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# Lipid profile as an evaluation tool for glycemic parameters in Type II Diabetes Mellitus

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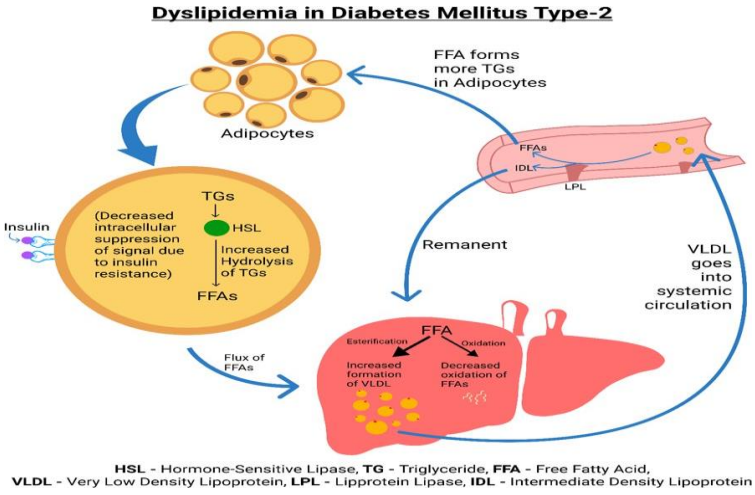
**Abstract:**

The study aimed to evaluate the correlation of glycemic parameters like fasting plasma glucose, glycated hemoglobin, fasting insulin levels with dyslipidemia in patients suffering from diabetes mellitus (Type II) at a multi-specialty hospital Dehradun Uttarakhand. The current analytical cross-sectional study was undertaken in a multispecialty hospital in Uttarakhand between May and December 2019. A total of one hundred Type-II diabetes patients participated in the study. The number of males and females were 49 and 51 in number respectively. The demographic statistics have been accrued via the patient profile form. Essentially, blood tests were done following 12 hours fast to test `fasting plasma levels of glucose, glycated hemoglobin, fasting insulin levels and lipid profile. The criteria of Glycated hemoglobin levels (HbA1c) were used to divide the subjects into three groups (Group A patients exhibiting HbA1c less than or equal to 7%, Group B with values from 7-9%, and Group C patients with HbA1c greater than 9%). The patient had a Body Mass Index range (BMI) of 26-33, putting them in the overweight and obese groups. Multivariate analysis demonstrated the values of Fasting blood sugar, HbA1c, and HOMA-IR(Homeostatic Model Assessment of Insulin Resistance) increased as dyslipidemia progressed from Group A to Group C. Bivariate correlation analysis on the total patient's data revealed that Fasting blood sugar, Glycated hemoglobin, duration of disease and HOMA-IR values show a direct positive correlation at $p<0.05$ for the total cholesterol, triglycerides and Low-density lipoprotein-C, but negative correlation at $p<0.05$ for High-density lipoprotein-C values. The glycated hemoglobin, fasting blood sugar, and insulin resistance are significantly correlated with abnormal lipid profiles, specifically the triglyceride levels. However, the lipid profile of the patients had no significant correlation with their BMI or age.

