

## Vitamin D and hematological indicators of inflammation in Prediabetes

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### ABSTRACT

**Objectives:** Prediabetes is characterized by the presence of inflammation. Hematological parameters provide the advantageous qualities of being cost-effective and readily reproducible, rendering them highly helpful for the purpose of disease surveillance. The impact of vitamin D on inflammatory mediators and its role in the progression from prediabetes to type 2 diabetes has been seen. This study aims to investigate hematological markers, glycemic management, and vitamin D status among individuals with prediabetes.

**Methods:** A retrospective investigation was performed on a cohort of 270 persons with prediabetes (5.7-6.4% glycated hemoglobin levels) and 299 participants with normal blood glucose levels. In order to conduct a comparison of hematological indicators between two groups, statistical analyses including chi square analysis and the t test were employed. The analysis of variance (ANOVA) statistical method was employed to analyze the components within three distinct categories of Vitamin D levels: acceptable (more than 75 nmol/L), inadequate (ranging from 50 to 74.9 nmol/L), and deficient (50 nmol/L). The odds ratio for prediabetes was obtained through the utilization of regression analysis. **Results:** The study observed a statistically significant decrease in vitamin D levels among individuals with prediabetes (mean  $57.91 \pm 20.83$ ,  $p = 0.05$ ). The group of individuals with prediabetes exhibited significantly higher values for the neutrophil lymphocyte ratio ( $2.10 \pm 0.85$ ;  $p = 0.05$ ), platelet lymphocyte ratio ( $137.70 \pm 43.70$ ;  $p = 0.05$ ), mean platelet volume ( $8.55 \pm 3.00$ ;  $p = 0.001$ ), and red cell distribution width ( $12.65 \pm 1.31$ ;  $p = 0.05$ ). The present study observed a statistically significant positive correlation between declining levels of vitamin D and increasing trends in the neutrophil lymphocyte ratio, platelet lymphocyte ratio, and red cell distribution width in individuals with prediabetes. The study revealed that the mean platelet volume had a noteworthy association with the development of prediabetes. **Conclusions:** The neutrophil lymphocyte ratio, platelet lymphocyte ratio, red cell distribution width, and mean platelet volume are emerging inflammatory markers that can be employed for monitoring purposes in patients with prediabetes. However, it is important to note that these indicators should be utilized in combination with an assessment of Vitamin D status.

**KEYWORDS:** Mean platelet volume, red cell distribution width, neutrophil lymphocyte ratio, and platelet lymphocyte ratio

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### INTRODUCTION

According to Hostalek et al. (2019), the prevalence of prediabetes among adults was approximately 7.3% in 2017, with a projected increase to 8.3% by the year 2045. Despite the absence of apparent symptoms, individuals with prediabetes are at a heightened risk of acquiring type 2 diabetes and its associated pathological changes (Tabak et al., 2012). Patients with prediabetes are more likely to develop CVD, stroke, and death than those with

normoglycemia, according to a meta-analysis (Donath et al., 2011). Hence, it is imperative to identify and address prediabetes at an early stage in order to impede its advancement and maybe mitigate the widespread proliferation of the diabetes pandemic.

Diabetes is distinguished by the presence of persistent low-grade inflammation and endothelial dysfunction generated by hyperglycemia (Huang et al., 2016). According to a study conducted by Donath et al. (2016), it was observed

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that persons with diabetes exhibited a mortality risk that was comparable to the risk associated with chronic inflammation. In recent years, there has been a growing acceptance of hematological markers such as the neutrophil-to-lymphocyte ratio (NLR), the platelet-to-lymphocyte ratio (PLR), the breadth of the red-cell distribution, and the mean platelet volume (MPV) as reliable indicators of inflammation and endothelial dysfunction. According to Duman et al. (2019), individuals with diabetes can effectively monitor their glucose management by utilizing the Neutrophil-to-Lymphocyte Ratio (NLR) as a valuable tool.

According to Malandrino et al. (2012), the presence of anisocytosis or an elevated red blood cell distribution width (RDW) suggests an increased level of oxidative stress and inflammation within the body. Sherif et al. (2013) established a correlation between elevated red cell distribution width (RDW) and an augmented susceptibility to macrovascular complications and cardiovascular disease among individuals with diabetes.

