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Correspondence between OCT Characteristics and Biochemical Parameters in Diabetic Macular Edema

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Abstract

Objective: The purpose of this study is to evaluate the potential association between peripheral blood parameters and the morphological characteristics of retinal imaging obtained via spectral-domain optical coherence tomography (SD-OCT) in patients with treatment-naïve diabetic macular edema (DME).

Materials and Methods: This cross-sectional study included 100 patients with treatment-naïve DME. All participants underwent spectral-domain optical coherence tomography (Optovue) and fundus photography. Peripheral blood samples were collected to assess complete blood count (CBC), glycated hemoglobin (HbA1c), blood glucose, serum urea, serum creatinine, and lipid profile.

Results: Central subfield thickness (CST) was significantly associated with serum HDL (*P*= 0.003). Intraretinal fluid (IRF) was linked to serum triglycerides (P=0.006), serum VLDL (P=0.001), and cholesterol-to-HDL ratio (*P*= 0.001). Subretinal fluid (SRF) showed an association with blood glucose (*P*= 0.028). Hyperreflective foci (HF) were related to total blood count (*P*= 0.001), monocyte count (*P*= 0.001), cholesterol-to-HDL ratio (*P*= 0.045), LDL-to-HDL ratio (*P*= 0.003), and serum urea (*P*= 0.051). Disorganization of the retinal inner layers (DRIL) correlated with total blood count (P=0.047), lymphocyte count (*P*= 0.008), blood glucose (*P*= 0.007), and LDL-to-HDL ratio (*P*= 0.046). Epiretinal membrane (ERM) was associated with blood glucose (*P*= 0.001), total cholesterol (*P*= 0.022), serum LDL (*P*= 0.025), cholesterol-to-HDL ratio (*P*= 0.013), and LDL-to-HDL ratio (*P*= 0.008). Ellipsoid zone (EZ) and external limiting membrane (ELM) disruptions were linked to blood glucose, serum LDL, and VLDL. Hard exudates correlated with blood cell counts, glucose, HbA1c, urea, and creatinine (*P*< 0.05).

CONCLUSION: Systemic factors are significantly associated with retinal morphological patterns in DME, highlighting the potential for modifying these factors to influence disease progression and treatment response.

Keywords: Diabetic macular edema, OCT, Biochemical parameters.

QR Code:

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Introduction

According to estimates from the World Health Organization, the global number of individuals with diabetes mellitus (DM) is projected to rise to 548 million by 2030 (1). All individuals with DM are at risk of developing diabetic retinopathy (DR), a progressive condition characterized by microvascular alterations that result in retinal ischemia, increased retinal permeability, retinal neovascularization, and macular edema (2). Diabetic macular edema (DME) is the leading cause of decreased visual acuity in patients with DR, with an overall prevalence of approximately 6.8% to 14% among DM patients (3). The natural course of DME can lead to significant vision loss in up to 50% of affected patients within two years (4).

DME is clinically manifested as retinal thickening due to the accumulation of intraretinal fluid, primarily in the inner and outer plexiform layers. This is thought to result from hyperpermeability of the retinal vasculature. DME can occur at any stage of diabetic retinopathy. The purpose of this study is to investigate the potential association between peripheral blood parameters and the morphological characteristics of retinal imaging obtained using spectral-domain optical coherence tomography (SD-OCT) in patients with treatment-naïve diabetic macular edema (DME).

Material and Methods

This cross-sectional study was conducted at M. N. Eye Hospital, Chennai, between February 2022 and May 2023, involving 50 patients (50 eyes). Written informed consent was obtained from all participants in their native language (Tamil). Data were collected using a pre-designed, validated proforma that included sociodemographic information, detailed history of diabetes mellitus (DM) duration, history of treatment, and the presence of other systemic conditions such as hypertension and renal disease.

Ophthalmic examinations were performed using slit-lamp biomicroscopy. After dilating the pupils with tropicamide eye drops, fundus examination was conducted using direct ophthalmoscopy, indirect ophthalmoscopy, and slit-lamp biomicroscopy with a +90D lens. Patients diagnosed with diabetic retinopathy (DR) and clinically significant macular edema (CSME) were classified according to the Early Treatment Diabetic Retinopathy Study (ETDRS) classification. For patients with bilateral diabetic macular edema (DME), only the more severely affected eye was included in the analysis.

