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# Impact of COVID-19 on Lipid Profile in Diabetic Retinopathy of the Central Rural Population of India

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## ABSTRACT

People with Diabetes, particularly poorly controlled blood sugar levels, are at an increased risk of severe illness if they contract COVID-19. Diabetes has weakened the immune system, with more difficult for the body to fight infections. Studies have suggested a potential link between lipid abnormalities and COVID-19 severity. High levels of cholesterol and triglycerides, a component of the lipid profile, have been associated with increased inflammation and impaired immune response. This factor may contribute to a more severe course of COVID-19. Our study aims to investigate the Impact of COVID-19 on Lipid profiles in Diabetic Retinopathy of rural populations. Our study reported the potential direct and indirect effects of COVID-19 on the development and progression of DR, including the impact of Lipid Profile and glycemic Control due to altered healthcare access, changes in lifestyle, potential viral involvement, and vaccinations. By examining existing literature, analyzing patient data, and conducting surveys, this study provides valuable insights into the intersection between COVID-19 and DR. The specific relationship between diabetic Retinopathy, lipids, and COVID-19 is not well-established, and limited research is available on this topic. However, the results of this study contributed to information about the relationship between COVID-19, Lipids, and Diabetic Retinopathy, offering a foundation for future research and guiding clinical practice to improve patient outcomes.

**Conclusion:** In this study, we concluded that Dyslipidemia and Hyperglycemia increase the risk of progressing on Diabetic Retinopathy, but due to the breakthrough of covid-19, there was no significantly changed observed in the lipid profile and glycemic control pattern of individuals with diabetic Retinopathy. However, the number of cases increased dramatically toward the progression of Diabetes to Diabetic Retinopathy with significantly reduced age of diabetic individuals and Duration of Diabetes compared to before the breakthrough of COVID-19.

***Keywords:*** COVID-19 pandemic, glycemic control, Diabetic Retinopathy, vaccination, World Health Organization, severe acute respiratory syndrome coronavirus 2, Diabetic Eye Disease

## INTRODUCTION

Severe diabetic Retinopathy (DR) was independently associated with poorer outcomes of COVID-19, including the need for critical care or death (1). The World Health Organization (WHO) lists DR (8) as a chronic eye disease. Early detection and treatment of sight-threatening DR can halve the risk of sight loss. Some highly effective DED treatments include corticosteroids, laser photocoagulation, and the intravitreal injection of anti-vascular endothelial growth factor (VEGF) agents are available. However, the efficacy of these approaches in

preventing vision loss depends on early diagnosis and glycemic control over time. In particular, individuals experience no symptoms in the preliminary stage, so screening for DED in diabetic patients is highly recommended worldwide, as illustrated in international and regional guidelines (3). The COVID-19 pandemic has impacted every individual's life. It has shown that mortality in people with underlying diseases, including Diabetes, has been very high. A study report on nationwide analysis in England shows that type 1 and type 2 diabetes are independently associated with significantly increased odds of in-hospital death with COVID-19 (4).

A study report on Mental Health, Substance Use, and Suicidal ideation during the COVID-19 Pandemic in the United States shows a dynamic reduction in routine medical care among diabetic patients after the emergence of COVID-19. The study also explains the factors that play an essential role in healthcare avoidance by using health insurance claims, which are behavioral-based measurements, and augmenting the finding via opinion surveys(5). The study report on factors influencing on development of COVID-19 pneumonia and its association with oral anti-diabetic drugs in hospitalized patients with diabetes mellitus states that DM increase mortality and morbidity in patients with coronavirus disease (COVID-19) with there is no oral anti-diabetics where associated with COVID-19 related death with factors affecting the development of COVID-19 pneumonia in patients with Diabetes mellitus is not well known(6). A Study reported that Microvascular diseases, including DR a positive association with poorer COVID-19 outcomes, including hospital admission and death. Further studies are required, using more standardized methods to allow for a direct comparison of results(1). A study of 187 patients with Diabetes hospitalized with COVID-19 observed a more than 5-fold increased risk of intubation in patients with diabetic Retinopathy (7).

However, several vulnerable populations did not include sufficient numbers in COVID-19 vaccine trials. Several studies have highlighted that several high-risk population groups should be at the top of the priority list for receiving a vaccination and also demonstrated that significant research gaps in this topic require more studies to determine whether these populations should receive COVID-19 vaccines. There is a need to determine the effectiveness of the vaccination with the various complications and side effects of several high–risk populations.

However, considering the paucity of data on participants with DM in the hitherto available clinical trials, the use of COVID-19 vaccines in this subgroup of subjects needs more research. Our study shows that after the breakthrough of COVID-19 with T2D and eye health. Aim of study "Investigating the Impact of COVID-19 on lipid profile in Diabetic Retinopathy.

This disease is usually asymptomatic in its early stages; consequently, people with Diabetes do not consider examination regularly. DR affects nearly half of the population with Diabetes. The global prevalence of Diabetes has been continually increasing, and current projections estimate that 438 million adults will be affected by 2030. With this estimate, a minimum of 2.4 million eyes would need to be evaluated for Retinopathy every day(8)

Diabetic Retinopathy is one of the most common complications and a leading cause of preventable blindness among the working population. It had estimated that around 93 million have diabetic Retinopathy, of whom 17 million (18%) have proliferative diabetic Retinopathy, 21 million (23 %) have diabetics macular edema, and 28 million (20%) have vision-threatening diabetic Retinopathy.

## CLASSIFICATION OF DIABETIC RETINOPATHY

Diabetic Retinopathy; classified according to disease progression. The initial stage, *nonproliferative DR* (NPDR; previously

termed "background" retinopathy (BDR)), can be further categorized as mild, moderate, or severe. *Proliferative DR* (PDR) represents the advanced stage of the disease.