Moreover, it has been suggested by Atak et al. (2019) that PLR serves as a simple and cost-effective measure for assessing the progression of diabetes. Mertoglu et al. (2017) discovered NLR (neutrophil-to-lymphocyte ratio) and PLR (platelet-to-lymphocyte ratio) as significant markers of inflammation in individuals with prediabetes. Vizioli et al. (2009) found a positive correlation between elevated mean platelet volume (MPV) and increased synthesis of thromboxane A<sub>2</sub>, a prothrombotic factor, hence indicating an augmented risk of thrombosis.

In a study conducted by Inoue et al. (2020), compelling evidence was discovered indicating the involvement of a certain factor in the pathogenesis of diabetes and its accompanying vascular complications.

Vitamin D (VD) is considered a vital vitamin due to its various physiological roles, such as supporting bone health and bolstering immune system functionality (Di Rosa et al., 2011). Zhang et al. (2012) demonstrated that at the molecular level, the regulation of innate and adaptive immunity is achieved through the utilization of cytokines and cell signaling pathways. According to Korf et al. (2012), the expression of VD receptors by both B and T cells allows for the regulation of their proliferation, differentiation, and suppression. The association between a deficiency in vitamin D and an elevated susceptibility to the development of type 2 diabetes mellitus has been established, however conclusive evidence is still insufficient. The role of inflammation in the metabolic dysregulation, initiation, and advancement of Vascular Dementia (VD) has been emphasized by Garbossa et al. (2017), indicating a potential association between VD and the pathophysiology of diabetes.

The objective of this study is to assess disparities in hematological indices between individuals without any health conditions and individuals who are susceptible to

acquiring diabetes. The potential of these novel markers lies in their ability to function as cost-effective and user-friendly tools for monitoring the extent of inflammation, a fundamental pathophysiological process implicated in the onset and progression of diabetes. Furthermore, the objective of this study is to ascertain if the presence of VD has an impact on the examined hematological indices in a manner that effectively regulates inflammation.

## METHODS

### Study Duration and Design

The retrospective case control research focused on individuals between the ages of 18 and 65 who were newly diagnosed with prediabetes and receiving treatment at a tertiary care hospital. The study included individuals who sought medical attention at the emergency department throughout the time frame of January 1, 2019, to December 31, 2020. Individuals having a documented history of Prediabetes were paired with an equivalent number of control subjects who were matched for age and did not exhibit this particular medical condition..

### Target Population

The inclusion criteria for this study encompassed individuals who were first diagnosed with prediabetes, as determined by a HbA1C level falling within the range of 5.7% to 6.4% (Pippitt et al., 2016).

### Sample calculation and collection

The study comprised patients who initially received a diagnosis of prediabetes based on their HbA1c levels and later underwent hemogram and vitamin D tests. In the analysis, only the initial set of data was considered for patients who had multiple appointments. Among the study population of 569 individuals, it was observed that 299 individuals exhibited normal blood sugar levels, whereas 270 individuals were found to be in the prediabetes stage.

### Exclusion criteria

Individuals with a medical background encompassing diabetes, cancer, or other acute or chronic ailments were excluded from the study. Likewise, participants who had already consumed Vitamin D or had incomplete data were also eliminated from consideration.

### Anthropometric and Laboratory parameters

The demographic information, including the ages and genders of all participants, was accurately encoded in a Microsoft Excel spreadsheet. The calculation of body mass index (BMI) was performed utilizing the provided data. The Body Mass Index (BMI) is calculated by dividing an individual's weight in kilograms by their height in meters. The measurement was conducted using two distinct methods: systolic and diastolic.