Spectral-domain optical coherence tomography (SD-OCT) was performed on all participants. Patients were instructed to fast overnight before blood samples were collected for the evaluation of hemoglobin (Hb), total count (TC), differential count (DC), HbA1c, blood urea, serum creatinine, and a lipid profile, including total cholesterol, LDL, HDL, VLDL, triglycerides (TGL), cholesterol-to-HDL ratio, and LDL-to-HDL ratio.

All OCT images were analyzed and categorized accordingly:

Central Macular Thickness (CMT)

CMT is defined as the thickness of the central subfield, representing the circular area with a 1 mm diameter centered on the foveal center. This measurement is provided as a quantifiable value by the OCT software.

Disorganization of Retinal Inner Layers (DRIL)

DRIL is defined as the inability to distinguish between the ganglion cell–inner plexiform layer complex, the inner nuclear layer, and the outer plexiform layer within the central fovea. It was classified as either absent or present.

External Limiting Membrane (ELM) and Ellipsoid Zone (EZ)

Integrity The integrity of the ELM and EZ was graded based on the visibility and continuity of the first and second hyperreflective bands of the outermost retinal layers. These were categorized as follows:

Intact: Discernible and continuous layers.

Disrupted: Partially visible layers.

Absent: Completely undetectable layers.

Hyperreflective Foci (HRF)

HRFs were defined as round, hyperreflective dots within the retina. To distinguish HRFs from hard exudates or microaneurysms, the following criteria were applied: 1. Reflectivity similar to the retinal nerve fiber layer (RNFL). 2. Diameter less than 30 μm. 3. Absence of back-shadowing. The number of HRFs was counted manually.

Subretinal Fluid (SRF)

SRF was defined as a subfoveal hypo-reflective area resulting from neurosensory detachment (5). It was categorized as either absent or present.

Ethical considerations

The study has been approved by ethics committee by Ethical Code (U85100TN2010 PTC077225).

Statistical analysis

Data were entered into an MS Excel sheet and analyzed using SPSS software version 21. Continuous or numerical variables, such as age, were expressed as mean ± standard deviation. Categorical variables, such as gender, were presented as frequencies and percentages. Pie charts and bar diagrams were used for visual representation where appropriate.

For the analysis of associations between continuous and categorical variables, the data were represented as mean ± standard deviation in tables. The significance of differences between means was tested using the Student's T-test for comparisons involving two categories and the ANOVA test for comparisons involving more than two categories. A *P* of less than 0.05 was considered statistically significant.

Results

The mean Age (years) was 56.72 (± 9.06) ranging from 38 to 81 years. Among the subjects, 55 (55%) were females and 45 (45%) were males.

1. Central macular thickness

The mean hemoglobin (g/dl) among patients with CMT> 300 μm was 11.1 (± 1.7), which was 1.05 lower than the mean hemoglobin of 12.15 (± 1.47) observed in patients with CMT< 300 μm. This difference was statistically significant (*P*= 0.001).

The mean total count among patients with CMT> 300 μm was 8020.94 (± 1993.05), which was 1055.5 higher compared to 6965.44 (± 1165.97) in patients with CMT < 300 μm. This difference was also statistically significant (*P*= 0.002).

The mean polymorph count in patients with CMT > 300 μm was 60.97 (± 8.83), 4.17 higher than the 56.8 (± 7.83) observed in patients with CMT < 300 μm. This difference was statistically significant (*P*= 0.014).

The mean lymphocyte count among patients with CMT > 300 μm was 32.45 (± 7.24), which was 3.92 lower than the 36.37 (± 7.71) in patients with CMT < 300 μm. This difference was statistically significant (*P*= 0.010).

The mean monocyte count in patients with CMT > 300 μm was 2.46 (± 2.08), 0.86 lower than the 3.32 (± 2.57) observed in CMT < 300 μm. However, this difference was not statistically significant.