## PROLONGED HYPERGLYCEMIA

It is the primary etiologic agent in the microvascular complications of Diabetes mellitus. Three mechanisms seem plausible for diabetic Retinopathy:

I. Alteration in the expression of one or more genes results in increased amounts of altered gene products, causing altered cell function.
II. Nonenzymatic glycation of proteins leads to cross-linking and altered protein function. These products have a very long cellular lifetime.
III. Chronic Hyperglycemia causes accelerated oxidative stress in cells resulting in toxic end products. Also, increased polyol pathway activity increases the NADH/NAD+ ratio, resulting in increased toxic end product by a hyperglycemic pseudo hypoxia mechanism.

## HIGH CHOLESTEROL AND HYPERLIPIDEMIA

Lipid abnormalities contribute to the development and progression of diabetic Retinopathy through various mechanisms. Elevated levels of lipids can cause damage to the blood vessels in the retina, leading to microvascular changes. The accumulation of lipids within the retinal blood vessels can impair blood flow and oxygen delivery to the retina, resulting in ischemia (lack of blood supply). This ischemic environment triggers the release of factors that promote the growth of abnormal blood vessels (neovascularization) or fluid leakage into the retina. In Lipoprotein retinopathy, lipid deposits may directly accumulate within the retina, leading to a condition known as lipoprotein retinopathy. Lipoprotein retinopathy has characterized by the prescience of lipid-filled yellowish deposits in the retinal layers, which can affect vision. Elevated serum cholesterol is associated with increased severity of hard exudates. Elevated serum triglyceride levels are associated with an increased risk of developing high-risk PDR and decreased visual acuity. Cheng et al. demonstrated that in overweight DM2 patients, high triacylglycerol levels had significantly associated with DR (9). A Chinese study on DM2 patients confirmed that elevated very low-density lipoprotein (VLDL) and Triglyceride (TG) concentrations were independent risk factors for DR(10). Also, Yau et al. found that increased total serum cholesterol levels correlated with an increasing prevalence of macular edema and severe Retinopathy in diabetic patients (11). In contrast, Wong et al. found that a higher total serum cholesterol level is a protective factor for DR(12).

Studies have shown that the treatment of hyperlipidemia improves DR and limits its progression into advanced stages. Statins, HMG-CoA reductase inhibitors, are commonly used to treat high cholesterol. Interestingly, their use had related to a significantly decreased rate of DR development(13). Fibrates are other medications used to treat hyperlipidemia. A study showed that using the fenofibrate was associated with a lower rate of progression of DR(14).

The National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) guidelines recommended a reasonable goal of LDL-cholesterol below 100 mg/dL (15). The intensive treatment group showed improved HDL-cholesterol ratio and decreased TG level, significantly associated with decreased risk of DR progression(16). In summary, controlling the high lipid profile levels can decrease the risk of developing and progressing DR in diabetic patients.

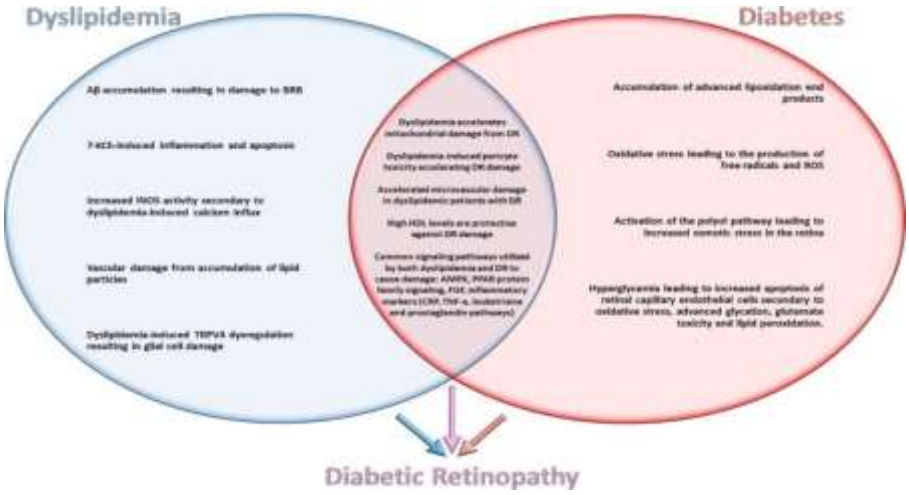


**Figure 1. Shared and distinct mechanisms underlying dyslipidemia and Diabetes contribute to the pathogenesis of diabetic Retinopathy. (17)**

Regarding the specific impact of COVID-19 on diabetic Retinopathy and its relationship with lipids, there is limited information available. However, it is possible to consider that the interplay of Diabetes, lipids, and COVID-19 could indirectly affect diabetic Retinopathy. COVID-19 can cause systematic inflammation and affect blood vessels, potentially aggravating existing vascular complications like diabetic Retinopathy. Individuals with Diabetic Retinopathy must follow preventive measures such as practicing good glycemic control, adhering to a healthy diet, and maintaining regular medical care to minimize the risks of COVID-19 complications.

Managing a lipid abnormality is an essential aspect of the overall management of Diabetes and diabetic Retinopathy. Lifestyle modification, including healthy regular exercise and weight management, are recommended to control lipid levels. A study on Diabetic Retinopathy in a Multitier Ophthalmology Network in India shows that the presentation of DR patients in hospitals is evolving because of the COVID-19 pandemic. The footfalls of patients during the unlock (phases 1-10) regained two-thirds of the pre-COVID-19 level. There was an increase in patients with sight-threatening DR and the need for vitreoretinal surgery and intravitreal injections during the lockdown (phases 1-4). (18) A study reported that Coronavirus disease 2019 (COVID-19) is known to cause thromboembolic episodes apart from acute respiratory distress syndrome (ARDS). With large vaccine drives worldwide, there are a few cases reports on post-vaccine thrombotic events seen with the vaccine. (19)

## METHODOLOGY

**Cross-Sectional Observational Study,**

**Study Population:** The Patients / Subjects of DM Randomly selected who are attending the OPD & IPD or medical camp of Index Medical College gram Khudel Indore and Amaltas Institute of Medical Science gram Banger Dewas Surroundings Rural Population Approximately 15 KM, between 2021 to 2023.

