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Original Article

Alterations in hematological parameters and fibrinolytic markers (D-dimer) among diabetic retinopathy patients

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ABSTRACT

Diabetic retinopathy remains a significant public health concern. The lack of proper disease control strategies and limited awareness further contribute to increased diabetes related complications. D. dimer and haematological parameters are simple and could be of great benefit in the prediction of complications. This study aims to evaluate haematological parameters and dimer levels in Sudanese diabetic patients with retinopathy to assess their clinical significance and diagnostic potential in the improvement of diabetic complications. This case-control study enrolled diabetic patients with type 2, who were diagnosed with vision issues, but most of them had cataract and retinal issues related to DM. The majority of subjects, 28(53.8%), were female; the selected diabetes patients were undergoing sample collection for CBC and dimer assessment. CBC conducted by BC3000, D. dimer assessed by Fine-care device, data obtained and analysed via SPSS. The study revealed that Haemoglobin levels were reduced in 19.2%of patients, low TWBC among 7.7%, and elevated in 3.8% of patients, platelet counts were decreased in 7.7%, but remained within the normal range in 88.5% of patients. Comparing data of the case group with data of the control group showed that PDW was decreased among diabetic patients with retinopathy than control), while monocyte %, MPV, and D dimer, all 3 parameters, were increased among diabetic patients with retinopathy, and the p-value for each was low than 0.05. This study highlights important haematological changes in T2DM patients with diabetic retinopathy, focusing on their potential role in disease progression and complications.

Keywords: Diabetic retinopathy, Type 2 diabetes mellitus (T2DM), D-dimer, Mean platelet volume, Platelet distribution width

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Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from impaired insulin secretion, insulin resistance, or both [1]. The metabolic disturbances of diabetes affect carbohydrate, lipid, and protein metabolism, primarily influencing skeletal muscle, adipose tissue, and the liver [2]. Long-term uncontrolled hyperglycemia leads to microvascular and macrovascular complications, which constitute major causes of disability and

mortality among affected patients [3]. Diabetic retinopathy (DR) is one of the most common microvascular complications and a leading cause of visual impairment and blindness worldwide [4]. DR develops due to progressive retinal microvascular damage exacerbated by chronic hyperglycemia, hypertension, and dyslipidemia, ultimately resulting in retinal ischemia and pathological neovascularization [5].

Recent studies indicate that diabetes is frequently accompanied by hematological and coagulation abnormalities that may contribute to vascular complications [6]. D-dimer, a fibrin degradation product and biomarker of fibrinolytic and coagulation system activation, has been identified as a potential marker associated with hypercoagulability in diabetic patients [7]. Elevated D-dimer levels have been linked to increased severity of microvascular complications, including proliferative diabetic retinopathy [8, 9].

In Sudan, the prevalence of diabetes continues to rise, particularly in populations with limited access to healthcare services and low awareness regarding disease management [10]. Consequently, diabetes-related complications such as DR represent a growing public health burden. Identifying simple, accessible hematological and coagulation biomarkers may support early detection, monitoring, and prevention of the progression of diabetic complications.

Therefore, this study aims to evaluate hematological parameters and D-dimer levels among Sudanese patients with diabetic retinopathy to assess their clinical relevance and potential diagnostic value in improving the management of diabetic complications [11-14].

Materials and Methods

This case-control study was conducted at Alsafwa Medical Ophthalmic Center in Shendi, River Nile State, Sudan, during the period from May 2024 to January 2025. The study population consisted of two groups: a case group of patients with type 2 diabetes mellitus who had been diagnosed with diabetic retinopathy based on fundoscopic examination, and a control group of apparently healthy non-diabetic individuals. All patients with T2DM who had confirmed diabetic retinopathy were included as study subjects. Patients with diabetic retinopathy who were suffering from other medical complications, such as liver disease, renal disease, ulcers, or other systemic conditions. A total of 82 participants were enrolled in the study, including 52 diabetic retinopathy patients in the case group and 30 healthy non-diabetic subjects in the control group. A simple direct verbal questionnaire was used to collect demographic and clinical data we excluded from the study.

