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General Medicine

# Association between Glycosylated Haemoglobin and Serum Lipid Profile in Patients with Type 2 Diabetes Mellitus

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| Abstract | | Original Research Article |
|---|---|---|

***Introduction:*** In India, diabetes is turning into an epidemic as currently, more than 62 million individuals suffer from the disease. To our knowledge, very few studies have evaluated the correlation between lipid profiles and glycated hemoglobin (HbA1c) in newly diagnosed type II diabetes patients with hypertension. The early detection of lipid abnormalities in these patients will help prevent the cardiovascular outcomes. ***Material and Methods:*** This is a prospective and cross-sectional study conducted at Tertiary care teaching centre and Hospital over a period of 6 months. In our study 70 patients of Type 2 diabetes mellitus were taken for the study after applying inclusion and exclusion criteria. Biochemical data such as fasting plasma glucose (FPG), HbA1c and lipid profile, along with the patient's age, BMI and gender, were also taken from the electronic file system. The inclusion criteria allowed for only patients who were regularly seeing their physician and whose electronic file was up to date. ***Results:*** In our study, among 80 Type 2 diabetic individuals included in this study, 47 were male and 33 were female. Distribution of Glucose Triad results of FBS, PPBS and HbA1c levels of patients presented as Mean±SD, mean FBS was 201.49±41.84, mean PPBS was 273.39±91.48 and mean HbA1c was 8.83±0.83. Mean total cholesterol was 201.38 ± 11.48, mean total triglyceride was 198.48 ± 12.39, Mean HDL was 36.48 ± 4.62, mean LDL was 140.09 ± 9.63 and VLDL was 24.81 ± 2.47. HbA1c positively and significantly correlated with total cholesterol (r=0.223), LDL (r=0.243), HbA1c negatively and significantly correlated with HDL (r= - 0.126), and did not show any show correlation with VLDL (r=0.039) and total triglycerides (r=0.17). ***Conclusion:*** This study showed a significant correlation between levels of glycosylated hemoglobin (HbA1c) and lipid profile. This may help in predicting the lipid profile levels from the degree of glycemic control and therefore, identifying the patients with increased risk of diabetic complications.
**Keywords:** Type 2 diabetes, Glycosylated haemoglobin, Dyslipidaemia.

## INTRODUCTION

Worldwide the people suffering from diabetes mellitus were estimated to increase from current 415 million people to 642 million by 2040 [1]. The number of type 2 diabetes mellitus (T2DM) patients is increasing in all countries and 75% of people with diabetes mellitus are living in developing countries [2]. The prevalence of dyslipidaemia was 39.9%, 46.8%, and 59.3% in participants with normal glucose, prediabetes, and type 2 diabetes mellitus (T2DM). Women had a lower dyslipidaemia prevalence than men (38.7% vs. 43.3%) [3-5].

Diabetes mellitus (DM) is a common secondary cause of hyperlipidaemia, particularly, if glycaemic control is poor. Based on the American diabetic association (ADA) abnormal lipid profiles are when total cholesterol level ≥200 mg/dl, triglyceride

level is ≥150 mg/dl, HDL level is <40 mg/dl in males and <50 mg/dl in females, LDL level is ≥100 mg/dl. These LDL particles have been identified as a major risk factor for chronic heart disease (CHD) by the National Cholesterol Education Programme (NCEP) Adult Treatment panel (ATP) III [6]. It has been shown that reducing the plasma LDL cholesterol levels sharply reduces the risk of subsequent clinical Coronary Heart Diseases in both patients with pre-existing Coronary Heart Diseases and in patients free of Coronary Heart Diseases. While LDL cholesterol is a strong risk factor for coronary artery disease (CAD) [7].

Consequently, dyslipidaemia was defined as the presence of one or more of the above-mentioned abnormalities in serum lipids [8]. The changes in lipid parameters in diabetes mellitus are due to increased free fatty acid flux secondary to insulin resistance [9].

Numerous studies were done to assess the correlation of glycaemic control of patients with T2DM with the serum lipid profile. The present study would help us to understand the pattern of dyslipidaemia and also in regulating the incidence of hyperlipidaemia in patients with T2DM.

## MATERIAL AND METHODS
This is a cross sectional study conducted at Tertiary care teaching centre and Hospital over a period of 6 months. Total 70 patients of Type 2 diabetes mellitus were taken for the study after applying inclusion and exclusion criteria.

**Inclusion criteria**: Adults aged above 30 years and having Type 2 Diabetes Mellitus

**Exclusion criteria**
Patients taking multivitamin supplementation, patients treated with lipid-lowering drugs at the time of referral or having hepatic, renal or metabolic bone disorders, including parathyroid-related problems, patients with history of haemoglobinopathies were excluded from the study. Those patients having history of malabsorption syndromes such as celiac disease or active malignancy or with active infection were also excluded from the study.

### Laboratory investigations
- Estimation of FBG was done using glucose oxidase-peroxidase method [10]
- Determination of HbA1c in blood [11]
- Lipid profile: Plasma levels of total cholesterol (TC), TG and HDL-cholesterol. [12] LDL-cholesterol was measured according to Friedewald formula. [13] LDL was calculated as follows: $LDL = TC - HDL - TG/5$; very low-density lipoprotein (VLDL) cholesterol was calculated as follows: $TG/5$.