The mean fasting blood glucose (mg/dl) in patients with CMT> 300 μm was 146.9 (± 36.46), which was 61.12 lower than the 208.02 (± 58.93) observed in patients with CMT< 300 μm. This difference was statistically significant (*P*= 0.001).

The mean post-prandial blood glucose (mg/dl) in patients with CMT> 300 μm was

244.62 (± 42.24), which was 78.44 lower compared to 323.06 (± 110.64) in CMT< 300 µm. This difference was also statistically significant.

The mean HbA1c among patients with CMT> 300 µm was 8.91 (± 1.58), which was 1.63 lower compared to 10.55 (± 2.09) in CMT< 300 µm. This difference was statistically significant (*P*= 0.001).

The mean serum HDL (mg/dl) in patients with CMT> 300 µm was 39.49 (± 8.2), 5.61 lower than the 45.1 (± 10.32) in patients with CMT< 300 µm. This difference was statistically significant.

The mean serum urea (mg/dl) in patients with CMT> 300 µm was 36.71 (± 18.92), 10.78 higher compared to 25.94 (± 8.99) in patients with CMT < 300 µm. This difference was statistically significant (*P*= 0.001).

Finally, the mean serum creatinine (mg/dl) in patients with CMT > 300 µm was 1.4 (± 1.1), 0.45 higher than the 0.96 (± 0.43) observed in patients with CMT< 300 µm. This difference was statistically significant (*P*= 0.009).

2. Intra retinal fluid

As shown in Table 1 intraretinal fluid (IRF) was linked to serum triglycerides (*P*= 0.006), serum VLDL (*P*= 0.001), and cholesterol-to-HDL ratio (*P*= 0.001).

3. Hyper reflective foci

Table 2 shows that hyperreflective foci (HF) were related to total blood count (*P*= 0.001), monocyte count (*P*= 0.001), cholesterol-to-HDL ratio (*P*= 0.045), LDL-to-HDL ratio (*P*= 0.003), and serum urea (*P*= 0.051).

4. Sub retinal fluid

Sub retinal fluid did not have any statistical significance with any of the laboratory parameters.

5. Disorganization of the inner retinal layers

The mean total count among patients with Disorganization of the Inner Retinal Layers (DRIL) was 8108.79 (± 2455.96), which was 918.8 higher compared to 7189.99 (± 1083.11) in those without DRIL. This difference was statistically significant (*P*= 0.047). The mean lymphocyte count among patients with DRIL was 31.52 (± 7.35), which was 4.31 lower than the 35.83 (± 7.52) observed in those without DRIL. This difference was statistically significant (*P*= 0.008).

Table 1. Association between laboratory variables and intra retinal fluid on optical coherence tomography

Variable	Intra Retinal Fluid		Mean diff.	*P*-value
	Present	No		
Hemoglobin (g/dl)	11.62 (± 1.6)	11.65 (± 2.17)	0.032	0.962
Total count	7558.94 (± 1744.4)	7011 (± 1388.31)	547.943	0.300
Polymorphs count	58.98 (± 8.61)	58.25 (± 8.59)	0.725	0.785
Lymphocyte count	34.43 (± 7.28)	34.25 (± 10.66)	0.181	0.940
Eosinophil count	5.12 (± 2.12)	5.75 (± 2.99)	0.631	0.492
Monocyte count	2.84 (± 2.46)	3.25 (± 1.54)	0.409	0.577
Basophil count	0.58 (± 0.62)	0.35 (± 0.43)	0.233	0.114
Fasting blood glucose (mg/dl)	175 (± 52.02)	195.5 (± 89.89)	20.500	0.455
Post prandial blood glucose (mg/dl)	274.75 (± 77.39)	350.5 (± 153.58)	75.750	0.119
HbA1C	9.59 (± 1.84)	10.78 (± 2.93)	1.186	0.197
Serum total cholesterol (mg/dl)	202.35 (± 47.36)	183.25 (± 36.77)	19.101	0.183
Serum HDL (mg/dl)	41.99 (± 9.37)	44.5 (± 12.01)	2.508	0.403
Serum LDL (mg/dl)	122.81 (± 42.39)	118.85 (± 22.88)	3.958	0.752
Serum triglycerides (mg/dl)	184.7 (± 103.42)	99.75 (± 39.58)	84.952	0.006
Serum VLDL (mg/dl)	32.91 (± 10.7)	19.85 (± 7.95)	13.064	0.001
Cholesterol HDL ratio	5.07 (± 1.88)	4.18 (± 0.41)	0.883	0.001
LDL HDL Ratio	3.07 (± 1.41)	2.74 (± 0.48)	0.332	0.423
Serum urea (mg/dl)	30.71 (± 14.35)	35.8 (± 23.77)	5.086	0.483
Serum creatinine (mg/dl)	1.09 (± 0.56)	1.83 (± 1.91)	0.739	0.210