Sample process

Whole blood samples were collected under hygienic conditions in ethylene diamine tetraacetic acid (EDTA), and tri-sodium citrate was added to blood containers for each patient to conduct a complete blood count and D-dimer, respectively. Patients were recruited from an ophthalmic clinic in Shendi city, where they used to follow up, as they suffer from complications of being diabetic.

CBC was conducted via hematology analyzer Mindray BC3000+, and D-dimer was measured by a fine-care device; each device has suitable reagents and kits.

Ethical consideration

This study was approved by the ethical committee of Medical Laboratory Science College -Alzaeim Alazhari University, as well as patients and the clinic administration [15-19]. Every patient verbally approved to participate in this study before enrolling.

Statistical analysis

Data were analyzed using the statistical package of social science (SPSS) version 23 with an independent t-test as the main statistical tool. Considering the P value is significant when it is less than 0.05. The Pearson correlation, as the R value, reflects the flow of data regarding age, duration of disease, with measured parameters, and observes if a significant difference occurred or not.

Results and Discussion

This case-control study enrolled diabetic patients with type 2, who were diagnosed with vision issues, but most of them had cataract and retinal issues related to DM. Males were 24 (46.2%), and females were 28 (53.8%). They were 52, their age ranged from 24 to 76 years with a mean ±SD of 60.4±13.9 years, the duration of DM ranged from 2 to 30 years with a mean +SD of 11.6±9.7 years, and eye sickness 2.2±0.1 years all data were summarized in **Table 1**.

Table 1. Frequency of age and duration of disease among the case group

	N	Minimum	Maximum	Mean+SD years
Age	**52**	24	76	60.4±13.9
Duration (years)		2	30	11.6±7.9
Eye sickness		0.1	7.0	2.2±1.9

Table 2 summarized measured parameters included CBC parameters and D-dimer levels. Decreased levels of Hb, TWBC, and platelet counts were observed, as well as increased TWBC count and relatively increased platelet count.

Table 2. Distribution of Hematological Indices and D-dimer Levels in the Study Population

	N	Minimum	Maximum	Mean+ SD
Hb	**52**	9.7	15.5	12.8±1.2
RBCs		4.1	7.5	4.9±0.7
PCV		33	48	40.5±3.4
MCV		71	97	84.7±61
MCH		21	30	26.0±2.2
MCHC		28	32	30.7±0.9
RDW-CV		12.3	17.7	14.9±1.9

TWBCs	3.7	17.2	6.8±2.7
Neutrophils	36	69	55.9±8.7
Lymphocyte	19	53	33.2±8.9
Monocyte	6	19	11.1±3.0
PLT	128	494	249.2±84.8
PDW	7.1	10.9	8.4±0.8
MPV	15.4	16.6	15.9±0.4
D dimer	.1	3.9	0.508±0.73

Sorting patients according to levels of blood counts showed that decreased Hb was observed among 19.2%, normal among 80.2%, low TWBC among 7.7%, normal 88.5% and high 3.8%, platelet with low counts 7.7%, normal 88.5% and high were 3.8% as in **Table 3**.

Table 3. Distribution of Hemoglobin, Total White Blood Cells, and Platelet Levels Among Study Participants

	Hb		TWBCs		Platelets	
	Frequency	Percent	Frequency	Percent	Frequency	Percent
Low	10	19.2	4	7.7	4	7.7
Normal	42	80.8	46	88.5	46	88.5
High	0	0.0	2	3.8	2	3.8
Total	52	100.0	52	100.0	52	100.0

No significant differences were observed between groups for most hematological parameters. However, PDW was significantly lower, while monocyte percentage, MPV, and D-dimer levels were significantly higher in diabetic patients with retinopathy compared to controls ($p < 0.05$), all data reported in **Table 4**

Table 4. Frequency of Complete Blood Count and D-Dimer Levels Between Diabetic Patients with Retinopathy and Control Group

