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# Correlation between diabetic retinopathy, type-2 diabetes mellitus, serum lipid profile, and BMI: A single center study

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**Abstract**
**Background:** Type-2 Diabetes Mellitus (T2DM) poses a significant global health challenge, impacting millions worldwide, with 422 million individuals affected. The majority reside in low and middle-income nations, contributing to 1.5 million annual fatalities. Projected data indicates a rise to 783.2 million cases by 2045. South Asians, including Bangladeshis, exhibit higher diabetes prevalence, possibly linked to visceral adiposity.
**Aim of the study:** This study aimed to investigate the correlation between blood lipid profiles, BMIs, and the severity of diabetic retinopathy in individuals with type 2 diabetes across different grades.
**Methods:** This cross-sectional study, conducted at the Department of Cardiology, District Hospital, Narail, Bangladesh, spanned one year from January 2023 December 2023 with 32 participants diagnosed with type 2 diabetes. Informed consent was obtained, and eligible patients meeting inclusion criteria (treated with oral hypoglycemic agents or insulin) were recruited. Exclusion criteria included malignancies, immunologic disorders, corticosteroid use, and pregnancy.
**Result:** This study involved 32 patients, predominantly aged 51-60 (31.25%), with the female majority (53%). Diabetic Retinopathy (DR) severity distribution included 34.375% moderate NPDR, 31.25% mild NPDR, and 18.75% severe NPDR. No significant correlation with DR severity was found when examining total cholesterol (TCL) and Triglyceride (TG) levels. However, lipoprotein levels (LDL and HDL) showed a notable association (p-value 0.014). Mean BMI values across DR severity groups ranged from 21.51 to 22.29, with a potential statistical significance (p-value 0.0562). The study provides insights into the demographic and biochemical factors associated with DR severity, emphasizing potential links with lipoprotein levels and BMI.
**Conclusion:** The findings highlight the intricate interplay of metabolic factors in diabetic ocular complications. The study recommends regular lipid profile monitoring for diabetic patients, emphasizing dyslipidemia interventions to prevent DR. Additionally, recognizing lower BMI's potential impact on DR emphasizes the need for tailored interventions based on individual metabolic profiles. Further research in larger, diverse populations is suggested for comprehensive insights into these associations.

**Keywords:** Association, serum lipid profile, BMI, diabetic retinopathy and type-2 diabetes mellitus

## Introduction
Type-2 Diabetes Mellitus (T2DM) stands as a pervasive global health challenge, affecting millions of individuals worldwide [1]. A total of 422 million people worldwide have diabetes, the majority of whom dwell in low and middle-income nations and are directly responsible for 1.5 million fatalities annually [2]. According to the 10th edition of the World Diabetes Federation, there will be 536.6 million cases of diabetes worldwide in 2021, and that number is expected to rise to 783.2 million by 2045 [3]. As a result, the World Health Organization (WHO) and the International Diabetes Federation (IDF) recommend using specific cut-off points for WC for this group. At similar BMI levels, diabetes prevalence has been identified as higher in Asians compared with Caucasians. These findings may be partly explained by a difference in body fat distribution: South Asians seem to have a higher risk of developing visceral adiposity, which is more closely associated with insulin resistance and T2DM than general adiposity [4]. According to the INTERHEART study, Bangladeshis were found to have the highest prevalence of CAD risk factors among the South Asian populations [5].