**Sample size:** Total sample size of 100 subjects. Assuming the expected population standard deviation to be five and employing t-distribution to estimate sample size, the study would require a sample size of- 100 to estimate a mean with 95% confidence and a precision of 0.5.

**SAMPLE SIZE CALCULATION:**

The sample size refers to the number of observations in a study. Sample size calculation used to power analysis Based on the "India Diabetes Report 2000 — 2045," the prevalence of Diabetes was 9.6% in 2021. (4) Among them, 16.9% Prevalence of diabetic Retinopathy in India: Results from the National Survey 2015-19 by Praveen Vashist et al. (20) People had a 1.62 %

prevalence of diabetic Retinopathy calculated.

Sample size formula:

$$n = p(1-p)\left(\frac{z_{1-\frac{\alpha}{2}}}{e}\right)^2$$

Here,

$\alpha = \text{Probability of typI error (usually 0.05).}$

$z = \text{Standard normal score for } (1-\alpha)100\% \text{ assurance.}$

$p = \text{Proportion of diabetic retinopathy}$

$e = \text{Allowable error in estimate.}$

$\alpha = 0.05, \quad z_{1-\frac{\alpha}{2}} = 1.96, \quad p = 0.0162, \quad e = 0.025$

The minimum sample size of 98 subjects had estimated, assuming the prevalence of DR is 1.62 % of the population at a 95% confidence interval, 5% significance level, and 2.5% allowable error in the estimate.

**INCLUSION CRITERIA:** T2D with covid vaccinated above 18 years, both genders

**EXCLUSION CRITERIA**: Nondiabetic, Patients with known cases of hypolipidemia, hypothyroidism, Cushing's syndrome, Patients with kidney disease, hepatic diseases, type 1 Diabetes Mellitus, Known / suspected pregnancy, and not capable of giving consent,

A careful history of the patients regarding their Age and sex, duration of Diabetes mellitus, covid-19 History with appropriate behaviors with their vaccination status, risk factors, smoking habits, associated systemic disorders like hypertension, coronary artery disease (CAD), and treatment of Diabetes recorded.

**WHO criteria diagnose Diabetes. (21)**

Diabetic Retinopathy is diagnosed by (ICO) the International Council of Ophthalmology (ICO) (3) with a confirmatory diagnosis by an ophthalmologist.

**LABORATORY PROCEDURE:**

5 milliliters of venous blood had taken with the standard method from the forearms of the subjects participating in the study. The collected blood sample was centrifuged and separated into serums. Serum samples were stored in a −20°C freezer until the study had done. Before the study, the serum samples were brought to room temperature and kept until thawed. Each serum sample was rendered ready for study by being vortexed for 20 s for biochemical investigation using standard clinical laboratory protocol, SOP of biochemical parameters, and EM-360 fully auto analyzer.

A sodium fluoride vacutainer uses to conduct glucose samples from interventional, whereas EDTA vacutainers use for HbA1c calculation. The Lipid profile had assessed by using Plain or red-top blood tubes.

**Quality Control:** Validation of calibration Multical-XL and control Erba Path and Erba Norm result were done before processing the sample.

**Biochemical Parameters estimation using the methodology:**

1. Blood glucose- glucose oxidase peroxidase (GOD) method
2. Glycosylated hemoglobin - Immunoturbidimetrique Method.
3. Cholesterol- CHOD-POD method
4. Triglyceride -GPO –PAP method
5. HDL-Cholesterol - Direct method
6. LDL cholesterol and VLDL cholesterol had calculated using Fried Wald's formulae.

**Data collection procedure**: Based on the eligibility inclusion and exclusion criteria, the participants were screened and selected from the study as mentioned above and after informed consent. The investigator interviewed selected participants, and one trained interviewer using a pretested semi-structured questionnaire. Information was obtained on the socio-demographic background and clinical History using a semi-structured questionnaire followed by a brief clinical examination with COVID-19 history.

## Statistical Analysis

Data were analyzed using IBM SPSS Statistics 20 software. Appropriate statistics (either student t-test if two groups or one-

way ANOVA if more) tests had used to compare the outcome between groups with Correlation.

**Ethics committee clearance:** Ethical approval obtained from hospital authorities and the institutional ethics committee (IEC) prior to the commencement of the study.

**Benefits to the participants:** No monetary benefits were given to the participants.

## OBSERVATION AND RESULTS

In evaluating biochemical parameters RBS, HbA1c, and lipid profile, the baseline values above the following levels are considered abnormal.

- Random blood glucose = >126mg/dl
- HbA1c - 6.5%
- Total cholesterol = 200 mg/dl
- HDL cholesterol = <40 mg/dl
- Triglycerides = 160 mg / dl
- LDL cholesterol = 100 mg/dl
- VLDL >30

**Table** 1 shows the Age and Duration of Diabetes. The two-tailed P value equals 0.31 and 0.67, respectively. The difference is bound to be insignificant. There is no significant change in Age and Duration of Diabetes among the DR participants.

Our study reported that Hyperglycemic Biochemical markers RBS and HbA1c mean scores were significantly higher in base value-126 mg/dl and 6.5%, respectively. The two-tailed P value is less than 0.000 and 0.000, respectively. The difference is bound to be extremely statistically significant among the DR participants.