	Case (n=52)	Control (n=30)	P. value
Hb	12.8 ± 1.2	12.9 ± 1.5	0.622
RBCs	4.9 ± 0.7	4.7 ± 0.5	0.112
PCV	40.5 ± 3.4	40.1 ± 3.9	0.661
MCV	84.7 ± 6.1	82.5 ± 14.9	0.351
MCH	26.0 ± 2.2	26.8 ± 2.6	0.182
MCHC	30.7 ± 0.9	31.23 ± 1.5	0.065
RDW-CV	14.9 ± 1.3	14.3 ± 1.9	0.099
TWBCs	6.8 ± 2.7	6.7 ± 2.2	0.795
Neutrophils	55.9 ± 8.7	59.7 ± 9.4	0.070
Lymphocyte	33.2 ± 8.9	30.1 ± 8.7	0.125
Monocyte	11.1 ± 3.0	9.5 ± 4.3	0.049*
PLT	249.2 ± 84.8	253.4 ± 86.8	0.834
PDW	8.4 ± 0.8	14.6 ± 2.4	0.000*
MPV	15.9 ± 0.4	10.2 ± 1.6	0.000*
D dimer	0.51 ± 0.10	0.25 ± 0.10	0.013*

Table 5 summarized the comparison of CBC and D-dimer Parameters According to Gender in the Case Group were significant gender-based differences were observed in total white blood cell count (TWBCs), lymphocyte percentage, and platelet count, all of which were significantly higher in females than males ($p < 0.05$). No significant differences were found between males and females for the remaining hematological parameters or D-dimer levels ($p > 0.05$).

Table 5. Comparison of CBC and D-dimer Parameters According to Gender in the Case Group

	Male (n=24)	Female (n=28)	P. value
Hb	12.9 ± 1.4	12.6 ± 0.9	0.321
RBCs	4.8 ± 0.4	5.0 ± 0.9	0.299
PCV	41.1 ± 3.7	39.9 ± 3.1	0.229
MCV	85.6 ± 5.1	84.0 ± 6.8	0.353
MCH	26.4 ± 2.2	25.7 ± 2.2	0.262
MCHC	30.8 ± 1.1	30.7 ± 0.7	0.889
RDW-CV	15.0 ± 1.4	14.7 ± 1.3	0.410
TWBCs	5.9 ± 1.3	7.7 ± 3.2	0.013*
Neutrophils	57.6 ± 7.4	54.6 ± 9.7	0.219
Lymphocyte	30.5 ± 7.7	35.5 ± 9.3	0.041*
Monocyte	11.7 ± 2.9	10.6 ± 3.1	0.229
PLT	215.7 ± 66.8	278.0 ± 89.0	0.007*
PDW	8.5 ± 0.9	8.3 ± 0.7	0.311
MPV	15.9 ± 0.4	15.9 ± 0.4	0.365
D dimer	0.31 ± 0.17	0.67 ± 0.18	0.083

Table 6 demonstrate significant correlations with MCHC ($r = -0.290$, $p = 0.037$), neutrophils ($r = 0.328$, $p = 0.018$), lymphocytes ($r = -0.332$, $p = 0.016$), and PDW ($r = -0.333$, $p = 0.016$). Other hematological parameters showed no statistically significant associations with age ($p > 0.05$).

Pearson's correlation analysis showed that age was positively correlated with neutrophil percentage ($p = 0.018$). Significant negative correlations were observed with MCHC ($p = 0.037$), lymphocyte percentage ($p = 0.016$), and PDW ($p = 0.016$). No significant correlations were found for the remaining parameters ($p > 0.05$), so age correlated positively with neutrophils and negatively with MCHC, lymphocytes, and PDW; duration of diabetes negatively correlated with Hb, PCV, and MCHC; duration of retinopathy correlated positively only with RBCs ($p < 0.05$).