The mean fasting blood glucose (mg/dl) in patients with DRIL was 159.67 (± 36.29), which was 26.56 lower compared to 186.22 (± 64.08) in those without DRIL. This difference was statistically significant (*P*= 0.010). The mean post-prandial blood glucose (mg/dl) among patients with DRIL was 248.58 (± 66.67), which was 52.63 lower than the 301.21 (± 98.29) in those without DRIL. This difference was statistically significant (*P*= 0.007). The mean LDL-to-HDL ratio among patients with DRIL was 3.51 (± 1.89), which was 0.71 higher compared to 2.8 (± 0.89) in those without DRIL. This difference was statistically significant (*P*= 0.046).

6. Epiretinal membrane

As shown in Table 3, epiretinal membrane (ERM) was associated with blood glucose (*P*= 0.001), total cholesterol (*P*= 0.022), serum LDL (*P*= 0.025), cholesterol-to-HDL ratio (*P*= 0.013), and LDL-to-HDL ratio (*P*= 0.008).

Table 2. Association between laboratory variables and Hyper reflective foci on optical coherence tomography

Variable	Hyper reflective Foci		Mean diff.	*P*-value
	Present	No		
Haemoglobin (g/dl)	11.51 (± 1.68)	12.03 (± 1.57)	0.515	0.210
Total Count	7737.38 (± 1789.5)	6574.57 (± 919.11)	1162.808	0.001
Polymorphs count	59.36 (± 9.02)	57.11 (± 6.47)	2.245	0.204
Lymphocyte count	33.72 (± 7.78)	37.01 (± 6.97)	3.298	0.081
Eosinophil count	5.38 (± 2.14)	4.49 (± 2.47)	0.898	0.102
Monocyte count	2.65 (± 2.23)	3.81 (± 2.69)	1.164	0.045
Basophil count	0.56 (± 0.64)	0.53 (± 0.46)	0.033	0.823
Fasting Blood Glucose (mg/dl)	172.61 (± 54.03)	195.71 (± 67.87)	23.107	0.160
Post Prandial Blood Glucose (mg/dl)	285.77 (± 75.37)	276.57 (± 140.82)	9.201	0.775
HbA1C	9.65 (± 2.13)	10.04 (± 1.51)	0.395	0.428
Serum Total Cholesterol (mg/dl)	201.87 (± 48.34)	193.24 (± 38.98)	8.628	0.452
Serum HDL (mg/dl)	41.68 (± 9.78)	44.6 (± 9.21)	2.921	0.221
Serum LDL (mg/dl)	123.96 (± 42.55)	116.23 (± 31.64)	7.727	0.440
Serum Triglycerides (mg/dl)	177.98 (± 108.7)	161.46 (± 69.94)	16.520	0.511
Serum VLDL (mg/dl)	31.09 (± 10.45)	32.31 (± 13.97)	1.225	0.711
Cholesterol HDL Ratio	5.12 (± 1.97)	4.36 (± 0.52)	0.766	0.003
LDL HDL Ratio	3.14 (± 1.46)	2.61 (± 0.57)	0.530	0.012
Serum Urea (mg/dl)	32.27 (± 17.36)	27.79 (± 5.28)	4.479	0.051
Serum Creatinine (mg/dl)	1.19 (± 0.95)	1.14 (± 0.42)	0.052	0.807

Table 3. Association between laboratory variables and Epiretinal membrane on optical coherence tomography

