

High-Density and Low-Density Lipoprotein Cholesterol in Diabetic Retinopathy Severity among Adults with Type 2 Diabetes Mellitus

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ABSTRACT

Introduction: Diabetic retinopathy remains one of the leading microvascular complications of type 2 diabetes mellitus. Although dyslipidaemia is widely implicated in retinal vascular injury, the relative clinical value of individual lipid fractions remains unevenly described across hospital-based cohorts. HDL and LDL cholesterol are especially relevant because they represent opposite ends of the atherogenic spectrum and may reflect vascular vulnerability beyond glycaemic control.

Aim: To examine the association of HDL and LDL cholesterol with the presence and severity of diabetic retinopathy in adults with type 2 diabetes mellitus.

Materials and Methods: This cross-sectional study included 279 adults aged more than 40 years attending a tertiary-care ophthalmology service between August 2023 and February 2025. Diabetic retinopathy was graded using worse-eye ETDRS classification. Fasting blood sugar, post-prandial blood sugar, HbA1c, HDL cholesterol, and LDL cholesterol were analysed. Group comparisons were performed using independent t-test and analysis of variance, with $p < 0.05$ considered statistically significant.

Results: Diabetic retinopathy was present in 151/279 participants (54.1%). Mean HDL cholesterol was lower in participants with retinopathy than in those without retinopathy (41.74 ± 9.31 mg/dL versus 46.81 ± 9.70 mg/dL, $p < 0.001$). Mean LDL cholesterol was higher in participants with retinopathy (118.21 ± 33.65 mg/dL versus 107.27 ± 31.47 mg/dL, $p = 0.006$). Across severity grades, HDL cholesterol declined significantly from no retinopathy to proliferative disease ($p < 0.001$), while LDL cholesterol showed an upward trend that did not reach statistical significance ($p = 0.076$). Low HDL cholesterol was present in 50.9% and high LDL cholesterol in 27.6% of the cohort.

Conclusion: Lower HDL cholesterol showed a clear association with increasing diabetic retinopathy severity, while LDL cholesterol was significantly higher in retinopathy overall and tended to rise with advanced grades. These findings support inclusion of HDL and LDL assessment in metabolic risk appraisal of adults with type 2 diabetes undergoing retinal evaluation.

Keywords: Diabetic retinopathy, HDL cholesterol, LDL cholesterol, type 2 diabetes mellitus, dyslipidaemia, ETDRS.

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INTRODUCTION

Diabetes continues to expand as a major public health burden. The most recent IDF Diabetes Atlas estimates that hundreds of millions of adults are living with diabetes worldwide, and the burden is expected to rise further over the coming decades [1]. Within that larger epidemic, diabetic retinopathy remains one of the most feared complications because it threatens vision during the most productive years of adult life [2]. In India, where delayed diagnosis, prolonged disease duration, and uneven access to retinal screening remain common, the retinal burden is especially relevant to routine ophthalmic practice [3].

The biological basis of diabetic retinopathy is not limited to elevated glucose alone. Chronic hyperglycaemia initiates oxidative, inflammatory, and endothelial changes that injure

the retinal capillary bed and eventually lead to haemorrhages, exudation, ischemia, and neovascularisation [4]. Disease severity is commonly staged using internationally accepted classifications that distinguish no retinopathy, mild to severe non-proliferative diabetic retinopathy, and proliferative diabetic retinopathy [5].

Another layer of risk comes from dyslipidaemia. In type 2 diabetes mellitus, low HDL cholesterol and qualitatively more atherogenic LDL particles are biologically plausible contributors to retinal injury because they reflect impaired reverse cholesterol transport, oxidative stress, and vascular inflammation [6,7]. Experimental and clinical work has suggested that lower HDL may reduce vascular resilience, whereas LDL-related atherogenic burden may intensify endothelial damage and capillary dysfunction within the

retinal microcirculation [7,8].

Still, the literature has not been completely uniform. Some reports have linked HDL and LDL more strongly to retinal hard exudation or macular disease, whereas others have found broader associations with retinopathy severity itself [8-10]. That uncertainty makes focused clinical data useful, especially in tertiary settings where patients often present with multiple metabolic risks at the time of first retinal evaluation. The present study was therefore undertaken to examine how HDL and LDL cholesterol relate to the presence and severity of diabetic retinopathy in adults with type 2 diabetes mellitus.