Table 6. Correlation of Age, Duration of DM and retinopathy with CBC and D-dimer

Parameters	Age		Duration of DM		Duration of retinopathy	
	Pearson Correlation	P. value	Pearson Correlation	P. value	Pearson Correlation	P. value
Hb	.046	.748	-.470	.000*	.103	.469
RBCs	.184	.193	-.226	.108	.427	.002*
PCV	.163	.248	-.423	.002*	.182	.197
MCV	.036	.798	-.166	.240	.190	.178
MCH	-.059	.680	-.220	.118	.006	.966
MCHC	-.290	.037*	-.317	.022*	-.177	.209
RDW-CV	.143	.312	.112	.430	-.217	.122

TWBCs	.034	.811	.237	.090	-.273	.050
Neutrophils	.328	.018*	.260	.062	-.220	.117
Lymphocyte	-.332	.016*	-.162	.252	.152	.281
Monocyte	.125	.379	-.230	.101	.147	.298
PLT	.154	.275	.239	.088	-.027	.851
PDW	-.333	.016*	-.080	.572	-.166	.239
MPV	-.137	.331	-.249	.075	-.111	.435
D dimer	.231	.099	.073	.605	-.053	.708

Diabetes mellitus is a chronic metabolic disorder associated with substantial morbidity and mortality worldwide. Persistent hyperglycemia contributes to widespread metabolic, cellular, and vascular disturbances, predisposing patients to microvascular and macrovascular complications, including diabetic retinopathy (DR). As reported globally, diabetes remains one of the top causes of adult mortality, accounting for an estimated 4 million deaths in 2017 [20, 21]. Understanding hematological and coagulation alterations in diabetic patients is essential for early detection and prevention of sight-threatening complications.

The present case–control study evaluated complete blood count (CBC) indices and D-dimer levels among Sudanese patients with diabetic retinopathy compared to a non-diabetic control group. The findings highlight important hematologic patterns that may contribute to the pathophysiology and progression of DR.

A significant elevation in D-dimer levels was observed in diabetic retinopathy patients, indicating enhanced fibrin turnover and hypercoagulability [22-26]. This supports the concept that a pro-thrombotic state contributes to retinal microvascular injury in diabetes. Our findings are consistent with the results of Shetty *et al*. who also reported increased D-dimer levels among patients with DR [27]. This reinforces the utility of D-dimer as a potential biomarker for monitoring vascular alterations associated with retinopathy [28-30]. Our findings are consistent with Zhao *et al*. (2021) [31], who demonstrated significantly elevated D-dimer levels among patients with non-proliferative and proliferative diabetic retinopathy. Their results support the concept that hypercoagulability and enhanced fibrinolysis accompany the microvascular damage observed in DR. However, our results contradict the report by Diabetes Care (2024) [32], where D-dimer did not show a significant association with diabetic retinopathy [33-36]. In addition, Matheus AS *et al*. (2022) [37] reported that biochemical markers of endothelial dysfunction, which could include coagulation-related biomarkers, did not significantly improve the prediction of diabetic retinopathy beyond traditional risk factors in type 1 diabetes. This suggests that while coagulation abnormalities (such as elevated D-dimer) might play a role, they may not be primary drivers of DR risk in all populations. Such discrepancies may be attributed to differences in study population, DR grading, sample size, and the variability of coagulation biomarker assays, highlighting the need for standardized methodologies.

In addition, Mean Platelet Volume (MPV) was significantly increased in the diabetic retinopathy group. Elevated MPV reflects platelet activation, larger platelet size, and increased thrombogenic potential—all of which are relevant in microvascular occlusion and retinal ischemia. This observation aligns with several studies that have also reported elevated MPV in patients with diabetic retinopathy, supporting the concept of increased platelet activation and microvascular thrombogenicity. Aldeewan *et al*. (2019) [38] and Zhang Y, *et al*. (2024) [39] all documented significantly higher MPV values among patients with NPDR and PDR, reinforcing the role of platelet hyperactivity in DR pathogenesis.

Conversely, other studies have shown inconsistent behavior of platelet indices. Demiray *et al*. (2020) [40] found no significant differences in MPV between DR and non-DR groups, while Güngör *et al*. (2014) [41] reported elevated PDW in DR, contrary to our results. Sheikh DA *et al*. (2024) [42] further noted that platelet indices may not reliably correlate with diabetic microvascular complications. Such variability may reflect differences in laboratory methods, patient demographics, disease duration, and ethnic factors, highlighting the need for standardized multicenter investigations.