Our study shows that Lipid profile or Cardio Vascular, Biochemical markers Total cholesterol, Triglyceride, HDL, LDL, and VLDL mean score significantly higher in base value-200 mg/dl, 160 mg/dl, 40 mg/dl, and 100 mg/dl and 30 mg/dl respectively. The P value is less than 0.000, 0.000, 0.000, 0.000, and 0.000, respectively. The difference is bound to be extremely statistically significant among the DR participants.

**Table:1 Mean of Biochemical variables in study participants**

| Variables | N | Mean | Std. Deviation | Sig. (2-tailed) |
|---|---|---|---|---|
| | Valid | | | |
| Age | 100 | 53.64 | 8.91 | 0.31 |
| Dur_DM | 100 | 6.61 | 4.77 | 0.67 |
| RBS | 100 | 252.35 | 95.78 | .000 |
| HbA1C | 100 | 10.11 | 2.59 | .000 |
| TC | 100 | 234.74 | 25.38 | .000 |
| TG | 100 | 171.31 | 29.13 | .000 |
| HDL | 100 | 44.04 | 07.96 | .000 |
| LDL | 100 | 156.43 | 28.21 | .000 |
| VLDL | 100 | 34.26 | 05.82 | .000 |

**99% Confidence Interval, 1% level of significance (p< 0.01)**
**95% Confidence Interval, 5% level of significance (p< 0.05)**

**Table: 2** Shows the Age and Duration of Diabetes using ANOVA between the groups and within the groups of Severity stages of DR. The two-tailed P value is less than 0.05 and 0.04, respectively. The difference is bound to be Extremely significant. There are significant changes in Age and Duration of Diabetes with severity stages of DR participants. The study reported that Hyperglycemic Biochemical markers RBS and HbA1c, using ANOVA between the groups and within the groups of Severity stages of DR. The two-tailed P value is less than 0.000 and 0.001respectively. The difference is bound to be Extremely significant. There are significant changes in RBS and HbA1C with the severity stages of DR participants. However, the study shows Lipid profile or Cardio Vascular, Biochemical markers, Total cholesterol, Triglyceride, HDL, LDL, and VLDL mg/dl. The P value is 0.37, 0.52, 0.39, 0.21, and 0.52, respectively. The difference is bound to be insignificant. There are no significant changes in Lipid profiles with DR participants' severity stages.

**Table: 2 Mean of Biochemical variables with stages of DR**

| Variables | Mild NPDR (N-57) Mean ± SD | Moderate NPDR (N-22) Mean ± SD | Severe NPDR (N-11) Mean ± SD | PDR (N-57) Mean ± SD | Sig. |
|---|---|---|---|---|---|
| Age | 51.91 ± 9.13 | 56.55 ± 9.81 | 53.09 ± 6.06 | 57.7 ± 5.64 | 0.05 |
| Dur-DM | 5.29 ± 4.43 | 8.95 ± 4.1 | 9.09 ± 5.24 | 6.19 ± 5.06 | 0.00 |
| RBS | 218.31 ± 87.52 | 262.3 ± 74.68 | 316 ± 94.07 | 354.53 ± 79.23 | 0.00 |
| HbA1C | 9.48 ± 2.26 | 10.36 ± 2.7 | 10.26 ± 2.69 | 13.02 ± 2.25 | 0.00 |
| TC | 232.75 ± 25.25 | 241.18 ± 27 | 227.27 ± 14.14 | 240.1 ± 31.13 | 0.37 |
| TG | 172.22 ± 33.08 | 175.23 ±25.54 | 170.18 ± 21.98 | 158.8 ± 15.9 | 0.52 |
| HDL | 44.46 ± 7.02 | 43.09 ± 9.06 | 46.55 ± 10.17 | 41 ± 8.03 | 0.39 |
| LDL | 153.85 ± 26.7 | 163.05 ± 30.71 | 146.69 ± 21.87 | 167.34 ± 34.51 | 0.21 |
| VLDL | 34.44 ± 6.62 | 35.05 ± 5.11 | 34.04 ± 4.4 | 31.76 ± 3.18 | 0.52 |

**99% Confidence Interval, 1% level of significance (p< 0.001)**
**95% Confidence Interval, 5% level of significance (p< 0.05)**

**Table .3** Shows there is no significant change in lipid profile with Gender, age, and Family History of Diabetes. However, triglycerides (P-value is 0.05) with Duration of Diabetes and total cholesterol (P-value is 0.05) with anti-Diabetes medication shows a significant change in lipid profile.