MATERIALS AND METHODS

Study design and setting

A hospital-based cross-sectional study was conducted in the Department of Ophthalmology, Adichunchanagiri Institute of Medical Sciences, B.G. Nagara, Karnataka.

Study period

August 2023 to February 2025.

Study population

Adults aged more than 40 years with known type 2 diabetes mellitus attending the ophthalmology outpatient or inpatient services were screened for enrolment.

Inclusion criteria

Known type 2 diabetes mellitus and age more than 40 years.

Exclusion criteria

Long-term corticosteroid use, pregnancy, accelerated hypertension, active infection, high myopia, mature cataract, uveitis, age-related macular degeneration, recent ocular surgery within six months, and known hypercholesterolaemia.

Sampling and sample size

Consecutive eligible participants were enrolled until the

calculated sample size of 279 was achieved.

Ophthalmic evaluation

A detailed ocular examination was performed in all participants. Visual acuity was assessed with Snellen chart, intraocular pressure was measured, and fundus evaluation was completed after pupillary dilatation. Retinopathy was graded according to worse-eye ETDRS classification as no diabetic retinopathy, mild NPDR, moderate NPDR, severe NPDR, or proliferative diabetic retinopathy.

Biochemical assessment

Fasting blood sugar, post-prandial blood sugar, glycated haemoglobin, HDL cholesterol, and LDL cholesterol were recorded for analysis.

Statistical analysis

Quantitative variables were expressed as mean±standard deviation and categorical variables as frequency and percentage. Independent t-test was used for comparison between no diabetic retinopathy and any diabetic retinopathy groups. Analysis of variance was used across severity grades. A p-value less than 0.05 was considered statistically significant.

Ethical considerations

Institutional Ethics Committee approval was obtained before recruitment, and written informed consent was secured from all participants.

RESULTS

A total of 279 adults with type 2 diabetes mellitus were analysed. Baseline demographic and clinical characteristics are shown in Table 1. The largest age band was 50-59 years (34.4%), followed by 60-69 years (29.4%). Hypertension was present in 52.3% of participants, and 59.9% were either overweight or obese.

Table 1. Baseline characteristics of the study population (N=279).

Characteristic	Category	n (%)
Age group (years)	40-49	70 (25.1)
	50-59	96 (34.4)
	60-69	82 (29.4)
	≥70	31 (11.1)
Sex	Male	158 (56.6)
	Female	121 (43.4)
BMI category	Normal (18.5-24.9)	112 (40.1)
	Overweight (25-29.9)	107 (38.4)
	Obese (≥30)	60 (21.5)
Duration of diabetes (years)	<5	87 (31.2)
	5-10	104 (37.3)
	>10	88 (31.5)
Hypertension	No	133 (47.7)
	Yes	146 (52.3)
Smoking/tobacco use	No	220 (78.9)
	Yes	59 (21.1)

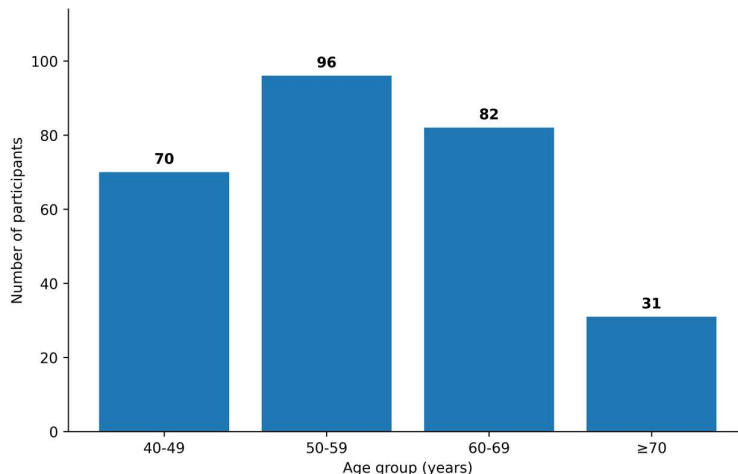


Figure 1. Bar chart showing age-group distribution of study participants.