**Keywords:** lipid profile, insulin resistance, glycated haemoglobin, Type II diabetes, dyslipidemia.




**Introduction**:

Diabetes mellitus essentially is a complicated set of continual sicknesses with varying aetiologies, clinical courses, and evolution. Still, a common link is hyperglycemia, which causes errors in insulin secretion and its mechanism of action, resulting in abnormalities in many organs and systems[1]. Diabetes mellitus is prevalent worldwide, including in India, and the sufferer's number is increasing at a disturbing rate[2]. India, a country undergoing tremendous socioeconomic development and urbanization, is responsible for a significant portion of the world's diabetes burden. As a result of the urbanization of lifestyle characteristics, studies in India have revealed an increasing prevalence of diabetes among urban and rural populations. In addition, prediabetes is also a common ailment. Therefore, diabetes probably is estimated to escalate from 40.6 million sufferers to 79.4 million from 2006 to 2030 in India alone.[3]According to studies, diabetes affects roughly 12.1 per cent of urban Indian individuals, with symptoms appearing a decade before their western counterparts[4]. Diabetes mellitus (DM) is a substantial factor covering risk for cardiovascular disorders (CVD), the essential driver of mortality amongst diabetics. Aside from the well-known microvascular complications of diabetes, such as nephropathy and retinopathy, macrovascular issues, such as coronary arteries, peripheral arteries, and carotid vessels related disordersare becoming more prevalent[5]. Obesity with type 2 diabetes (T2D) is a global chronic disorder. Patients with T2D and obesity are more likely to develop cardiovascular disease, which increases morbidity and death. [6].The A1C test is recommended in clinical trials to demonstrate enhanced control over glycemic status. Itis the most used way to monitor the glycemic index. Self-monitoring of blood glucose[7] assists the management of an individual's health and medication, especially for people who take insulin. Dyslipidemia ismore common in Type II diabetes (T2DM) patients, which raises their risk of cardiovascular disease (CVDs). Glycated haemoglobin may be used as a prognosticator of dyslipidemia, further to a legitimate glycemicindex. [8]. Thus, the early prediction of imbalance in lipid profile through HbA1c values may be hired as a preventive method for delaying or avoiding cardiovascular issues in sufferers with type II diabetes mellitus. [9].

Dyslipidemia is the most common comorbidity in T2DM patients with uncontrolled hyperglycemia [10]. In those afflicted with diabetes mellitus (Type II), glycosylated haemoglobin (HbA1c) is the gold standard of glycemic management. It's a good predictor of blood glucose control over time. HbA1c levels above 7% have been documented as an alarming factor for cardiovascular disorders in people with diabetes. Dyslipidemia is marked by an elevation in triglycerides and Low-Density Lipoprotein values, accompanied by a

decline in High-Density Lipoprotein-cholesterol levels in persons with poor glycemic control [11].Glycated haemoglobin (HbA1c) blood testing provides information on the subject's average levels of bloodglucose through the preceding 2-3 months, reflecting the estimated half-life of erythrocytes [12]. The glycated haemoglobin test is now acknowledged as a standard to diagnose and monitor diabetes, principallytype II diabetes. [13]. According to the reviewed literature, hypertriglyceridemia is associated with elevatedblood glucose values and an augmented hazard of diabetes mellitus [14]. Hypertriglyceridemia, which is frequent in diabetes mellitus that is non-insulin-dependent, is also connected with insulin resistance. High triglycerides characterize insulin resistance. Sugar does not enter the body cells if there is insulin resistance. As a result, there is an excess of insulin in the body system because the pancreas produces more. The link between hypertriglyceridemia and insulin resistance is unclear but could be due to glucose and lipid substrate competition[15].This study investigates the relationship between HbA1c, fasting blood sugar, disease duration, and insulinresistance with dyslipidemias in Type II diabetic patients.

**Materials and methods:**

The investigation was performed in Dehradun, Uttarakhand, India, at a Multi-specialty Hospital. An observational, cross-sectional and prospective study was conducted in the medicine department, including inpatient and outpatient departments. The Institutional Ethics Committee accepted the protocol. All subjects agreed to sign a written informed consent document that covered the entire research project, and they were informed about its purpose. The study subjects' confidentiality was preserved. The patient's information was gathered through patient profile forms and the medical history. The study includes both genders, which came for the regular check-up and follow-up to the Hospital during the study period.

*Inclusion criteria:* The investigations covered all subjects suffering from Type 2 Diabetes Mellitus, regardless of age or gender. "American Diabetes Association" (ADA) standards was followed [16] for diagnosis of diabetes.

*Exclusion criteria:* Seriously ill patients, Patients suffering from cardio-respiratory disease, hepatic complications, endocrinopathies, thyroid and renal issues or any other systemic disease and those on cholesterol-lowering medications were not involved in the study. Pregnant female patients and patients who have Type 1 Diabetes were also excluded.