**Table 3 Demographic and clinical characteristics of Distributions with Lipid Profile of Diabetic Retinopathy.**

| S. No. | Characteristics | | Number (%) | TC Mean ± SD | TG Mean ± SD | HDL Mean ± SD | LDL Mean ± SD | VLDL Mean ± SD |
|---|---|---|---|---|---|---|---|---|
| 1 | Gender | Female | 41 (41%) | 236.44 ± 25.68 | 171.68 ± 30.83 | 44.02 ± 8.24 | 158.07 ± 26.98 | 34.34 ± 6.17 |
| | | Male | 59 (59%) | 233.56 ± 25.33 | 171.06 ± 28.17 | 44.05 ± 7.84 | 155.3 ± 29.21 | 34.21 ± 5.63 |
| P-value | | | | 0.579 | 0.917 | 0.987 | 0.63 | 0.917 |
| 2 | Age (Year) | < 40 | 09 (09%) | 256.33 ± 13.43 | 156.11 ± 31.3 | 43.22 ± 6.32 | 181.89 ± 16.83 | 31.22 ± 6.26 |
| | | 41-50 | 24 (24%) | 230.54 ± 28.8 | 176.38 ± 27.52 | 9 ± 43.83 | 9 ± 151.43 | 9 ± 35.28 |
| | | 51-60 | 52 (52%) | 232.21 ± 21.96 | 172.53 ± 25.76 | 6.32 ± 24 | 16.83 ± 24 | 6.26 ± 24 |
| | | 61-70 | 12 (12%) | 234.67 ± 31.75 | 164.83 ± 36.04 | 43.83 ± 8.49 | 151.43 ± 32.05 | 35.28 ± 5.5 |
| | | >70 | 3 (03%) | 247.67 ± 32.62 | 181.33 ± 59.6 | 24 ± 43.69 | 24 ± 154.01 | 24 ± 34.51 |
| P-value | | | | 0.073 | 0.383 | 0.753 | 0.069 | 0.383 |
| 3 | Duration of DM (Year) | <5 | 47 (47%) | 237.34 ± 28.59 | 164.59 ± 31.92 | 44.34 ± 6.41 | 160.08 ± 30.92 | 32.92 ± 6.38 |
| | | 6-10 | 33 (33%) | 231.94 ± 23.26 | 172.7 ± 24.6 | 47 ± 43.3 | 47 ± 154.1 | 47 ± 34.54 |
| | | 11-15 | 16 (16%) | 235.5 ± 22.41 | 187.19 ± 26 | 6.41 ± 33 | 30.92 ± 33 | 6.38 ± 33 |
| | | 15-20 | 04 (04%) | 224.25 ± 10.21 | 175.5 ± 21.49 | 43.3 ± 8.61 | 154.1 ± 25.66 | 34.54 ± 4.92 |
| P-value | | | | 0.667 | 0.05 | 0.298 | 0.441 | 0.05 |
| 4 | Family History of DM | Absent | 83 (83%) | 235.57 ± 25.57 | 170.07 ± 28.87 | 43.95 ± 8.14 | 157.6 ± 29 | 34.01 ± 5.77 |
| | | Present | 17 (17%) | 230.71 ± 24.77 | 177.41 ± 30.59 | 44.47 ± 7.29 | 150.75 ± 23.95 | 35.48 ± 6.12 |
| P-value | | | | 0.475 | 0.346 | 0.808 | 0.365 | 0.346 |
| 5 | Anti-dibetic medicine | No | 09 (09%) | 250.44 ± 16.7 | 158 ± 41.01 | 41.44 ± 6.69 | 177.4 ± 18.44 | 31.6 ± 8.2 |
| | | Yes | 91 (91%) | 233.19 ± 25.63 | 172.63 ± 27.66 | 44.3 ± 8.07 | 154.36 ± 28.23 | 34.53 ± 5.53 |
| P-value | | | | 0.05 | 0.152 | 0.308 | 0.019 | 0.152 |
| 6 | DR groups | NPDR | 90 (90%) | 234.14 ± 24.8 | 172.71 ± 29.99 | 44.38 ± 7.93 | 155.23 ± 27.39 | 34.54 ± 6 |
| | | PDR | 10 (10%) | 240.1 ± 31.13 | 158.8 ± 15.9 | 41 ± 8.03 | 167.34 ± 34.51 | 31.76 ± 3.18 |
| P-value | | | | 0.484 | 0.153 | 0.205 | 0.199 | 0.153 |

**99% Confidence Interval, 1% level of significance (p< 0.001)**
**95% Confidence Interval, 5% level of significance (p< 0.05)**

**Table 4** shows Covid-19 characteristics with Lipid Profile of Diabetic Retinopathy. According to this, there is no significant change in lipid profile with administered Vaccine (Covisheild and Covaxin), H/O Covid positive (RT-PCR), and H/O Covid-like Symptoms. However, H/O Provided Treatment – No Treatment, Isolation, and Hospitalization with Total cholesterol, Triglyceride, LDL, and VLDL mg/dl. The P values are 0.0.01, 0.01, 0.00, and 0.01. The difference is bound to be extremely statistically significant among the DR participants. However, with HDL, the P-value is 0.108. The difference is bound to be insignificant. There are no significant changes in Lipid profiles with DR participants' severity stages.

**Table:4 Covid-19 Characteristics with Lipid Profile of Diabetic Retinopathy**

| S. No. | Characteristics | | Number (100%) | TC Mean ± SD | TG Mean ± SD | HDL Mean ± SD | LDL Mean ± SD | VLDL Mean ± SD |
|---|---|---|---|---|---|---|---|---|
| 1 | Administered Vaccine | Covisheld | 78 (78%) | 234.31 ± 24.73 | 168.47 ± 29.14 | 43.86 ± 7.69 | 156.76 ± 27.12 | 33.69 ± 5.83 |
| | | Covaxin | 22 (22%) | 236.27 ± 28.16 | 181.41 ± 27.45 | 44.68 ± 9.06 | 155.31 ± 32.46 | 36.28 ± 5.49 |
| P-value | | | | 0.750 | 0.066 | 0.671 | 0.833 | 0.066 |
| 2 | H/O Covid positive (RTPCR) | No | 78 (78%) | 236.05 ± 27.03 | 174.18 ± 28.24 | 43.56 ± 7.95 | 157.65 ± 29.41 | 34.84 ± 5.65 |
| | | Yes | 22 (22%) | 230.09 ± 18.17 | 161.16 ± 30.65 | 45.73 ± 7.98 | 152.13 ± 23.6 | 32.23 ± 6.13 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| P-value | | | | 0.333 | 0.064 | 0.263 | 0.421 | 0.064 |
| 3 | H/O Covid like Symptoms | No | 68 (68%) | 236.56 ± 26.19 | 173.25 ± 28.68 | 43.63 ± 7.67 | 158.28 ± 28.69 | 34.65 ± 5.74 |
| | | Yes | 32 (32%) | 230.88 ± 23.49 | 167.2 ± 30.13 | 44.91 ± 8.63 | 152.53 ± 27.2 | 33.44 ± 6.03 |
| P-value | | | | 0.299 | 0.336 | 0.459 | 0.345 | 0.336 |
| 4 | H/O Provided Treatment | No Treatment | 62 (62%) | 236.05 ± 25.63 | 177.5 ± 28.61 | 43.1 ± 7.6 | 157.45 ± 28.4 | 35.5 ± 5.72 |
| | | Isolation | 19 (19%) | 243.89 ± 26.17 | 156.53 ± 25.79 | 43.68 ± 8.58 | 168.91 ± 30.2 | 31.31 ± 5.16 |
| | | Hospitalization | 19 (19%) | 221.32 ± 18.65 | 165.92 ± 28.93 | 47.47 ± 8.02 | 140.66 ± 17.41 | 33.18 ± 5.79 |
| P-value | | | | 0.017 | 0.014 | 0.108 | 0.007 | 0.014 |