Italic note: Values above bars represent participant counts. Diabetic retinopathy was identified in 151 of 279 participants (54.1%), while 128 (45.9%) had no retinopathy.

Mild and moderate NPDR together accounted for 35.4% of the cohort, whereas severe NPDR and proliferative diabetic retinopathy together constituted 18.6% [Table 2, Figure 2].

Table 2. Prevalence and severity distribution of diabetic retinopathy based on worse-eye ETDRS grading (N=279).

Retinopathy grade	n	%
No DR	128	45.9
Mild NPDR	52	18.6
Moderate NPDR	47	16.8
Severe NPDR	31	11.1
PDR	21	7.5

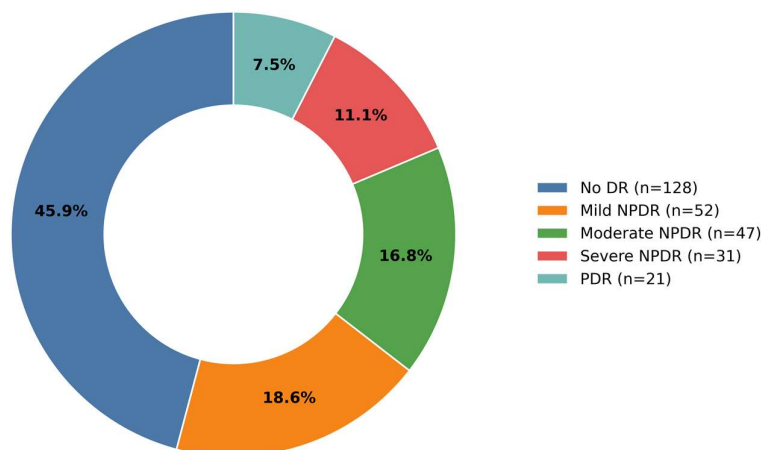


Figure 2. Donut chart showing the proportional distribution of diabetic retinopathy grades.

Italic note: Segment labels denote percentages; legend entries show raw counts.

The cohort showed generally poor metabolic control. Mean fasting blood sugar was 159.23±44.75 mg/dL, mean post-prandial blood sugar was 244.85±65.63 mg/dL, and mean HbA1c was 8.43±1.42%. For the lipid fractions retained in this focused analysis, mean HDL cholesterol was

44.07±9.81 mg/dL and mean LDL cholesterol was 113.19±33.07 mg/dL. Low HDL cholesterol was observed in 50.9% of participants, whereas high LDL cholesterol was present in 27.6% [Table 3, Figure 3].

Table 3. Overall glycaemic profile and HDL-LDL burden in the study population (N=279).

Parameter	Value
Fasting blood sugar, mg/dL	159.23 ± 44.75 (range: 80-306)
Post-prandial blood sugar, mg/dL	244.85 ± 65.63 (range: 120-436)
HbA1c, %	8.43 ± 1.42 (range: 5.60-12.79)
HDL cholesterol, mg/dL	44.07 ± 9.81 (range: 20-76)
LDL cholesterol, mg/dL	113.19 ± 33.07 (range: 40-218)
Low HDL, n (%)	142 (50.9)
High LDL, n (%)	77 (27.6)