Subjects of both genders who presented to outpatient and inpatient departments between May and December 2019 were chosen. Thus, 100 patients fit our criteria. Their histories and examination data comprise presenting symptoms, complications, treatment, BMI, Fasting blood sugar, Glycated Hemoglobin, duration of diabetes, Triglycerides, LDL, HDL, Total cholesterol and Fasting insulin levels.The National Cholesterol Education Program Adult Treatment Panel III[17] guiding principles were considered for evaluating the lipid profile ranges. Hypercholesterolemia is characterized by a total cholesterol level of more than 200 mg/dl, triglycerides levels greater than 150 mg/dl, LDL-C of higher than 100 mg/dl,and HDL-C(High-Density Lipoprotein-cholesterol) below 40 mg/dl. [18]For the assessment of biochemical parameters, patients' venous samples were taken after a 12-hour fast.A "high-performance liquid chromatography[19]" method was employed to measure glycosylated haemoglobin. Glycerol kinase was used to quantify serum triglycerides using an enzymatic colorimetric method-ology. VITROS GLU Slide[20]was used to measure Glucose concentration in blood plasma quantitatively. The insulin levels were assessed using an Immunometric Immunoassay technique[21]. The demographic information and relevant medical history

were recorded with the help of patient profile forms.The participant subjects were grouped into two categories based on glycated haemoglobin values in theirblood for analysis. Group A comprised the subjects with glycosylated haemoglobin ≤ 7, Group B subjects with 7-9% levels, and Group C patients with HbA1c greater than 9%.[22]

IBM SPSS Statistics 20 software was utilized to evaluate and analyze the datasets. The data exhibited normal distribution confirmed by the Shapiro–Wilk test[23] combined with the Kolmogorov-Smirnov test[24]. Data were denoted as mean with standard deviation. Pearson correlation coefficient was used to determine the correlation of patients' lipids profiles with the glycemic state. In addition, Multivariate investigation (MANOVA) was conducted for comparingvariable means, differences in-between groups. When the value of p was less than 0.05, the results werestately substantial.

*Informed Consent:* All patients agreed and signed informed consent papers, according to the protocol.

*Ethical approval:* Approval from the Institutional Ethics Committee of Shri Guru Ram Rai Institute of Medical and Health Sciences, Shri Guru Ram Rai University, Patel Nagar Dehradun Uttarakhand((reg no. ECR/710/INST/UK/2015/RR-18A) was obtained for all test procedures.

**Results:**

This analysis involved 100 participants, including 49 males and 51 females. Females had higher values for FBS (Fasting Blood Sugar), Glycated haemoglobin, Fasting Insulin, HOMA-IR, and Triglycerides than males at a significance level of <0.05. However, the total cholesterol, HDL-C, and LDL-C (Low-Density Lipoprotein-cholesterol) levels in males and females were not substantially different. The mean values of variables are shown in Table 1. The Mean with standard deviation values for subjects` age, FBS, HbA1c, BMI, Total cholesterol levels, Tri- glyceride levels, LDL values, HDL values, duration of diabetes, Fasting Insulin and HOMA-IR values are 76.96±7.288, 165.43±52.674, 9.423±3.0004, 28.862±1.44710, 202.907±44.612, 172.4023±43.97,126. 8523±33.651, 41.1901±10.20, 9.48±6.443, 8.611±3.3290 and 3.123±1.9435 respectively. The patients were segregated into three categories based on glycated haemoglobin levels There were 26 patients in the category with glycated haemoglobin levels< 7%,42 patients of the 7-9% category, and 32 patients had glycated haemoglobin values>9%. The GroupWise baseline values for variables are demonstrated in Table 2. Comparing the three groups, hypercholesterolemia was seen in 24%,61.9% and 50% of patients in Group A, Group B and Group C, respectively. In addition, 50% of patients in Group A had elevated triglycerides and LDL. Group C had abnormal triglycerides in 64.4%. The HDL levels were less than normal in 50% of patients in Group C. In total, 52.4 % of patients fulfilled the criteria of dyslipidemia in compliance with the "NCEP ATP III guideline". Multivariate analysis was used to compare the performance of the cases in each independent variable level (Group A, B, and C) on the dependent variable (Biochemical and glycemic parameters). Box's Test of Equality of Covariance Matrices[25] assesses` whether dependent variable covariance matrices were equal across different independent variable levels (Group). In this set of data, the presumption is incorrect. (Box's M= 1173.981, p<0.001).