The hematological indicators that were used in the study encompassed the total lymphocyte count, absolute neutrophil count, mean platelet volume, red cell distribution width, neutrophil to lymphocyte ratio, and platelet to lymphocyte

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ratio. In addition, measurements were taken for fasting blood sugar (FBS), hemoglobin A1c, and vitamin D. Various ratios, such as the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR), were derived from the hemogram, while additional ratios were calculated. The researchers in the study conducted by Aksoy et al. (2000) utilized serum 25(OH) vitamin D as a means of assessing the status of vitamin D (VD). This particular form of vitamin D was chosen due to its stability and lack of susceptibility to external factors such as food intake or physical activity. The 25-hydroxyvitamin D levels were analyzed using the Alinity i Abbott platform, while the complete blood count was obtained using the Cell Dyn-Ruby Hematology Analyzer, both manufactured by Abbott. The laboratory has obtained certification from the College of American Pathologists. In this study conducted by Holick et al. (2007), the levels of vitamin D (VD) were categorized into three groups: acceptable ( $>75$  nmol/L), inadequate (50-74.9 nmol/L), and deficient ( $<50$  nmol/L). The researchers analyzed several factors for both prediabetic and normoglycemic patients falling within these specified ranges. The study did not incorporate any form of animal or human experimentation. All procedures employed in this study were granted approval

by the ethical committee at our institution.

### Data Analysis

The statistical analysis was conducted using SPSS 20.0. The quantitative data was presented in the form of a mean and standard deviation, while the qualitative data was reported as frequency and percentage. The application of chi-square analysis was employed to assess the association between categorical variables, while the t-test was utilized to examine the differences between continuous variables. The patients were classified into two groups, namely prediabetic and normoglycemic, based on the stratification criteria for VD using ANOVA. Prior to conducting the regression analysis to ascertain the odds ratio of prediabetes, adjustments were made to the model for age, gender, and body mass index. A p-value below the threshold of 0.05 was deemed to possess statistical significance.

### RESULTS

Among the cohort of 569 individuals, it was determined that 299 exhibited blood sugar levels within the normal range, but the remaining 270 individuals were identified as being susceptible to the development of diabetes.

**Table 1. Clinical and Biochemical parameters of all subjects**

	Normoglycemic (n=299)	Pre diabetic (n=270)	P value
Gender (Female/Male)	157/142	136/134	0.61
BMI	22.79±1.92	25.53±2.89	<0.001*
HbA1C (%)	4.89±0.29	5.93±0.19	<0.001*
FBS (mmol/L)	6.50±27.88	5.41±0.59	0.52
TLC( $\times 10^3$ /uL)	6.46±1.49	6.79±1.86	0.01*
ANC( $\times 10^3$ /uL)	3.80±1.11	4.12±1.47	0.003*
ALC( $\times 10^3$ /uL)	2.15±0.66	2.08±0.68	0.22
NLR	1.89±0.70	2.10±0.85	0.001*
TPC( $\times 10^3$ /uL)	251.93±22.56	262.15±34.99	<0.001*
MPV(fl)	7.61±0.39	8.55±3.00	<0.001*
PLR	127.30±43.57	137.70±43.70	0.005*
RDW (%)	12.47±0.80	12.65±1.31	0.05
Vitamin D (nmol/L)	63.27±23.78	57.91±20.83	0.005*
Deficient VD (%)	81(43.1%)	107(56.9%)	0.003*
Insufficient VDt (%)	146(59.6%)	99(40.4%)	
Sufficient VD (%)	72(52.9%)	64(47.1%)	

The statistical measures for continuous variables are shown as the mean and standard deviation (SD), whereas categorical data is displayed as frequency and proportion (\*). Fasting blood sugar (FBS), total leukocyte count (TLC), absolute neutrophil count (ANC), absolute lymphocyte count (ALC), neutrophil lymphocyte ratio (NLR), total platelet count (TPC), mean platelet volume (MPV), platelet lymphocyte ratio (PLR), and red cell distribution width (RDW) are abbreviations commonly used in academic literature. Vitamin D (VD) is a micronutrient that plays a crucial role in various physiological processes within the human body. The mean age in the prediabetic group ( $44.98 \pm 9.4$  years)

was found to be substantially higher compared to the other group ( $35.72 \pm 8.43$  years). Individuals classified as prediabetic exhibited body mass indexes and systolic blood pressures that were greater than the average values. On average, patients with prediabetes exhibited an average HbA1c level of  $5.9 \pm 0.19\%$ . Individuals who are susceptible to developing diabetes exhibited a significantly reduced average level of vitamin D ( $57.9$  20). Prediabetic individuals had significantly elevated values when comparing TLC, TPC, MPV, RDW, NLR, and PLR.