Like in all other South Asian countries, T2DM and related cardiovascular complications develop 5–10 years earlier in Bangladesh than in Western countries, and consequently, fatality rates are high among young adults [6, 7]. Despite advances in diabetes management, the intricate interplay between various factors contributing to DR remains a subject of intense research scrutiny [8]. Among these factors, the roles of serum lipid profile and Body Mass Index (BMI) have gained prominence, offering a promising avenue for understanding the complex pathophysiology of diabetic ocular complications [9]. Dyslipidemia, characterized by aberrations in lipid metabolism, has been implicated in the development and progression of diabetic microvascular complications, including DR [10]. The intricate relationship between lipid profile parameters and the risk of DR necessitates a comprehensive investigation to delineate their specific contributions to the ocular pathology in T2DM [11]. Simultaneously, the role of BMI as a surrogate marker for adiposity and overall body composition has garnered attention in the context of diabetic complications [12]. While the link between obesity and insulin resistance is well-established, the association between BMI and DR remains nuanced and multifaceted [13]. The complex interplay between adipose tissue, inflammatory mediators, and vascular dysfunction introduces layers of intricacy in understanding how body composition influences the onset and severity of DR [14]. Employing advanced statistical methodologies, the investigation seeks not only to identify potential risk factors but also to discern patterns that may facilitate the development of targeted interventions and personalized treatment strategies. Through a meticulous review of pertinent literature, coupled with the analysis of clinical data derived from a diverse patient population, this study aims to provide a comprehensive understanding of the relationships between serum lipid levels, BMI, and the incidence and severity of DR. This study aimed to investigate the correlation between blood lipid profiles, BMIs, and the severity of diabetic retinopathy in individuals with type 2 diabetes across different grades.

## Methodology and Materials

This cross-sectional study, conducted at the Department of Cardiology, District Hospital, Narail, Bangladesh, spanned one year from January 2023 December 2023 with 32 participants diagnosed with type 2 diabetes. Eligible patients who satisfied all inclusion criteria were invited to join the study and provided their consent by signing the consent form. Before data collection, informed consent was acquired from each participant for their involvement and sample contribution to the research.

### Inclusion Criteria

- Patients diagnosed with type 2 diabetes.
- Participants were treated with either oral hypoglycemic agents (OHA) or insulin therapy.

### Exclusion criteria

- Individuals with malignancies, immunologic disorders, or infectious inflammatory diseases.
- Those receiving corticosteroids or cytostatic.
- Pregnant women were not considered for participation.
- Individuals with other eye conditions, such as mature cataracts, uveitis, or age-related macular degeneration.

A comprehensive physical examination was conducted, including a thorough ophthalmic assessment. Blood samples for laboratory testing were obtained after a 12-hour fast from 08:00 to 10:00 am. Both clinical and ophthalmic examinations were completed. A detailed fundus evaluation was carried out utilizing direct ophthalmoscopy, indirect ophthalmoscopy, and slit lamp bio microscopy with a +90D lens. The lipid profile (total cholesterol, HDL, LDL, and triglycerides) and HbA1c values were determined. The relationship between various lipid values, severity of retinopathy, and HbA1c was assessed using analysis of variance and chi-square tests.

### Data analysis

All data were organized into tables and graphs based on relevance, with detailed descriptions provided for better comprehension. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) program on the Windows platform. Continuous parameters were presented as mean ± SD and categorical parameters as frequency and percentage. Group comparisons for continuous parameters were conducted using Student's t-test. A significance level of $P<0.05$ was considered statistically significant in interpreting results.