**Table 1: Baseline characteristics**

| | Minimum value | Maximum value | Mean | std. deviation |
|---|---|---|---|---|
| **Age in yrs** | 65 | 87 | 76.96 | 7.288 |
| **FBS (mg/dl)** | 120 | 315 | 165.43 | 52.674 |
| **HbA1c (%)** | 5.7 | 14.9 | 9.423 | 3.0004 |
| **BMI(Kg/m2)** | 26.00 | 33.00 | 28.8620 | 1.44710 |
| **Total cholesterol(mg/dl)** | 120.00 | 306.00 | 202.9070 | 44.61296 |
| **Triglyceride (mg/dL)** | 53.32 | 332.00 | 172.4023 | 43.97910 |
| **LDL-C (mg/dL)** | 53.60 | 232.54 | 126.8523 | 33.65121 |
| **HDL-C (mg/dL)** | 20.00 | 68.18 | 41.1901 | 10.20660 |
| **Duration of Diabetes (Yrs)** | 1 | 24 | 9.48 | 6.443 |
| **Fasting Insulin (MIU/L)** | 4.0 | 16.8 | 8.611 | 3.3290 |
| **HOMAIR** | .9 | 8.2 | 3.123 | 1.9435 |
| **Valid N (listwise)= 100** | | | | |

BMI, Body Mass Index; FBS, fasting blood sugar; HbA1c, Glycated haemoglobin; LDL-C, Low-Density Lipoprotein-cholesterol; HDL-C, High-Density Lipoprotein-cholesterol; HOMA-IR, Homeostatic Model Assessment of Insulin Resistance; N, sample size:

**Table 2: Groupwise Anthropometric and clinical characteristics of Group A, B and C**

| | **GROUP A Glycated haemoglobin less than 7%** | | **GROUP B Glycated haemoglobin between 7-9%** | | **GROUP C Glycated haemoglobin more than 9%** | |
|---|---|---|---|---|---|---|
| **Variables** | mean | standard deviation | mean | standard deviation | mean | standard deviation |
| **Age (Yrs)** | 72.38 | 6.152 | 75.64 | 6.469 | 78.03 | 6.332 |
| **FBS (mg/dl)** | 120.31 | 15.740 | 174.26 | 19.974 | 198.63 | 44.255 |
| **HbA1c (%)** | 6.069 | .3159 | 8.024 | .6176 | 10.859 | 1.0978 |
| **BMI(Kg/m2)** | 28.7115 | 1.56623 | 28.7476 | 1.32743 | 29.1344 | 1.50518 |
| **Total cholesterol(mg/dl)** | 171.6346 | 26.42918 | 210.5095 | 23.42294 | 218.3375 | 62.63334 |
| **Triglyceride (mg/dL)** | 144.2915 | 30.60447 | 183.2305 | 19.78690 | 181.0303 | 63.28672 |
| **LDL-C (mg/dL)** | 101.3446 | 23.68324 | 135.2510 | 18.27837 | 136.5541 | 44.53933 |
| **HDL-C (mg/dL)** | 48.1169 | 8.85108 | 37.5707 | 4.96053 | 40.3125 | 13.34834 |
| **Duration of Diabetes (Yrs)** | 7.92 | 3.045 | 6.11 | 3.612 | 12.06 | 9.312 |
| **Fasting Insulin(MIU/L)** | 5.342 | 3.4990 | 8.034 | 3.7680 | 9.169 | 4.6107 |
| **HOMAIR** | 1.562 | .9916 | 3.257 | 1.6848 | 3.903 | 1.9081 |