**99% Confidence Interval, 1% level of significance (p< 0.001)**
**95% Confidence Interval, 5% level of significance (p< 0.05)**

**Table 5** shows no significant change in this study in Lipid profile with Associated Risk Factors like- Hypertension, CVD, and HTN with CVD and Bad Habits like- Smoking, Alcohol, and Smoking with alcohol of Diabetic Retinopathy. However, their mean value is higher than no risk and bad habits.

**Table:5 Associated Risk Factors and Bad Habits with Lipid Profile of Diabetic Retinopathy**

| S. No. | Characteristics | | Number (100%) | TC Mean ± SD | TG Mean ± SD | HDL Mean ± SD | LDL Mean ± SD | VLDL Mean ± SD |
|---|---|---|---|---|---|---|---|---|
| 1 | Associated Risk Factor | No Risk | 88 (88%) | 234.48 ± 26.15 | 170.28 ± 30.15 | 43.75 ± 7.66 | 156.67 ± 28.45 | 34.06 ± 6.03 |
| | | HTN | 8 (08%) | 237.13 ± 17.4 | 183.75 ± 11.82 | 46.88 ± 10.41 | 153.5 ± 27.12 | 36.75 ± 2.36 |
| | | CVD | 1 (01%) | 196 ± 0 | 182 ± 0 | 45 ± 0 | 114.6 ± 0 | 36.4 ± 0 |
| | | HTN+CVD | 3 (03%) | 249 ± 2.65 | 165 ± 35 | 44.67 ± 13.32 | 171.33 ± 19.43 | 33 ± 7 |
| P-value | | | | 0.344 | 0.612 | 0.768 | 0.377 | 0.612 |
| 2 | Associated Bad Habits | No | 75 (75%) | 234.31 ± 25.24 | 172.31 ± 29.7 | 43.64 ± 7.74 | 156.21 ± 27.23 | 34.46 ± 5.94 |
| | | Smoking | 10 (10%) | 233 ± 27.67 | 164 ± 27.51 | 43.7 ± 8.67 | 156.5 ± 30.36 | 32.8 ± 5.5 |
| | | Alcohol | 6 (06%) | 232.83 ± 27.82 | 167.5 ± 17.81 | 48.67 ± 10.07 | 150.67 ± 36.57 | 33.5 ± 3.56 |
| | | Smoking+Alcohol | 9 (09%) | 241.56 ± 25.99 | 173.72 ± 34.72 | 44.67 ± 8.08 | 162.14 ± 32.5 | 34.74 ± 6.94 |
| P-value | | | | 0.865 | 0.834 | 0.521 | 0.894 | 0.834 |

**99% Confidence Interval, 1% level of significance (p< 0.001)**
**95% Confidence Interval, 5% level of significance (p< 0.05)**

**Table 6:** Shows a significant Correlation of HbA1c with RBS, Urea, Creatinine, Total cholesterol, and LDL. Their Pearson Correlation (r) values r= 0.416, 0.217, 0.337, and 0.424, respectively, lie between -1 to +1. The Correlation of HbA1C with RBS is to be moderate, Positive relationship and significance (p<0.000) at the 0.01 level (2-tailed); Urea is to be weak, Positive relationship and significant (p<0.030) at the 0.05 level (2-tailed), Creatinine is to be moderate, Positive, relationship and significant (p<0.001) at the 0.01 level (2-tailed), Total Cholesterol is to be Moderate, Positive, relationship and significant (p<0.000) at the 0.01 level (2-tailed), and LDL is to be Moderate, Positive, relationship and significant (p<0.000) at the 0.01 level (2-tailed). However, there is no significant correlation between HbA1c with Triglycerides, HDL, and VLDL.

**Table: 6 Correlation between RBS, Urea, Creatinin, and Lipids with HbA1C in Diabetic Retinopathy**

| Variables | HbA1C | |
|---|---|---|
| | r value | Sig. (2-tailed) |
| RBS | .416** | .000 |
| Urea | .217* | .030 |
| creatinine | .337** | .001 |
| TC | .402** | .000 |
| TG | -.168 | .094 |
| HDL | -.097 | .336 |
| LDL | .424** | .000 |
| VLDL | -.168 | .094 |

***. Correlation is significant at the 0.05 level (2-tailed).**
****. Correlation is significant at the 0.01 level (2-tailed).**