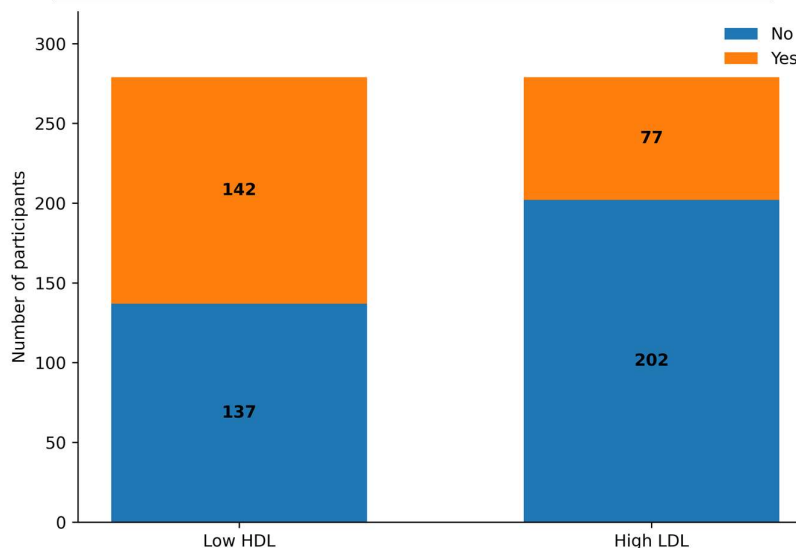


Figure 3. Stacked bar chart showing the distribution of low HDL and high LDL cholesterol in the cohort.
Italic note: Each bar represents the full cohort; segment labels show participant counts.

Participants with diabetic retinopathy had consistently worse glycaemic indices and less favourable HDL-LDL values than those without retinopathy. Mean HDL cholesterol was significantly lower in the retinopathy group, whereas LDL cholesterol was significantly higher [Table 4, Figure 4].

Table 4. Comparison of glycaemic and HDL-LDL parameters between participants with no diabetic retinopathy and any diabetic retinopathy.

Parameter	No DR (n=128) Mean ± SD	Any DR (n=151) Mean ± SD	p-value
Fasting blood sugar, mg/dL	153.41 ± 39.10	164.16 ± 48.61	0.042
Post-prandial blood sugar, mg/dL	231.12 ± 57.43	256.50 ± 69.96	0.001
HbA1c, %	7.91 ± 1.12	8.87 ± 1.49	<0.001
HDL cholesterol, mg/dL	46.81 ± 9.70	41.74 ± 9.31	<0.001
LDL cholesterol, mg/dL	107.27 ± 31.47	118.21 ± 33.65	0.006

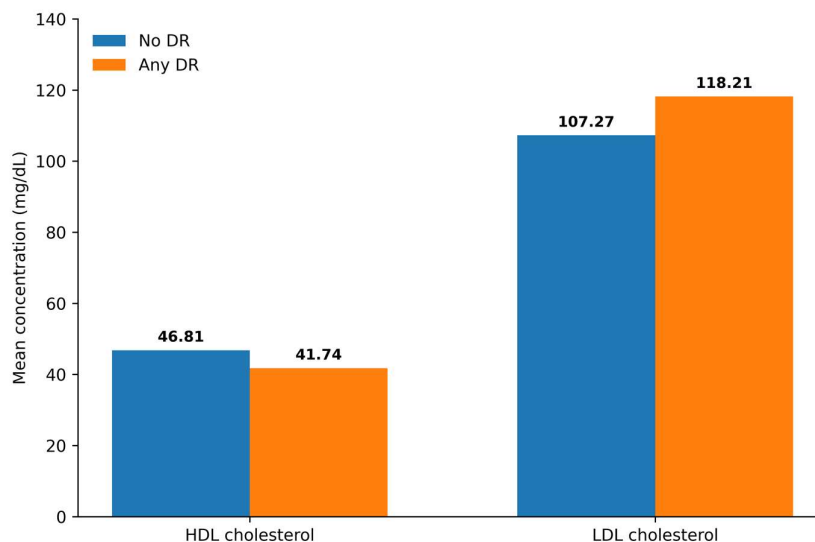


Figure 4. Grouped bar chart comparing mean HDL and LDL cholesterol in participants with no diabetic retinopathy and any diabetic retinopathy.

Italic note: Values above bars indicate mean concentrations in mg/dL.

Across retinopathy severity grades, HDL cholesterol showed a significant decline from no diabetic retinopathy to proliferative disease ($p < 0.001$). LDL cholesterol rose across grades, though the trend did not reach statistical significance

($p = 0.076$). The pattern still suggested a gradual shift towards a less favourable lipoprotein profile with worsening retinal disease [Table 5].

Table 5. HDL and LDL cholesterol across diabetic retinopathy severity categories (ANOVA).