Tables 2 and 3 present a comparative analysis of Vitamin D-related variables between individuals with prediabetes and

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those with normal glycemic levels, respectively. A notable disparity in body mass index (BMI) was seen across the three cohorts susceptible to diabetes onset, upon evaluating their respective vitamin D levels. The HbA1c had a comparable trend, displaying a substantial increase from the range considered acceptable to the range classified as deficient. Although no clear pattern was observed, it was found that the average fasting blood sugar (FBS) level was highest among

prediabetic patients with a deficiency in vitamin D. A noticeable elevation in the values of RDW, NLR, and PLR was seen after transitioning from the range considered adequate to the range classified as poor. Nevertheless, in individuals with normal blood glucose levels, all indices, with the exception of mean platelet volume (MPV), did not exhibit a distinct increase when the level of vascular disease (VD) decreased.

**Table 2. Clinical and Biochemical parameters of Prediabetic subjects under Vitamin D Categories.**

Pre diabetes n= 270	Deficient VD (<50 nmol/L)	Insufficient VD (50-74.9 nmol/L)	Sufficient VD (>=75 nmol/L)	P value
Age	43.71±9.45	44.73± 8.86	47.51± 9.77	0.03*
Gender (Female/Male)	61 / 46	50 / 49	23 / 41	0.02*
BMI	26.69 ±3.04	25.07±2.78	24.31±2.02	<0.001*
HbA1C (%)	6.00± 0.21	5.90 ±0.17	5.86 ±0.14	<0.001*
FBS (mmol/L)	5.50±0.5657	5.36 ±0.57	5.34±0.64	0.09
TLC(x10 <sup>3</sup> /uL)	7.90±1.91	6.31±1.59	5.67 ±0.97	<0.001*
ANC(x10 <sup>3</sup> /uL)	5.01±1.54	3.68 ±1.25	3.32±0.78	<0.001*
ALC(x10 <sup>3</sup> /uL)	2.26±0.76	2.02±0.61	1.86± 0.52	<0.001*
NLR	2.39±0.95	1.91±0.74	1.90±0.67	<0.001*
TPC(x10 <sup>3</sup> /uL)	287.71±22.05	253.07±28.3	233.46±32.98	<0.001*
MPV(fl)	8.93±4.66	8.29±0.74	8.31±0.83	0.24
PLR	141.67±48.51	135.38±39.50	134.65 ±41.50	0.48
RDW (%)	13.56 ±1.10	12.31±1.18	11.65±0.79	<0.001*
Median Vitamin D level	38.65±7.194	59.49±6.87405	87.65±12.691	<0.001*

In the realm of statistical analysis, it is customary to determine the average and standard deviation for continuous data, whereas for categorical data, the focus shifts towards evaluating the frequency and percentage. The one-way analysis of variance (ANOVA) produced a p-value of (\*) that was found to be statistically significant. The NLR (neutrophil

lymphocyte ratio), ALC (absolute lymphocyte count), TLC (total leukocyte count), ANC (absolute neutrophil count), MPV (mean platelet volume), PLR (platelet lymphocyte ratio), RDW (red cell distribution width), VD (vitamin D), and FBS (fasting blood sugar) are all important parameters used in academic research and clinical practice.