## DISCUSSION

Dyslipidemia with Hyperglycemia increases the progression of Diabetic Retinopathy. Dyslipidemia is associated with increased inflammation and oxidative stress, which can contribute to the pathogenesis of diabetic Retinopathy. (17) Oxidative stress can cause damage to retinal cells and blood vessels, exacerbating the progression of the disease. Dyslipidemia can lead to increased vascular permeability, causing the linkage of fluid and protein into the retina. It can result in macular edema, a common complication of diabetic Retinopathy. (10) Dyslipidemia can also promote the growth of abnormal blood

vessels (neovascularization) in the retina, further worsening retinal damage. Hyperglycaemia and its biochemical sequelae either alter endothelial function directly or influence endothelial cell functioning indirectly by affecting the pathways of growth factors, cytokines, and vasoactive agents. (24)

In our study, the mean baseline total cholesterol, TG LDL, HDL, and VLDL levels in DR were 234.74 mg/dl, 171.31 mg/dl, 44.04 mg/dl, LDL 156.437 mg/dl and 34.26 mg/dl respectively which was strongly significant with their abnormal ranges. The mean baseline Random blood Glucose and HbA1c were 252.35 mg/dl and 10.11%, respectively, which was strongly significant with their abnormal ranges. The mean baseline RBS and HbA1C in Mild NPDR, Moderate NPDR, Severe NPDR, and PDR were 281.31 mg/dl, 262.30 mg/dl, 316 mg/dl, 354.53 mg/dl and 9.48%, 10.36%, 10.26%, 13.02% respectively. In this study, we observed a significant change between and within groups. Due to the breakthrough of covid, there is no change in pattern with an increasing number of individuals of people with Diabetes toward the progression of DR. Total Cholesterol and LDL were higher in all NPDR and PDR. HDL was lower in PDR. It correlated with Klein et al. 1988, and Chew et al. 1996 showed a significant trend for increased severity of Retinopathy with increased cholesterol. (22,23)

The Gender wise distribution showed preponderance for the male sex. The ratio being 1.6:1, most of the male sex was associated with severe forms of Retinopathy. (22) The Predominant age group affected with DR was 51-60. Our study shows a significant change in lipid profile, age, and Gender with the severity of DR; after the Covid-19 breakthrough, both genders increased mild NPDR cases with increasing Prevalence of Diabetic Retinopathy in the low age group of Diabetic Populations. Many factors like medical facility, DM medication, Economical, and other psychological factors were associated with this. However, there are no significant changes observed in their lipid profile.

Our study found significant changes in TG and VLDL with a duration of Diabetes and significant change in Total cholesterol and LDL with anti-diabetic medications. Lipid-lowering therapy was been shown to have some beneficial effects on DR.(23). With the family history of Diabetes, change in lipid profile is insignificant.

Our study found an insignificant change in lipid profile with administered COVID-19 Vaccine (Covisheld and Covaxin), History of COVID-19 Positive (RT-PCR), and History of Covid-like symptoms. However, our studies observe significant changes between the History of Provided treatments during COVID-19 (No treatment. Isolation, and hospitalization) and Total cholesterol, Triglyceride, LDL, and VLDL. However, there is a change in HDL insignificant. This study found an insignificant change between lipid profile and Associated Risk Factors (No Risk, HTN, CVD, and HTN+CVD), Associated Bad Habits (No bad habits, Smoking, Alcohol, and Smoking +Alcohal).

Our study found a significant correlation between HbA1c and total cholesterol, and LDL, but there was no association between serum lipids and DR. In this study, we observed a significant change in lipid profile, but an insignificant change was observed with the severity of DR. Due to the breakthrough, covid number of cases increased in DR with decreasing age and duration of Diabetes. However, there is no major change in the observation of the lipid profile pattern of individual diabetics toward the progression of DR. Diabetic Retinopathy is a preventable cause of blindness, especially in developing countries. Strict glycemic control, routine Biochemical investigation, and their good control, Early Diagnosis of DR, and treatment save the individual from severe visual loss by controlling the progression of Retinopathy.

## CONCLUSION

We found there are no significant changes in patterns of lipid profile due to the COVID-19

Pandemic and with administered vaccines, associated risk factors (HTN, CVD, and CVD+HTN), and bad habits (smoking, alcohol, and smoking+alcohal) along with significant association between lipid profile except HDL-C and History of Provided treatment during the Covid-19. The study also showed a significant correlation between the mean blood glucose, HbA1c, Urea Creatinine, and total cholesterol. However, there was no significant association between serum lipids and the severity of DR.

**Limitation of the study:** The study was limited to 100 patients only. The study is limited to only two rural populations around the two specific medical colleges, hence suffers from selection bias.

**Benefits to the participants:** No monetary benefits were given to the participants.

***Declaration by Authors***

**Ethical Approval:** Approved

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**Conflict of Interest:** The authors declare no conflict of interest.