This discrepancy may be attributed to differences in sample size, population characteristics, disease duration, or laboratory methodologies [43-48]. Population-specific variations may also influence platelet indices, highlighting the need for multicenter studies to establish consistent trends.

Regarding leukocyte parameters, monocyte percentage was significantly higher in the case group, suggesting an inflammatory response contributing to retinal vascular injury. Elevated monocytes have been implicated in endothelial dysfunction and microvascular inflammation, both of which are central to DR progression. Gender-based analyses showed significantly higher total WBC count, lymphocyte percentage, and platelet count among females, although the clinical significance of these differences warrants further investigation.

Correlation analyses revealed notable relationships between hematologic markers, disease duration, and age. Duration of diabetes showed significant negative correlations with Hb, PCV, and MCHC, suggesting progressive hematological deterioration with long-standing disease. Age correlated positively with neutrophil percentage and negatively with lymphocyte percentage and PDW, reflecting age-related inflammatory and hematologic changes among diabetic individuals. Interestingly, the duration of retinopathy was positively correlated with RBC count, although most other parameters showed weak or non-significant associations [49-54].

Overall, the study demonstrates that hematological and coagulation abnormalities—particularly elevated D-dimer, increased MPV, and altered monocyte levels—are associated with diabetic retinopathy. These results highlight the significance of regularly evaluating haematologic markers as additional screening methods for identifying early vascular and inflammatory alterations in diabetes individuals.

Future research with a larger, multicenter sample and longitudinal follow-up is recommended to validate these findings, explore their predictive value, and assess whether targeting coagulation or platelet activation could provide

therapeutic benefits. Additionally, further evaluation of anticoagulant therapies may offer insights into potential strategies for preventing or slowing the progression of diabetic retinopathy.

Conclusion

This study demonstrated that D-dimer levels were elevated among patients with type 2 diabetes mellitus (T2DM) with retinopathy, indicating enhanced coagulation activity in diabetic microvascular complications. Hematological abnormalities were also observed, with anemia present in 19.2%, thrombocytopenia in 7.7%, and leukopenia in 7.7%, while leukocytosis was detected in 3.8% of patients.

Both mean platelet volume (MPV) and monocyte percentage were significantly higher in the diabetic retinopathy group, suggesting increased platelet activation and chronic inflammatory status, respectively. A negative correlation between diabetes duration and hemoglobin levels indicated a higher risk of anemia with disease progression.

Gender-related differences were observed, where female patients exhibited significantly higher total white blood cell and platelet counts than males ($P < 0.05$). Additionally, there was a negative correlation with lymphocyte count and platelet distribution width (PDW) and a positive correlation with neutrophil levels. These findings collectively point toward systemic inflammation, immune dysregulation, and evolving microvascular changes among patients with diabetic retinopathy.

Limitations of the study

This study was influenced by several contextual and logistical constraints. Limited financial resources restricted the sample size and the ability to include additional study sites. In addition, the ongoing conflict in Sudan significantly disrupted healthcare services and patient accessibility, which affected participant recruitment and the availability of stable research infrastructure. As a result, conducting a larger, multicenter study with extended follow-up and advanced diagnostic investigations was not feasible.

Recommendation

Implementing routine laboratory screening of hematological indices—such as mean platelet volume (MPV), platelet distribution width (PDW), monocyte count, and neutrophil and lymphocyte percentages—together with D-dimer testing and periodic ophthalmologic evaluations, is recommended to enhance early detection of complications among diabetic patients. In parallel, strengthening community awareness and education regarding the seriousness of diabetes, its systemic consequences, and effective preventive measures is essential for reducing disease burden. Additionally, further rigorously designed studies are warranted to assess the potential role of anticoagulant therapies in mitigating the progression of diabetic retinopathy. Future research involving larger, multicenter cohorts with longitudinal follow-up is strongly recommended to validate current findings and to elucidate their clinical applicability.

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