Parameter	No DR (n=128)	Mild NPDR (n=52)	Moderate NPDR (n=47)	Severe NPDR (n=31)	PDR (n=21)	p-value
HDL cholesterol, mg/dL	46.81 ± 9.70	44.04 ± 9.52	40.74 ± 10.16	41.00 ± 7.13	39.38 ± 9.06	<0.001
LDL cholesterol, mg/dL	107.27 ± 31.47	116.17 ± 34.65	116.70 ± 34.12	121.42 ± 31.28	121.86 ± 35.22	0.076

DISCUSSION

This study found diabetic retinopathy in just over half of the enrolled adults with type 2 diabetes mellitus, and nearly one-fifth already had severe non-proliferative or proliferative disease. That pattern is clinically important because it suggests that many participants were reaching ophthalmic care after appreciable microvascular injury had already accumulated. Given the continuing diabetes burden globally and the uneven uptake of routine retinal surveillance in India, such a distribution is not unexpected [1-3].

The metabolic direction of the findings was coherent. Participants with retinopathy had poorer glycaemic indices and a less favourable HDL-LDL profile than those without retinal disease. That fits the known biology of diabetic retinal injury, where hyperglycaemia, oxidative stress, inflammation, and endothelial dysfunction converge on the retinal microvasculature [4,7]. In the present cohort, low HDL cholesterol was common and showed a clear stepwise decline across worsening retinopathy grades. HDL is often discussed as a protective lipoprotein because of its anti-

inflammatory and antioxidative functions. In diabetic states, however, the issue is not only lower concentration, but also impaired function. Lower HDL may therefore represent reduced vascular resilience in a retinal circulation already exposed to chronic metabolic stress [6,8].

LDL cholesterol behaved somewhat differently. It was significantly higher in the retinopathy group overall and rose numerically across advancing severity grades, although the ANOVA trend did not cross the threshold for statistical significance. That pattern is still clinically meaningful. LDL-related atherogenic burden has repeatedly been linked with endothelial injury, oxidised lipoprotein activity, and microvascular dysfunction, even when individual cohort studies differ in the strength of association observed with retinal stage [8-10]. The present findings therefore support LDL as a relevant companion marker, even if HDL appeared to track severity more sharply in this sample.

The present results also fit earlier hospital-based work suggesting that serum lipid fractions do not behave identically in diabetic retinopathy. Some studies have reported stronger associations for HDL and LDL, whereas

others have found broader dyslipidaemic patterns or more specific links with exudative disease [9-12]. The value of the current analysis lies in its narrower focus. By retaining HDL and LDL alone, the study highlights two clinically interpretable markers that can be reviewed quickly in routine diabetes care without diluting the message across multiple lipid fractions.

Duration of diabetes and hypertension added further context. Retinopathy prevalence increased sharply with longer disease duration, and hypertension remained highly prevalent in the cohort. These observations are biologically credible and align with previous work showing chronic disease exposure and elevated vascular pressure to be major modifiers of retinal damage [2,13,14]. The practical implication is straightforward: HDL and LDL should not be read in isolation, but as part of a broader metabolic profile in which glucose burden, disease duration, and blood pressure continue to matter.

There are strengths to this study. The sample size was adequate for descriptive and comparative analysis, retinopathy grading followed ETDRS classification, and the study captured a clinically relevant tertiary-care population. The limitations are equally important. The cross-sectional design prevents causal inference. Lipoprotein fractions were measured at one time point, so long-term exposure could not be assessed. Information on lipid-lowering therapy and lipoprotein functionality was not analysed separately. These constraints should temper causal interpretation, but they do not erase the consistency of the observed HDL-LDL pattern. Even with those limitations, the study carries a practical message for ophthalmology and diabetes care. Adults with type 2 diabetes who show low HDL, raised LDL, longer disease duration, and poor glycaemic control may merit closer retinal surveillance. In resource-variable settings, that kind of metabolic clustering can help identify patients who are more likely to harbour advanced retinal disease before vision loss becomes the first clinical signal.

CONCLUSION

More than half of the participants in this study had diabetic retinopathy, and one in five had sight-threatening disease. Retinopathy was associated with poorer glycaemic control, lower HDL cholesterol, and higher LDL cholesterol. Of the two lipid fractions examined, HDL showed the clearest gradient across worsening retinopathy severity, while LDL was significantly elevated in retinopathy overall and showed a rising trend with advanced grades. These findings support inclusion of HDL and LDL assessment in the metabolic appraisal of adults with type 2 diabetes undergoing retinal evaluation.

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Conflict of Interest: None.

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