## Result

A total of 32 patients were enrolled and analyzed in this study, where 10(31.25%) patients were from the age group 51-60 age and 25.00% were from both 61-70 and 41-50 age groups, respectively (Table 1). Figure 1 displays the gender distribution of the study population; the majority were female (53%), and the rest (47%) were male. Table 2 presents the type of Diabetic Retinopathy (DR) severity. Among the study participants, 11(34.375%) patients exhibit moderate NPDR, 10(31.25%) patients exhibit mild NPDR and 8(18.75%) patients exhibit severe NPDR, respectively. The relationship between Total Cholesterol (TCL) and Triglycerides (TG) levels (measured in mg/dl) concerning the severity of DR of the study is shown in Table 3. For the Total Cholesterol Level (TCL) in the Mild NPDR group, the mean ± SD is 211.41±37.35, and the associated p-value is 0.059. Similarly, for Triglycerides (TG) in the Mild NPDR group, the mean±SD is 256.10±71.90, with a p-value of 0.234. In the case of Moderate NPDR, the mean ± SD of TCL is 224.74±39.34 mg/dl, and the mean±SD of TG is 255.81±66.72 mg/dl. The same pattern is followed for the other DR Severity categories, where mean ± SD values are provided for both TCL and TG, and p-values are indicated. The p-value does not show any statistical significance between DR severity and cholesterols. Table 4 shows the relationship between lipoprotein levels and DR severity. The p-value of DR severity and LDL is 0.014. Similarly, HDL shows the same value, suggesting a notable association between both LDL and HDL levels and the severity of DR. Table 5 presents the mean body mass index (BMI) values along with standard deviations for different diabetic retinopathy (DR) severity levels. The mean BMI values for each severity group are as follows: Mild NPDR (22.15±2.83), Moderate NPDR (22.27±3.13), Severe NPDR (21.97±3.54), Very Severe NPDR (21.51±4.79), and PDR (22.29±3.9). Notably, a p-value of 0.0562 is associated with the DR group, indicating a potential statistical significance, albeit falling just above the conventional significance threshold of 0.05.

**Table 1:** Age distribution of the study population (N=32).

| Age | Frequency (n) | Percentage (%) |
|---|---|---|
| 20-30 | 1 | 3.13 |
| 31-40 | 5 | 15.63 |
| 41-50 | 8 | 25.00 |
| 51-60 | 10 | 31.25 |
| 61-70 | 8 | 25.00 |
| Total | 32 | 100.00 |

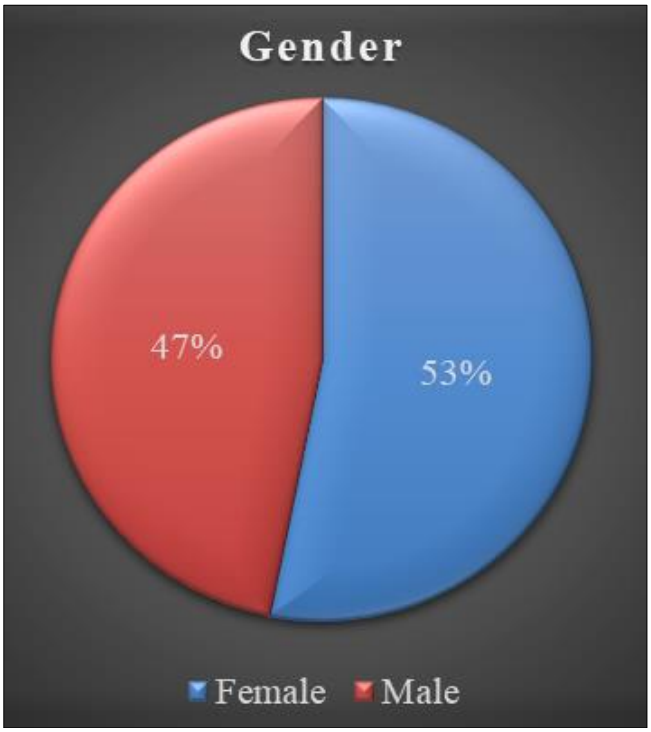


**Fig 1:** Gender distribution of the study population (N=32).

**Table 2:** Type of DR severity (N=32).

| DR Severity | Frequency (n) | Percentage (%) |
|---|---|---|
| Mild NPDR | 10 | 31.25 |
| Moderate NPDR | 11 | 34.375 |
| Severe NPDR | 6 | 18.75 |
| Very Severe NPDR | 2 | 6.25 |
| PDR | 3 | 9.375 |

**Table 3:** Relation of TCL & TG (mg/dl) and severity of DR**.**

| DR Severity | TCL | | TG | |
|---|---|---|---|---|
| | Mean ± SD | p-value | Mean ± SD | p-value |
| Mild NPDR (n=10) | 211.41 ± 37.35 | 0.059 | 256.10 ± 71.90 | 0.234 |
| Moderate NPDR (n=11) | 224.74 ± 39.34 | | 255.81 ± 66.72 | |
| Severe NPDR (n=6) | 249.87 ± 30.87 | | 267.37 ± 56.06 | |
| Very Severe NPDR (n=2) | 250.26 ± 17.66 | | 256.14 ± 79.70 | |
| PDR (n=3) | 264.38 ± 18.96 | | 295.71 ± 44.56 | |