Variable	Epiretinal Membrane		Mean diff.	*P*-value
	Present	No		
Hemoglobin (g/dl)	11.81 (± 1.59)	11.52 (± 1.71)	0.291	0.407
Total Count	7883.2 (± 2330.61)	7283.18 (± 1226.26)	600.015	0.162
Polymorphs count	59.98 (± 8.84)	58.3 (± 8.42)	1.680	0.352
Lymphocyte count	32.48 (± 7.16)	35.45 (± 7.83)	2.972	0.065
Eosinophil count	4.69 (± 1.77)	5.46 (± 2.42)	0.770	0.072
Monocyte count	2.77 (± 2.68)	2.95 (± 2.2)	0.182	0.715
Basophil count	0.56 (± 0.59)	0.55 (± 0.62)	0.012	0.925
Fasting Blood Glucose (mg/dl)	154.46 (± 43.49)	189.85 (± 60.71)	35.389	0.001
Post Prandial Blood Glucose (mg/dl)	241.57 (± 59.24)	306.6 (± 98.87)	65.029	0.001
HbA1C	8.98 (± 1.66)	10.13 (± 2.09)	1.151	0.006
Serum Total Cholesterol (mg/dl)	214.52 (± 56.44)	192.27 (± 38.39)	22.243	0.022
Serum HDL (mg/dl)	40.59 (± 9.69)	43.21 (± 9.64)	2.613	0.200
Serum LDL (mg/dl)	137.08 (± 53.86)	114.39 (± 28.48)	22.688	0.025
Serum Triglycerides (mg/dl)	190.16 (± 119.33)	166.08 (± 90.71)	24.080	0.261
Serum VLDL (mg/dl)	32.35 (± 9.86)	30.81 (± 11.92)	1.542	0.515
Cholesterol HDL Ratio	5.72 (± 2.58)	4.55 (± 0.97)	1.172	0.013
LDL HDL Ratio	3.64 (± 1.92)	2.71 (± 0.72)	0.933	0.008
Serum Urea (mg/dl)	37.59 (± 18.23)	27.95 (± 13.1)	9.646	0.003
Serum Creatinine (mg/dl)	1.39 (± 0.74)	1.07 (± 0.91)	0.324	0.072

7. Ellipsoid zone disruption

Based on Table 4, there was an association between fasting blood glucose (*P*= 0.001), post-prandial blood glucose (*P*= 0.001), LDL (0.035), and VLDL (*P*= 0.044) with ellipsoid zone disruption.

8. Hard exudates

Table 5 shows Hard exudates correlated with polymorph count (0.001), eosinophil count (0.034), monocyte count (0.002), basophil count (0.007), fasting blood glucose (0.001), HbA1C (0.001), serum urea (0.009), and serum creatinine (0.001).

Discussion

The mean Central Macular Thickness (CMT) among the study population was 383.24 (± 157.76) µm, indicating a significant degree of macular thickening in patients with diabetic macular edema (DME). The observed wide range of CMT values, with a median of 302 µm (ranging from 218 to 793 µm), highlights the heterogeneity in DME

Table 4. Association between laboratory variables and Ellipsoid Zone disruption on optical coherence tomography

Variable	Ellipsoid Zone disruption		Mean diff.	*P*-value by T-test
	Present	No		
Hemoglobin (g/dl)	11.48 (± 1.19)	11.69 (± 1.86)	0.214	0.488
Total Count	7278.55 (± 2043.73)	7598.91 (± 1523.45)	320.365	0.381
Polymorphs count	59.45 (± 7.41)	58.61 (± 9.12)	0.846	0.645
Lymphocyte count	33.07 (± 5.69)	35.07 (± 8.48)	1.994	0.167
Eosinophil count	4.83 (± 1.83)	5.37 (± 2.4)	0.544	0.213
Monocyte count	3.06 (± 2.61)	2.81 (± 2.26)	0.255	0.616
Basophil count	0.62 (± 0.69)	0.52 (± 0.56)	0.094	0.466
Fasting Blood Glucose (mg/dl)	150.03 (± 35)	190.97 (± 61.85)	40.940	0.001
Post Prandial Blood Glucose (mg/dl)	229.94 (± 64.12)	310.39 (± 92.64)	80.449	0.001
HbA1C	9.41 (± 1.16)	9.89 (± 2.32)	0.476	0.175
Serum Total Cholesterol (mg/dl)	190.07 (± 34.72)	204.98 (± 50.81)	14.909	0.132
Serum HDL (mg/dl)	40.7 (± 10.4)	43.08 (± 9.3)	2.383	0.249
Serum LDL (mg/dl)	110.2 (± 25.45)	128.31 (± 45.1)	18.104	0.035
Serum Triglycerides (mg/dl)	201.64 (± 117.48)	161.14 (± 90.96)	40.495	0.061
Serum VLDL (mg/dl)	34.26 (± 8.86)	29.91 (± 12.01)	4.356	0.044
Cholesterol HDL Ratio	5.05 (± 2.06)	4.92 (± 1.66)	0.136	0.723
LDL HDL Ratio	2.91 (± 1.08)	3.09 (± 1.46)	0.187	0.514
Serum Urea (mg/dl)	31.51 (± 9.03)	31.23 (± 18.17)	0.273	0.920
Serum Creatinine (mg/dl)	1.07 (± 0.44)	1.23 (± 1)	0.164	0.373