**Table 3. Clinical and Biochemical parameters of Normoglycemic subjects under Vitamin D Categories.**

Normoglycemic n= 299	Deficient VD (<50 nmol/L)	Insufficient (50-74.9 nmol/L)	Sufficient (>=75 nmol/L)	P value
Age	43.71±9.45	44.73±8.86	47.51±9.77	0.03*
Gender (Female/Male)	61 / 46	50 / 49	23 / 41	0.02*
BMI	26.69±3.04	25.07±2.78	24.31 ± 2.02	<0.001*
HbA1C (%)	4.91±0.29	4.88±0.30	4.88±0.25	0.47
FBS (mmol/L)	4.85±0.40	4.85±0.40	4.9±0.40	0.14
TLC (x10 <sup>3</sup> /uL)	6.56 ±1.57	6.35±1.38	6.56 ±1.62	0.48
ANC (x10 <sup>3</sup> /uL)	3.87 ± 1.23	3.76±1.04	3.79 ±1.12	0.77
ALC (x10 <sup>3</sup> /uL)	2.15 ±0.61	2.10±0.65	2.24 ±0.75	0.37
NLR	1.90±0.73	1.91±0.71	1.82±0.67	0.66
TPC (x10 <sup>3</sup> /uL)	248.37±20.4	252.90 ±22.60	253.97 ±24.56	0.23
MPV (fl)	7.71± 0.43	7.59 ±0.39	7.53±0.31	0.02*
PLR	124.11±42.42	130.72±43.12	123.92±45.78	0.41
RDW (%)	12.41± 0.81	12.40±0.80	12.67 ±0.77	0.06
Median Vitamin D	38.65 ±7.19	59.49±6.87	87.65±12.69	<0.001*

The provided data consists of mean values and standard deviations for continuous variables, while categorical variables are represented by frequencies and percentages.

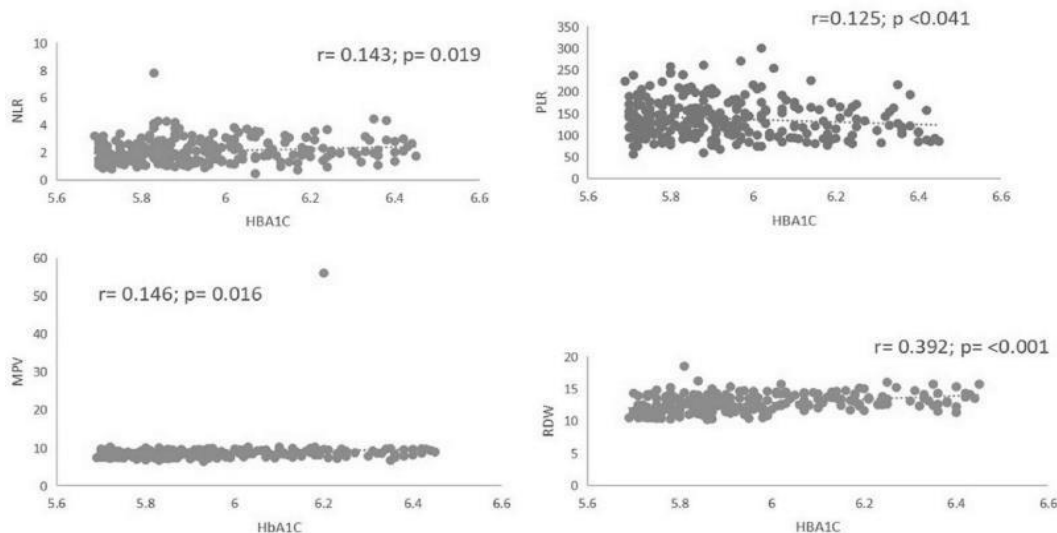
Statistical significance was assessed using one-way analysis of variance (ANOVA). The blood cell measurements included total leukocyte count (TLC), absolute neutrophil

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count (ANC), absolute lymphocyte count (ALC), neutrophil lymphocyte ratio (NLR), mean platelet volume (MPV), platelet lymphocyte ratio (PLR), and red cell distribution width (RDW). The topic of interest is the combination of Vitamin D and Magnesium, specifically referred to as VD Magnesium D3.

The study revealed a significant correlation between HbA1c

and hematological indices among individuals with prediabetes, as demonstrated in Table 4 and Figure 1. However, there was an inverse correlation observed with cardiovascular disease (CVD). The findings shown in Table 5 indicate that even after controlling for age and BMI, both TLC and MPV continue to exhibit a substantial association with the presence of prediabetes.