**Table 4:** Relation of LDL & HDL (mg/dl) with different grades of DR.

| DR Severity | LDL | | HDL | |
|---|---|---|---|---|
| | Mean ± SD | p-value | Mean ± SD | p-value |
| Mild NPDR (n=10) | 42.61 ± 6.34 | 0.014 | 43.09 ± 5.86 | 0.014 |
| Moderate NPDR (n=11) | 42.02 ± 6.54 | | 41.82 ± 6.74 | |
| Severe NPDR (n=6) | 41.02 ± 5.05 | | 41.12 ± 4.95 | |
| Very Severe NPDR (n=2) | 39.04 ± 5.65 | | 38.54 ± 6.15 | |
| PDR (n=3) | 39.20 ± 4.28 | | 38.9 ± 4.58 | |

**Table 5:** Age distribution of the study population based on groups (N=30).

| DR Severity | BMI | |
|---|---|---|
| | Mean ± SD | p-value |
| Mild NPDR (n=10) | 22.15 ± 2.83 | 0.0562 |
| Moderate NPDR (n=11) | 22.27 ± 3.13 | |
| Severe NPDR (n=6) | 21.97 ± 3.54 | |
| Very Severe NPDR (n=2) | 21.51 ± 4.79 | |
| PDR (n=3) | 22.29 ± 3.9 | |

## Discussion

Limited research has been conducted on the role of diabetic dyslipidemia in the onset of microvascular complications [15]. Furthermore, diverse outcomes have been observed in various studies examining the relationship between Diabetic Retinopathy (DR) and Body Mass Index (BMI) [15]. This study explored the correlation between blood lipid profiles, BMIs, and the severity of diabetic retinopathy in individuals with type 2 diabetes across different grades. The study's results align with research findings from various countries. Consistent with the Early Treatment Diabetic Retinopathy Study (ETDRS), individuals with elevated levels of low-density lipoprotein cholesterol or high total serum cholesterol at baseline were reported to have twice the likelihood of developing diabetic retinopathy compared to those with normal blood levels [16]. For this study, type 2 diabetic patients aged 20 to 70 were selected, with 31.25% of respondents aged 51-60 which is comparable with other similar studies [17, 18]. The study included more females (53%) than males. However, Sergio showed that the diabetic male/female ratio was less than 1 [19]. In our study, the distribution of DR severity among the sample population reveals that the majority of cases fall within the mild to moderate range, followed by severe NPDR. Similar result found in the study of Agroiya *et al*. [20]. Al-Bdour *et al*. identified a notable correlation (p=0.04) between hypercholesterolemia and diabetic retinopathy when investigating risk factors associated with the condition in individuals with diabetes. This outcome is consistent with the results observed in the present study [21]. Moreover, Larsson *et al*. identified a robust association between retinopathy and elevated levels of total blood cholesterol [22]. In the CURES eye research, Rema *et al*. investigated the relationship between blood lipids and diabetic retinopathy in South Indian urban populations. Individuals with diabetic retinopathy had higher blood triglyceride (p=0.001) and total cholesterol (P=0.014) levels than individuals without the condition. Similar results were also obtained by Haddad *et al*. [23]. In our study, both total cholesterol and triglyceride levels were elevated in Mild NPDR compared to Moderate NPDR, and both were statistically significant. Patients with diabetic retinopathy had lower levels of HDL/LDL cholesterol ratio and higher levels of total and LDL cholesterol, according to studies by Agarwal *et al*. and Sachdev *et al*. [24, 25]. Hard exudates and retinopathy are associated with higher blood total and LDL cholesterol levels, according to the Hoorn Study, a sizable population-based investigation to identify possible risk factors for retinopathy in diabetic and non-diabetic persons [26]. These findings are consistent with our investigation, which identified elevated LDL and hypercholesterolemia as risk factors for retinopathy. Observations made by Gupta *et al*. demonstrated that the higher the LDL level (>130 mg/dl),