Table 5. Association between laboratory variables and Hard Exudates on optical coherence tomography

Variable	Hard Exudates		Mean diff.	*P*-value by T-test
	Present	No		
Haemoglobin (g/dl)	11.78 (± 1.86)	11.29 (± 1.1)	0.483	0.108
Total Count	7500.44 (± 1922.57)	7477.78 (± 1156.26)	22.660	0.942
Polymorphs count	56.7 (± 8.59)	63.53 (± 6.48)	6.824	0.001
Lymphocyte count	35.2 (± 7.79)	32.73 (± 7.35)	2.467	0.136
Eosinophil count	4.87 (± 2.2)	5.88 (± 2.18)	1.009	0.034
Monocyte count	3.38 (± 2.41)	1.84 (± 1.94)	1.539	0.002
Basophil count	0.44 (± 0.53)	0.79 (± 0.7)	0.347	0.007
Fasting Blood Glucose (mg/dl)	193.43 (± 57.89)	143.53 (± 40.15)	49.895	0.001
Post Prandial Blood Glucose (mg/dl)	294.12 (± 100.53)	262 (± 67.58)	32.118	0.104
HbA1C	10.29 (± 1.78)	8.54 (± 2)	1.751	0.001
Serum Total Cholesterol (mg/dl)	200.79 (± 51.83)	198.5 (± 33.03)	2.293	0.790
Serum HDL (mg/dl)	41.69 (± 10.42)	43.57 (± 7.91)	1.877	0.369
Serum LDL (mg/dl)	120.53 (± 46.15)	126.18 (± 24.66)	5.650	0.518
Serum Triglycerides (mg/dl)	187.53 (± 113.94)	146.84 (± 61.75)	40.692	0.062
Serum VLDL (mg/dl)	32.29 (± 10.6)	29.33 (± 12.36)	2.963	0.219
Cholesterol HDL Ratio	5.12 (± 2.08)	4.63 (± 0.84)	0.492	0.096
LDL HDL Ratio	3.07 (± 1.56)	2.96 (± 0.7)	0.111	0.702
Serum Urea (mg/dl)	27.43 (± 6.11)	39.6 (± 24.55)	12.165	0.009
Serum Creatinine (mg/dl)	0.9 (± 0.23)	1.78 (± 1.3)	0.888	0.001

presentation.

Studies have shown variability in mean CMT values depending on the type of OCT instrument used, the definition of center-involved DME, and disease severity. For example, a study using Stratus OCT and Cirrus HD-OCT reported a mean CMT of 316.8 μm for DME patients (6).

Another study using OCT angiography noted a mean CMT of 302.8 μm for center-involved DME patients (7). Using Spectralis OCT, a study reported a mean CMT of 381.9 μm (8). Additionally, Roca et al. (9) documented a prevalence of 43% for CMT≥ 450 μm, while Dimitriou et al. (1) reported a mean CMT of 439.2 (± 79.1) μm. The current study found a significant association between increased CMT and elevated WBC counts.