**Table 3: Multivariate tests of statistical significance**

| Effect | | Value | F | Hypothesis df | Error df | Sig. |
|---|---|---|---|---|---|---|
| **Intercept** | **"Pillai's Trace"** | 1.000 | 37988.083[b] | 15.000 | 83.000 | .000 |
| | **"Wilks' Lambda"** | .000 | 37988.083[b] | 15.000 | 83.000 | .000 |
| | **"Hotelling's Trace"** | 6865.316 | 37988.083[b] | 15.000 | 83.000 | .000 |
| | **"Roy's Largest Root"** | 6865.316 | 37988.083[b] | 15.000 | 83.000 | .000 |
| **GROUP** | **"Pillai's Trace"** | 1.405 | 13.216 | 30.000 | 168.000 | .000 |
| | **"Wilks' Lambda"** | .048 | 19.800[b] | 30.000 | 166.000 | .000 |
| | **"Hotelling's Trace"** | 10.477 | 28.636 | 30.000 | 164.000 | .000 |
| | **"Roy's Largest Root"** | 9.476 | 53.064[c] | 15.000 | 84.000 | .000 |

b represents the Exact statistic

c represents that the statistic is upper bound on F, giving a lower bound on the significancelevel.

We described the results using the "Pillai's Trace" test (Table 3), owing to the statistical importance of Box's M. For all biochemical parameters, FBS, HbA1c, Fasting Insulin, and HOMA-IR, Levene's test of homogeneity of variance returned statistically relevant results[26]. Tamhane's T2 post hoc tests for the dependent variables revealed that all three groups differed significantly on Fasting blood sugar and HbA1c ($p<0.05$). In addition, Groups A and B and Group A and C differ significantly ($p<0.05$) for Triglycerides levels, LDL-C levels, HDL-C levels, Total Cholesterol, Fasting Insulin levels and HOMA-IR values. There is no substantial difference between Group B and C for the same parameters, though, at $p>0.05$. The glycemic status and lipid profiles on comparison through bivariate correlation analysis provided significant results. Table 4 illustrates the Pearson correlation values obtained. Triglycerides, LDL and Total cholesterol positively correlate with Fasting blood sugar, HbA1c, diabetes duration, and HOMA-IR. On theother hand, HDL shows a poorly negative correlation with Fasting blood sugar, HbA1c, diabetes duration and HOMA-IR.

**Discussion:**

As a metabolic disorder, Diabetes mellitus is inextricably linked with cardiovascular disease[27], the prime root of morbidity and even death among the patients. Obesity, hypertension, and dyslipidemia are CV risk factors in diabetes, putting them at higher risk for heart attacks and strokes[28]. Diabetic dyslipidemia is a combination of increased triglycerides, declined high-density lipoprotein cholesterol, and a surplus of small and dense low-density lipoproteins. Lipid anomalies predominantly develop in diabetes due to poor insulin sensitivity disturbs critical enzymes and pathways involved in lipid metabolism[29].

**Table-4: Summaries of Correlation of glycemic status and Lipid Profile**

| | | FBS (mg/dl) | Glycosylated haemoglobin (%) | Duration of diabetes (Yrs) | HOMA-IR |
|---|---|---|---|---|---|
| **Triglyceride (mg/dL)** | **Pearson Correlation** | .246** | .375** | .328** | .283** |
| | **Sig. (2-tailed)** | .000 | .000 | .001 | .004 |
| **LDL (mg/dL)** | **Pearson Correlation** | .168** | .428** | .298** | .304** |
| | **Sig. (2-tailed)** | .000 | .000 | .003 | .002 |
| **HDL (mg/dL)** | **Pearson Correlation** | -0.159 | -.312** | -.218* | -.244* |
| | **Sig. (2-tailed)** | .000 | .002 | .029 | .014 |
| **Total cholesterol(mg/dl)** | **Pearson Correlation** | .174** | .447** | .335** | .280** |
| | **Sig. (2-tailed)** | .000 | .000 | .001 | .005 |