the higher the prevalence of DR (38%) compared to others (28.3%) (p=0.05) [27]. Our study result matches this result, showing that LDL value is significantly higher in patients with diabetic retinopathy with a P-value of 0.013 (<0.05). A study conducted by Hove *et al*. reported no association between Total Cholesterol (TCL), Triglycerides (TG), and High-Density Lipoprotein (HDL) with diabetic retinopathy [28]. In contrast, when assessing the serum lipid levels of participants in the Wisconsin Epidemiologic Study of Diabetic Retinopathy, Klein *et al*. identified a significant trend, indicating an increase in the severity of both retinal hard exudate and diabetic retinopathy with higher cholesterol levels [29]. As per Larsson *et al*., a linear correlation exists between the severity of diabetic retinopathy and blood cholesterol levels [30]. Our study also found that serum total cholesterol is significantly associated with the severity of diabetic retinopathy. Lyons *et al*. investigated serum lipoprotein subclass profiles in the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Study (DCCT/EDIC) cohort. Their findings revealed an inverse correlation between the degree of retinopathy and HDL cholesterol and a positive correlation with triglycerides and LDL [31]. Our study results partly agree with previous research. Triglyceride levels significantly varied in diabetic retinopathy, though not across different grades and severity (p-value = 0.323 > 0.05). Consistent with our findings, lower HDL and higher LDL levels correlated with increased retinopathy severity, displaying statistical significance. Regarding BMI, our study revealed a significantly lower BMI (23.46±1.92) in patients with diabetic retinopathy compared to those without DR (23.95±1.46), with a p-value of 0.01492, indicating an association between lower BMI and diabetic retinopathy changes. However, no significant relationship was found between BMI and clinically significant macular edema (CSME) development. This aligns with findings of other study, suggesting an increased incidence of DR in patients with lower BMI [32]. However, Araki *et al* found no association between BMI and Diabetic Retinopathy. At the same time, Ballard DJ *et al*. reported higher BMI and obesity associated with Diabetic Retinopathy in certain Western population studies [33, 34].

**Limitations of the study:** Despite the valuable insights provided by this study on the correlation between diabetic retinopathy (DR), type-2 diabetes mellitus (T2DM), serum lipid profile, and body mass index (BMI), certain limitations should be acknowledged. Firstly, the small sample size of 32 participants may limit the generalizability of findings to a broader population. Additionally, the study's cross-sectional design only allows for the observation of associations at a single point in time, preventing the establishment of causation. The exclusion of pregnant women and those with specific eye conditions may further restrict the applicability of results to these subgroups. Moreover, the study's reliance on a single center and its geographic location in Bangladesh may introduce regional biases, necessitating cautious interpretation when extrapolating findings globally. Despite these limitations, this research contributes valuable insights into the intricate relationship between serum lipid levels, BMI, and the severity of DR in T2DM, warranting further exploration with more extensive, diverse cohorts and longitudinal designs to enhance the robustness and generalizability of conclusions.

## Conclusion and Recommendations

In conclusion, our study elucidated significant correlations between serum lipid profiles, BMI, and the severity of diabetic retinopathy (DR) in individuals with type 2 diabetes. Notably, elevated LDL and total cholesterol levels were associated with increased severity of DR, while lower BMI was linked to DR changes. These findings underscore the complex interplay of metabolic factors in diabetic ocular complications. The study recommends regular monitoring of lipid profiles in diabetic patients, emphasizing interventions targeting dyslipidemia for DR prevention. Moreover, recognizing the potential impact of lower BMI on DR highlights the need for tailored interventions based on individual metabolic profiles. For comprehensive insights, further research should explore these associations in larger, diverse populations.

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