**Figure 1. Scatter plot showing correlation of HbA1c with hematological indices**

r = Pearson's correlation coefficient

NLR-neutrophil lymphocyte ratio; MPV-mean platelet volume; PLR-plateletLymphocyte ratio, RDW- Red cell distribution width,

**Table 4 Correlation between HbA1c and hematological Parameter in prediabetic subjects**

Variable		Hba1c (%)
TLC( $\times 10^3/\mu\text{L}$ )	r	0.502
	p value	<0.001*
ANC( $\times 10^3/\mu\text{L}$ )	r	0.451
	p value	<0.001*
ALC( $\times 10^3/\mu\text{L}$ )	r	0.313
	p value	<0.001*
NLR	r	0.143
	p value	0.019*
TPC( $\times 10^3/\mu\text{L}$ )	r	0.430
	p value	<0.001*
MPV(fl)	r	0.146
	p value	0.016*
PLR	r	-0.125
	p value	0.041*
RDW (%)	r	0.392
	p value	<0.001

(\*) statistically significant r = pearson's correlation coefficient; Red cell distribution width (RDW), mean platelet volume (MPV), neutrophil lymphocyte ratio (NLR), absolute

neutrophil count (ANC), absolute lymphocyte count (ALC), and total platelet count (TPC).

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**Table 5. Hematological parameters and risk of prediabetes by Regression analysis**

Variable	UnAdjusted		Adjusted	
	Odds ratio (95%CI)	P value	Odds ratio (95%CI)	P Value
TLC( $\times 10^3/\mu\text{L}$ )	1.32 (0.73-2.36)	0.349	1.07 (0.55- 2.07)	0.84
ANC( $\times 10^3/\mu\text{L}$ )	1.22 (0.54- 2.74)	0.63	1.49 (0.55- 4.05)	0.42
ALC( $\times 10^3/\mu\text{L}$ )	0.28 (0.09- 0.83)	0.02*	0.26 (0.06- 1.04)	0.05*
NLR	0.44 (0.14 -1.39)	0.16	0.36 (0.08- 1.61)	0.18
TPC( $\times 10^3/\mu\text{L}$ )	1.14 (1.07 -1.22)	<0.001*	0.99 (1.01- 1.21)	0.02*
MPV(fl)	9.16 (6.03- 13.93)	<0.001*	13.6 (7.67- 24.11)	<0.001*
PLR	1.00 (0.98 -1.01)	0.89	0.99 (0.97- 1.01)	0.81
RDW (%)	0.07 (0.02- 0.27)	<0.001*	0.10 (0.02- 0.62)	0.01*

Model adjusted for age, gender, BMI (\*) p value significant

The parameters of interest in this study include the neutrophil lymphocyte ratio (NLR), absolute lymphocyte count (ALC), absolute neutrophil count (ANC), and total leukocyte count (TLC). The variables of interest in this study are the total platelet count (TPC), confidence interval (CI), red cell distribution width (RDW), mean platelet volume (MPV), and platelet lymphocyte ratio (PLR).

### DISCUSSION

In their study, Alam et al. (2015) conducted a comprehensive assessment of the existing literature and observed that hematological parameters exhibit alterations in individuals diagnosed with Type 2 Diabetes mellitus. The brief elevation of oxidative stress, leading to inflammation through cytokine activation, is attributed to prolonged hyperglycemia due to the glycosylation of hemoglobin, prothrombin, fibrinogen, and other proteins involved in the clotting mechanism. The relationship between chronic inflammation, glycemic management, and insulin resistance forms a self-perpetuating circle (Xia et al., 2017). Karonova et al. (2020) have demonstrated the efficacy of vitamin D (VD) in ameliorating diabetes-related inflammation and attenuating pathogenic mechanisms.

In accordance with a recent investigation conducted by Shankar et al. (2011), our findings indicate a significant decrease in vitamin D levels among patients with prediabetes in comparison to those with normal blood glucose levels. In alignment with prior studies, our findings revealed elevated total leukocyte count (TLC), absolute neutrophil count (ANC), and neutrophil-to-lymphocyte ratio (NLR) in those classified as prediabetic. In a study conducted by Shiny et al. (2014), it was discovered that the neutrophil-to-lymphocyte ratio (NLR) exhibited more accuracy as a predictive indicator compared to the total leukocyte count (TLC) for vascular complications, diabetic nephropathy, and retinopathy. The levels of total platelet count (TPC), mean platelet volume (MPV), and platelet-to-lymphocyte ratio (PLR) exhibited a statistically significant increase in individuals with prediabetes. Previous studies have reported comparable findings among persons with prediabetes and diabetes in different investigations (Aktas et al., 2018; Zuberi et al.,

2008).