Neutrophils serve as markers of inflammation, while lymphocytes indicate physiological stress, with both parameters and their neutrophil-to-lymphocyte ratio being predictors of inflammatory conditions. In DME, chronic low-grade inflammation may trigger the release of inflammatory cytokines, leading to increased vascular permeability.

This process is reflected in elevated neutrophil and lymphocyte counts in the blood and their association with increased CMT (10). Dimitriou et al. (4) also demonstrated that patients with CMT> 405 μm had significantly higher neutrophil and lymphocyte counts, as well as an elevated neutrophil-to-lymphocyte ratio.

Conversely, the present study did not identify a significant association between lipid profile parameters and increased CMT, despite observing higher lipid values. This finding aligns with the results of Dimitriou et al. (4), which reported a significant association only with lipoprotein (a).

Intra retinal fluid

Among the study subjects, 88 (88%) had Intra Retinal Fluid (IRF). The prevalence of IRF in patients with diabetic macular edema (DME) varies based on factors such as treatment type, duration of follow-up, and the definition of IRF. Serra et al. (11), using Aflibercept, reported that 88.9% of DME patients had IRF at baseline, which decreased to 25.9% at 12 months. Similarly, studies using OCT angiography, such as Chung et al. (12), observed a prevalence of 75.6%. Dimitriou et al. (4) reported that 100% of its study population had IRF.

In the current study, a significant association was observed between IRF and increased serum VLDL levels and the cholesterol-to-HDL ratio. However, other studies, such as Dimitriou et al. (1), found no significant association between the lipid profile and the presence of IRF.

Sub retinal fluid

Among the study subjects, 31 (31%) had Sub Retinal Fluid (SRF).

Similarly, Park et al. (13) reported a prevalence of 22% SRF among DME patients. Other studies have documented a wide range of SRF prevalence, varying from 18% to 32% in DME patients (14,15).

Dimitriou et al. (4) observed a prevalence of 25% SRF among their DME cohort. The present study did not identify any significant association between SRF and blood counts or biochemical parameters. This finding is consistent with studies such as Dimitriou et al. (4), which also reported no significant associations.

Hyper reflective foci

The current study population revealed that 79% of participants had hyperreflective foci (HRF), a finding comparable to Davoudi et al. (16), who identified HRF in 70% of patients with diabetic macular edema (DME). In contrast, Dimitriou et al. (4) reported HRF in 41.7% of DME patients. These findings suggest that more than half of DME patients are likely to present with HRF.

Our study demonstrated a significant association between HRF and an increased total white blood cell (WBC) count. Furthermore, HRF was significantly correlated with the cholesterol-to-HDL ratio and the

LDL-to-HDL ratio, consistent with the findings of Davoudi et al. (16). Specifically, Davoudi et al. reported significant odds ratios for the association of HRF with total cholesterol (TC) and LDL (1.13) and with HDL and triglycerides (1.17).

Additionally, they noted a strong association between HRF and elevated HbA1C levels (>8%) as well as higher systolic blood pressure. On the other hand, Dimitriou et al. (4) found no statistically significant association between HRF and biochemical parameters, despite observing elevated lipid profile markers in patients with HRF. Similarly, Chung et al. (12) reported that HRF in DME was more common in patients with high serum cholesterol levels and was associated with serous retinal detachment. Previous studies have suggested that distinct HRF in DME may represent subclinical, early stages in the development of intraretinal hard exudates. These may include subclinical lipid deposits, lipid-laden macrophages, or proteinaceous materials (17,18). Collectively, this evidence highlights the potential role of lipid profiles in the pathogenesis of HRF in DME.

Disorganization of the inner retinal layers

In the current study, 33% of the population exhibited Disorganization of the Inner Retinal Layers (DIRL). Similarly, Dimitriou et al. (4) reported a DIRL prevalence of 16.7% among patients with diabetic macular edema (DME).