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

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

Chronic uncontrolled hyperglycemia causes microvascular and macrovascular consequences in diabetics, comprising cardiovascular disorders, neuropathy, retinopathy and nephropathy. Therefore, one step toward lowering CVD risk is early detection and treating dyslipidemia associated with diabetes[30]. Our study evaluated the correlation of glycated haemoglobin, fasting blood sugar, insulin resistance, and duration of diabetes with lipid assessing parameters in Type II diabetes patients. In compliance with the "NCEP ATP III guideline", 54.8 per cent of women and 49.2 per cent of men were confirmed to have dyslipi-daemia. This is similar to previous study results [31].Total cholesterol, triglycerides, and Low-Density Lipoprotein are all hazard determinants for Coronary heart issues in women, as are low values of High-Density Lipoprotein[32]. Therefore, women's hyperlipidaemia might be due to the impact of female hormones on fat distribution in the body, resulting in disturbances in lipoprotein composition. The patient's lipid profile indicated clear distinction in the groups designed based on glycemic control[33,34]. The people in the first group with diabetes under control (HbA1c<7%) had 24% cases of hypercholesterolemia. However, most patients in groups B and C had high total cholesterol, elevated triglycerides, and low HDL with an obese profile[35]. The patients exhibited BMI in the range of 26-33, consisting of overweight and obese categories. The HOMA-IR values show an increasing trend from group A to B. A link was discovered between a lower percentage of body fat and lower HOMA2-IR values and triglyceride levels by Bocca *et al*. Obesity is a hazard factor for poor insulin sensitivity, dyslipidemia, with hypertension later in life, all of which are referred [36] as metabolic syndrome (MS) Between groups A and B and A and C, triglycerides, total

cholesterol, LDL values, HDL values, fasting insulin, and HOMA-IR differ significantly at $p<0.05$. Group B and C, on the other hand, do not have significant differences ($p>0.05$) for the same parameters. This explains that poor glycemic control (HbA1c>7%) in- variably affects the lipid profile.

Similar to our results, Biadgo *et al*. postulated that Type II diabetes patients had escalated serum values of fasting blood glucose, triacylglycerol, total cholesterol and Low-Density Lipoprotein, and decreased levels of High-Density Lipoprotein-cholesterol[37]. Moreover, these fasting blood sugar correlated positively with total cholesterol, triglycerides, LDL-C, and negatively with High-density lipoprotein-cholesterol.The glycated haemoglobin shows a similar trend like fasting blood sugar with ($p<.005$) increasing dyslipidaemias in the patients. Duration of the disease shows a positive correlation with the lipid profile. Thagele *et al*. reported that, asthe duration of the disease rises, so does the altered lipid metabolism, indicating that adequate therapy is required to avoid the subsequent consequence of cardiovascular disease. In both genders, the degree of dyslipidemia increases as they get older[38]. Diabetes dyslipidemia is linked to several factors. These include effects of insulin on liver apoprotein formation, modulation of lipoprotein lipase, actions of cho- lesteryl ester transfer protein (CETP), and peripheral insulin actions on adipose and muscle tissue are all linked to diabetes dyslipidemia. [39]. Similarly, in our study, the patients show increased HOMA-IR values as dyslipidemia increases from Group A to C.

**Conclusion :**

The study confirms a correlation between HbA1c, fasting blood sugar, disease duration and insulin resistance with several circulating lipid markers in the three groups, namely, the good, moderate and poor diabetic control groups. Conclusively, lipid profile can be used as an evaluation tool for glycemic parameters in Type II Diabetes Mellitus patients. As a result, high-risk diabetic patients can be screened for timely lipid-lowering drug intervention using low-cost blood tests, allowing for early identification. Furthermore, hyperlipidemia, hyperglycemia, a large waist circumference, and a high BMI are all strong indicators of cardiovascular disorders later in life. As a result, it is suggested to check the glycemic markers so that necessary intervention can be done as far as cardiovascular diseases are concerned before it is too late.

**Abbreviations:**

T2D, Type 2 diabetes mellitus; HbA1c, Glycosylated haemoglobin; A1C, Glycosylated haemoglobin; CVD, Cardiovascular disease; FBS, fasting blood sugar; HOMA-IR, Homeostatic Model Assessment of Insulin Resistance LDL-C, Low-Density Lipoprotein-cholesterol; HDL-C, High-Density Lipoprotein-cholesterol; MANOVA, Multivariate analysis of variance; BMI, Body Mass Index:

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**Data sharing statement:**

As per request, data compiled during the proceedings of this study will be provided by the corresponding author.

**Author contributions:**

All authors helped with data compilation, analysis, drafting the paper, providing final approval to the published version.

**Conflict of Interest:**

The authors declare that they have no conflicts of interest to disclose.

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