The reason for this phenomenon is attributed to the induction of oxidative stress and inflammation by hyperglycemia, which subsequently leads to an increase in platelet hyperactivity and turnover. The present study conducted by Yin et al. (2018) observed an elevated RDW in the prediabetic cohort, which aligns with previous research. The occurrence of prediabetes was found to be substantially associated with mean platelet volume (MPV), with an odds ratio of 9.1 and a p-value of 0.05. The lack of a meaningful relationship between NLR, PLR, and RDW in the regression analysis may be attributed to the relatively smaller sample size. Prior studies have established a negative association between vitamin D (VD) and glycated hemoglobin (HbA1c) levels (Aldossari et al., 2017). This conclusion is consistent with the present study, which observed a rising trend in HbA1c levels across different categories of vitamin D sufficiency. The hematological indicators, including NLR (neutrophil-to-lymphocyte ratio), PLR (platelet-to-lymphocyte ratio), and RDW (red cell distribution width), exhibited an upward trajectory from satisfactory to substandard values in the prediabetes cohort, similar to several other hematological measures, as observed through stratified analysis in comparison to the control group. While the VD deficient category had the highest mean MPV value ( $8.93 \pm 4.66$ ), it should be noted that MPV did not conform to this trend. Patients with a VD deficit who were pre-diabetic had the highest means for NLR (2.390.95), PLR (141.6748.51), and RDW (13.561.10). In individuals without diabetes, none of the patients exhibited an increase, except for mean platelet volume (MPV), which showed a concurrent decrease in venous diameter (VD).

The findings of our retrospective study were nevertheless statistically significant. VD is lower among pre-diabetic people, for starters. Furthermore, individuals with prediabetes are more inclined to undergo assessment of their vitamin D (VD) levels compared to those with normal blood glucose levels due to the heightened influence of VD status on hematological markers in the former cohort. Moreover, it elucidates the underlying reasons for the significant role of vascular dysfunction (VD) in the inflammatory pathway that culminates in the development of prediabetes.

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### LIMITATIONS

Nevertheless, it is important to note that there are certain limitations to the conclusions of this study. Potential bias in the sample procedure could have arisen due to the retrospective nature of the research. The study's limited scope and single-center design preclude generalization to other populations and consideration of factors such as ethnicity and environment. The absence of a shown cause-and-effect relationship in this cross-sectional study could potentially be addressed through longterm prospective investigations. However, this study holds significance due to the limited existing research on the association between vitamin D levels and blood counts in individuals with prediabetes.

### CONCLUSIONS

Consequently, persons with prediabetes exhibit decreased levels of Vitamin D, which demonstrates an inverse correlation with HbA1c. Prediabetes is correlated with elevated levels of novel hematological markers, namely NLR, PLR, RDW, and MPV, with MPV exhibiting the highest predictive value for identifying individuals at risk of developing prediabetes. In addition to a reduction in venous diameter (VD), there are observed elevations in neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and red cell distribution width (RDW). Therefore, it is crucial to thoroughly evaluate the Vitamin D level when interpreting hematological indices, as it has the potential to modify these indices and the associated illness condition. This is significant despite the low cost and ease of repetition of these inflammatory indicators, which are commonly used for monitoring prediabetes. However, further validation of the usefulness of these novel hematological indicators as monitoring tools in prediabetes may be derived from extensive research on a larger scale.

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### Author contributions

The research process involves several key stages, including ideation and design, data collecting, data analysis and interpretation, paper outline development, drafting and revising, and final approval before publication. The process involves several stages, including data gathering, analysis, editing, and the final approval of the published version. Research Question: The process of data gathering, analysis, and revision/final approval before to publication.

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### Conflict of interests

The authors assert that there are no conflicts of interest.

### Data and materials availability

The article encompasses comprehensive material pertaining to this inquiry.

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