## REFERENCES

1. Boden I, Bernabeu MO, Dhillon B, Dorward DA, MacCormick I, Megaw R, et al. Pre-existing diabetic Retinopathy as a prognostic factor for COVID-19 outcomes amongst people with Diabetes: A systematic review. Diabetes Res Clin Pract. 2022 May 1; 187:109869.
2. Lee R, Wong TY, Sabanayagam C. Epidemiology of diabetic Retinopathy, diabetic macular edema, and related vision loss. Eye Vis. 2015 Sep 30; 2:17.
3. Wong TY, Sun J, Kawasaki R, Ruamviboonsuk P, Gupta N, Lansingh VC, et al. Guidelines on Diabetic Eye Care: The International Council of Ophthalmology Recommendations for Screening, Follow-up, Referral, and Treatment Based on Resource Settings. Ophthalmology. 2018 Oct 1;125(10):1608–22.
4. Barron E, Bakhai C, Kar P, Weaver A, Bradley D, Ismail H, et al. Associations of type 1 and type 2 diabetes with COVID-19-related mortality in England: a whole-population study. Lancet Diabetes Endocrinol. 2020 Oct 1;8(10):813–22.
5. Czeisler MÉ, Lane RI, Petrosky E, Wiley JF, Christensen A, Njai R, et al. Mental Health, Substance Use, and Suicidal Ideation During the COVID-19 Pandemic - United States, June 24-30, 2020. MMWR Morb Mortal Wkly Rep. 2020 Aug 14;69(32):1049–57.
6. Elibol A, Eren D, Erdoğan MD, Elmaağaç M, Dizdar OS, Çelik İ, et al. Factors influencing on development of COVID-19 pneumonia and association with oral anti-diabetic drugs in hospitalized patients with diabetes mellitus. Prim Care Diabetes. 2021 Oct 1;15(5):806–12.
7. Corcillo A, Cohen S, Li A, Crane J, Kariyawasam D, Karalliedde J. Diabetic retinopathy is independently associated with increased risk of intubation: A single-center cohort study of patients with Diabetes hospitalized with COVID-19. Diabetes Res Clin Pract. 2021 Jan 1; 171:108529.
8. Goh JKH, Cheung CY, Sim SS, Tan PC, Tan GSW, Wong TY. Retinal Imaging Techniques for Diabetic Retinopathy Screening. J Diabetes Sci Technol. 2016 Feb 1;10(2):282–94.
9. Cheng Y, Zhang H, Chen R, Yang F, Li W, Chen L, et al. Cardiometabolic Risk Profiles Associated with Chronic Complications in Overweight and Obese Type 2 Diabetes Patients in South China. PLoS ONE [Internet]. 2014 Jul 3 [cited 2022 Aug 13];9(7):e101289. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4081665/
10. Zhang H yan, Wang J Yong, Ying G Shuang, Shen L Ping, Zhang Z. Serum lipids and other risk factors for diabetic Retinopathy in Chinese type 2 diabetic patients. J Zhejiang Univ Sci B [Internet]. 2013 May [cited 2022 Aug 13];14(5):392–9. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3650453/
11. Yau JWY, Rogers SL, Kawasaki R, Lamoureux EL, Kowalski JW, Bek T, et al. Global Prevalence and Major Risk Factors of Diabetic Retinopathy. Diabetes Care [Internet]. 2012 Mar [cited 2022 Aug 13];35(3):556–64. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3322721/
12. WONG TY, KLEIN R, ISLAM FMA, COTCH MF, FOLSOM AR, KLEIN BEK, et

al. Diabetic Retinopathy in a Multi-ethnic Cohort in the United States. Am J Ophthalmol [Internet]. 2006 Mar [cited 2022 Aug 13];141(3):446–55. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2246042/
13. Nielsen SF, Nordestgaard BG. Statin use before diabetes diagnosis and risk of microvascular disease: a nationwide nested matched study. Lancet Diabetes Endocrinol. 2014 Nov;2(11):894–900.
14. Rasoulinejad SA. Evaluating the Risk Factors of Development and Progression of Diabetic Retinopathy: A Review Study. Shiraz E-Med J [Internet]. 2022 [cited 2022 Aug 13];23(5). Available from: https://brieflands.com/articles/semj-117171.html#abstract
15. Talbert RL, National Cholesterol Education Program Adult treatment panel III. Role of the National Cholesterol Education Program Adult treatment panel III guidelines in managing dyslipidemia. Am J Health-Syst Pharm AJHP Off J Am Soc Health-Syst Pharm. 2003 Jul 1;60(13 Suppl 2):S3-8; quiz S25.
16. Sasongko MB, Wong TY, Nguyen TT, Kawasaki R, Jenkins A, Shaw J, et al. Serum Apolipoprotein AI and B Are Stronger Biomarkers of Diabetic Retinopathy Than Traditional Lipids. Diabetes Care [Internet]. 2011 Feb [cited 2022 Aug 19];34(2):474–9. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3024371/
17. Rao H, Jalali JA, Johnston TP, Koulen P. Emerging Roles of Dyslipidemia and Hyperglycemia in Diabetic Retinopathy: Molecular Mechanisms and Clinical Perspectives. Front Endocrinol [Internet]. 2021 [cited 2023 May 23];12. Available from: https://www.frontiersin.org/articles/10.3389/fendo.2021.620045
18. Das AV, Narayanan R, Rani PK. Effect of COVID-19 Pandemic on Presentation of Patients With Diabetic Retinopathy in a Multitier Ophthalmology Network in India. Cureus. 2021 Oct;13(10):e19148.
19. Sonawane NJ, Yadav D, Kota AR, Singh HV. Central retinal vein occlusion post-COVID-19 vaccination. Indian J Ophthalmol [Internet]. 2022 Jan [cited 2022 Jul 16];70(1):308–9. Available from: https://journals.lww.com/ijo/Fulltext/2022/01000/Central_retinal_vein_occlusion_post_COVID_19.68.aspx
20. Vashist P, Senjam SS, Gupta V, Manna S, Gupta N, Shamanna BR, et al. Prevalence of diabetic Retinopathy in India: Results from the National Survey 2015-19. Indian J Ophthalmol. 2021 Nov;69(11):3087–94.
21. WHO-UCN-NCD-20.1-eng.pdf.
22. Cherchi S, Gigante A, Spanu MA, Contini P, Meloni G, Fois MA, et al. Sex-Gender Differences in Diabetic Retinopathy. Diabetology. 2020 Dec;1(1):1–10.
23. Keech AC, Mitchell P, Summanen PA, O'Day J, Davis TME, Moffitt MS, et al. Effect of fenofibrate on the need for laser treatment for diabetic Retinopathy (FIELD study): a randomized controlled trial. Lancet Lond Engl. 2007 Nov 17;370(9600):1687–97.

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