The study by Midena et al. (18) highlighted that DIRL is correlated with Müller cell activation in eyes with DME. Müller cells, which are glial cells that support the structural and functional integrity of the retina, produce glial fibrillary acidic protein (GFAP). GFAP serves as a marker of inflammation and retinal stress. Furthermore, DIRL was associated with elevated levels of vascular endothelial growth factor (VEGF) and interleukin-6 (IL-6) in the aqueous humor. These cytokines are key mediators of angiogenesis and inflammation within the retina. Additionally, the study found that DIRL was linked to altered serum lipid profiles in patients with DME. Patients with DIRL exhibited significantly higher levels of total cholesterol, low-density lipoprotein cholesterol (LDL-C), and triglycerides compared to those without DIRL. The findings suggested that DIRL may reflect the accumulation of lipid deposits within the inner retina, likely due to leakage from damaged retinal blood vessels.

Epiretinal membrane

In the current study, 35% of the population had an Epiretinal Membrane (ERM), which is notably higher compared to other studies. Roca et al. (9) reported a prevalence of 7%, and Dimitriou et al. (4) identified ERM in 5.6% of diabetic macular edema (DME) patients. Our study revealed a significant association between ERM in DME patients and elevated serum cholesterol, LDL, cholesterol-to-HDL ratio, and LDL-to-HDL ratio.

Ellipsoid zone disruption

In this study, 33% of participants exhibited Ellipsoid Zone Disruption (EZD), a finding consistent with Dimitriou et al. (4), who reported a similar prevalence of 36.1% among DME patients.

The study by Dimitriou et al. (4) demonstrated significantly reduced red blood cell (RBC) count, hematocrit, and hemoglobin levels in DME patients with EZD. Similarly, our study observed reduced hemoglobin levels in EZD patients, though the association was not statistically significant.

Furthermore, our study found a significant association between increased LDL and VLDL levels and the presence of EZD in DME patients. Although Dimitriou et al. (4) reported elevated lipid profile parameters in EZD patients, these findings were not statistically significant. However, their study noted that lipoprotein (a) levels were significantly higher in EZD patients.

Hard exudates

In the current study, 68% of diabetic macular edema (DME) patients had hard exudates, a prevalence notably higher than previous studies. Davoudi et al. (16) reported a prevalence of 31%, while Dimitriou et al. (4) found hard exudates in 36.1% of DME patients.

Chew et al. (18) observed that patients with elevated total cholesterol and LDL levels were more likely to develop retinal hard exudates compared to those with a normal lipid profile. However, the current study did not identify a significant association between hard exudates and lipid profile parameters.

Interestingly, this study found a significant increase in monocyte counts among patients with hard exudates. Monocytes, as indicators of inflammation, play a crucial role in secreting inflammatory cytokines and serve as biomarkers for ischemic conditions. These processes may contribute to the development of hard exudates in the retina.

Further research with a larger sample size is required to better understand these correlations and evaluate their implications for treatment strategies.

Conclusion

We have concluded that CST is associated with Serum HDL (mg/dl). IRF is associated with Serum Triglycerides (mg/dl), Serum VLDL (mg/dl), and Cholesterol HDL ratio. SRF is associated with Fasting blood glucose (mg/dl). HF is associated with Total blood count, Monocyte count, Cholesterol HDL ratio and LDL HDL ratio. DRIL is associated with Total count, Lymphocyte Count, Fasting blood glucose, Post prandial blood glucose and LDL HDL ratio. ERM is associated with Fasting blood glucose, post prandial blood glucose, Total cholesterol, serum LDL, Cholesterol HDL ratio and LDL HDL ratio. EZ disruption is associated with fasting blood glucose, post prandial blood glucose, serum LDL and serum VLDL. ELM disruption is associated with fasting and post prandial blood glucose, serum VLDL. Presence of Hard Exudates is associated with Polymorphs count, Eosinophil count, Basophil count, and Fasting blood glucose, HbA1C, Blood Urea and Serum Creatinine.

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Conflict of Interest

No conflict of interest

Authors' contributions

SVO carried out supervision stages of project and conceived of the study, and participated in writing the manuscript as well and participated in the design of the study. SSh performed the statistical analysis and writing the manuscript. NM carried out collect samples and helped to draft the manuscript. PDN conceived of the study, and participated in its design and coordination and helped to draft the manuscript. LS carried out collect samples and helped to draft the manuscript.

All the authors critically revised the manuscript, agree to be fully accountable for the integrity and accuracy of the study, and read and approved the final manuscript.

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