditions can significantly alter CBC results, leading to potential misinterpretations in the context of DM. For example, infections often trigger an inflammatory response that elevates WBC counts as the body attempts to combat pathogens. In patients with acute infections, leukocytosis (an increased WBC count) may occur, which could be mistakenly attributed to the effects of diabetes if the underlying infection is not properly identified [124]. Additionally, chronic infections can impact the bone marrow's function, subsequently affecting the production of RBCs and platelets. Anemia is another critical co-existing condition that can skew CBC interpretations [125–127]. In diabetic patients, the presence of anemia may lead to lower hemoglobin levels, complicating the assessment of HbA1c, a vital measure of long-term glucose control. Different types of anemia, such as iron deficiency or

TABLE 2 | Summary of inflammatory markers in the patients with diabetes mellitus.

Parameters	M/F (%)	Median/mean age	Patient no.	Statistical significance	*p* value	Ref.
NLR	34/66	66.60 ± 4.20	145	2.46 ± 1.26	0.001	[93]
MPVLR	36/64	65 [50–78]	42	3.9 (1.4–13.2)	0.02	[115]
MHR	60/40	60.71 ± 9.07	494	10.92 (8.34–14.02)	< 0.001	[51]

Abbreviations: MHR, monocyte high-density lipoprotein ratio; MPVLR, mean platelet volume lymphocyte ratio; NLR, neutrophil-lymphocyte ratio.

anemia of chronic disease, produce distinct effects on CBC readings, making it imperative to differentiate these conditions [128]. Therefore, a thorough understanding and assessment of co-existing medical conditions are crucial for accurately interpreting CBC parameters in relation to diabetes [124, 129].

6.2 | Medication Use

The influence of medication use on CBC parameters is a critical factor in understanding their relationship with DM. Various medications prescribed for diabetes management can have hematological side effects that may complicate CBC interpretations. For instance, metformin, a common first-line treatment for type 2 diabetes, has been associated with vitamin B12 deficiency, which can lead to macrocytic anemia [130, 131]. This condition often results in altered MCV and MCH values, making it challenging to accurately assess a patient's hematological status. Additionally, other pharmacological treatments, such as corticosteroids, can induce leukocytosis, while immunosuppressants may lead to leukopenia, both of which impact WBC counts and overall CBC results. It is essential to document all medications taken by patients to ensure that the influence of these drugs is accounted for when evaluating CBC parameters in the context of diabetes [131, 132]. By thoroughly considering medication use, researchers and clinicians can attain a clearer understanding of how these factors interact with diabetes, thereby enhancing the accuracy of their assessments and improving patient care.

6.3 | Statistical Considerations

Statistical considerations play a crucial role in accurately assessing the relationship between CBC parameters and DM by controlling for confounding factors. Employing multivariate statistical techniques allows researchers to adjust for the influence of co-existing medical conditions and medication use while evaluating the direct impact of diabetes on CBC results. This approach enables the isolation of specific effects attributed to DM, leading to more reliable and valid findings. Additionally, stratification of the analysis based on the presence or absence of certain confounding factors can enhance understanding of how these variables interact with diabetes. For example, examining CBC parameters in diabetic patients with and without anemia can reveal critical insights into the interplay between these conditions. By using appropriate statistical methods, researchers can ensure that their conclusions about the relationship between CBC parameters and diabetes are robust and clinically relevant, ultimately contributing to better-informed clinical practices and improved patient outcomes [133, 134].

7 | Limitations

In this study, which explores the prognostic value of CBC parameters in diabetic patients, it is crucial to acknowledge the body of evidence that presents conflicting or nonsignificant findings. While many studies have emphasized the importance of parameters such as NLR, MPV, RDW, and MHR in predicting complications or disease progression in diabetes, several others have reported results that challenge these conclusions. For example, certain studies have failed to establish a statistically significant association between NLR and the severity of cardiovascular complications in diabetic populations, suggesting that its predictive power may be limited to specific subgroups or clinical contexts [135–137]. Similarly, MPV, although widely regarded as an indicator of platelet activation, has not shown consistent prognostic significance across all studies, with some investigations reporting no correlation with glycemic control or diabetic complications [138–140].

These discrepancies may stem from several factors, including variability in sample sizes, differences in the demographic and clinical characteristics of the study populations (e.g., age, comorbidities, or diabetes duration), or methodological variations such as the time frame of data collection and the definitions of outcomes. Furthermore, environmental factors, dietary habits, and genetic predispositions, which are often underexplored, could also contribute to the observed inconsistencies [136, 141, 142].

Recognizing these limitations, it becomes clear that while CBC parameters hold promise as prognostic tools, their application should be context-dependent. To solidify their utility, future studies should prioritize large-scale, multi-center trials with standardized methodologies, ensuring better comparability and reproducibility of findings. Additionally, exploring interactions between these parameters and other inflammatory or metabolic markers could provide a more comprehensive understanding of their role in diabetes pathophysiology.

Based on the diagnostic criteria for diabetes mellitus, all studies were included to ensure a comprehensive analysis with high sensitivity. However, a limitation of this study is the variability in the design of the included studies. Some studies focused on comparisons between diabetic and nondiabetic groups, while others examined diabetic patients with various complications. This heterogeneity may influence the interpretation of the results and the generalizability of the findings.

8 | Conclusion and Future Perspective

Nowadays the prognostic and diagnostic value of CBC parameters in DM patients become a hot research topic. It is predicted that CBC testing can be a cheap, accessible, simple, practical, and valuable test that can be used as a new prognostic tool for DM patients in health care centers. Therefore, the physician as the first line of diagnosis and follow-up of DM patients can determine the prognosis and treatment effects more confidently by standard principles of hematology clinical laboratories, especially CBC results. According to the previous studies the four parameters RDW, MPV, WBC, NLR are more relevant and efficient in determining the prognosis of DM patients compared to other CBC parameters. Additionally, we suggest that two new markers, MPVLR and MHR, can be used to determine the more accurate prognosis of DM patients. Additionally, considering the stability of RBC parameters such as Mean carpascular volume (MCV), Mean corpuscular hemoglobin (MCH), and Mean corpascular hemoglobin concentration (MCHC) in different populations, we

suggest that these parameters can be used separately or beside other inflammatory and platelet parameters.

Author Contributions

Mojtaba Aghaei: data curation, investigation, methodology, writing – review and editing, writing – original draft, conceptualization. **Seyed Sobhan Bahreiny:** methodology, writing – review and editing. **Zeynab Deris Zayeri:** investigation, methodology, writing – original draft. **Nader Davari:** software, data curation, writing – review and editing. **Mohammad Mehdi Abolhasani:** methodology, investigation. **Najmaldin Saki:** writing – review and editing, conceptualization, supervision.

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Ethics Statement

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Transparency Statement

The lead author Najmaldin Saki affirms that this manuscript is an honest, accurate, and transparent account of the study being reported, that no important aspects of the study have been omitted, and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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