### Statistical Analysis:
The data was analysed with SPSS version 25.0. The mean, SD and correlation(Pearson's) test was used to interpret the results. Correlation coefficient (r) $\geq +1$ is taken as positive correlation, $\leq -1$ is taken as negative correlation and between $-1$ and $+1$ as no correlation. Correlation (Pearson's) test was used to interpret the result.

### RESULT
In our study, among 80 Type 2 diabetic individuals included in this study, 47 were male and 33 were female.

**Table 1: Sex Distribution of study population**

|  | Total | Males | Females |
|---|---|---|---|
| **No. of patients** | 80 | 47 | 33 |
| **Percentage** | 100 | 58.7 | 41.2 |
| Chi-Square test p=value | 0.482 | | |

**Table 2: Distribution of Glucose Triad**

| Parameters | Mean ± SD |
|---|---|
| FBS | 201.49±41.84 |
| PPBS | 273.39±91.48 |
| HbA1C | 8.83±0.83 |

In table 2, distribution of Glucose Triad results of FBS, PPBS and HbA1c levels of patients presented as Mean±SD, mean FBS was 201.49±41.84, mean PPBS was 273.39±91.48 and mean HbA1c was 8.83±0.83.

**Table 3: Distribution of Lipid Profile and HbA1c**

| Parameters | Mean ± SD |
|---|---|
| Total cholesterol | 201.38 ± 11.48 |
| Triglycerides | 198.48 ± 12.39 |
| Mean HDL | 36.48 ± 4.62 |
| Mean LDL | 140.09 ± 9.63 |
| Mean VLDL | 24.81 ± 2.47 |

In table 3, Mean total cholesterol was 201.38 ± 11.48, mean total triglyceride was 198.48 ± 12.39, Mean HDL was 36.48 ± 4.62, mean LDL was 140.09 ± 9.63 and VLDL was 24.81 ± 2.47.

**Table 4: Biochemical parameters of type 2 diabetes mellitus patients with glycated haemoglobin ≥7 and glycated haemoglobin <7.**

| Parameters | Glycated Haemoglobin (HbA1c) | | p - value |
|---|---|---|---|
| | <7 (n=29) | ≥7 (41) | |
| FBS | 163.48±37.32 | 203.48±36.49 | 0.001 |
| Total cholesterol | 199.38 ± 12.84 | 204.21 ± 12.73 | 0.048 |
| Triglycerides | 183.51 ± 13.93 | 214.73 ± 14.93 | 0.003 |
| Mean HDL | 36.86 ± 3.67 | 31.82 ± 3.28 | 0.051 |
| Mean LDL | 125.82 ± 7.48 | 129.44 ± 7.27 | 0.072 |

**Table 5: Correlation analysis between serum Lipid profile and HbA1c.**

| Parameters | Correlation coefficient (r) | p - value |
|---|---|---|
| Total cholesterol-HbA1c | 0.223 | 0.029 |
| Triglyceride-HbA1c | 0.017 | 0.424 |
| HDL-HbA1c | - 0.126 | 0.021 |
| LDL-HbA1c | 0.243 | 0.036 |
| VLDL-HbA1c | 0.039 | 0.683 |

In our study table 4, HbA1c positively and significantly correlated with total cholesterol (r=0.223), LDL (r=0.243), HbA1c negatively and significantly correlated with HDL (r= - 0.126), and did not show any show correlation with VLDL (r=0.039) and total triglycerides (r=0.17).

## DISCUSSION

In the present study, we have evaluated the pattern of lipid profile parameters in diabetic subjects and its correlation with HbA1c. This study demonstrates the typical dyslipidaemia in diabetics characterized by high triglyceride, low HDL. Although there was no significant difference between male and female, the levels of TC and LDL were significantly higher in female as compared to male Type 2 diabetic patients. This finding is in agreement with the previous studies [11-13]. Hyperlipidaemia in females may be attributed to the effects of sex hormones on body fat distribution, which leads to differences in altered lipoproteins [14]. Another reason includes differences in coagulation, the pattern of obesity between men and women, and possible role for hyperinsulinemia [15].

In our study reveals high prevalence of hypercholesterolemia, hypertriglyceridemia, high LDL and low HDL levels which are well known risk factors for CVD and abnormality of cholesterol metabolism may lead to heart attacks. Insulin affects the liver apolipoprotein production. It regulates the enzymatic activity of lipoprotein lipase and Cholesterol ester transport protein. All these factors are likely cause of dyslipidemia in Diabetes mellitus [16]. Moreover, insulin deficiency reduces the activity of hepatic lipase and several steps in the production of biologically active lipoprotein lipase may be altered in DM [17]. The main disorder in lipid metabolism was hypertriglyceridemia in our study. This finding is in concord with our previous study [18]. In the study of Reddy AS et al, 54% diabetic individuals had elevated LDL and > 50% individuals had increased TG [19]. These findings are similar to our study. But in contrast to our present study, they reported low HDL in 73% individuals.

In our study, a highly significant correlation between HbA1c and Lipid profile which is similar with various previous studies [20]. We also observed significant correlations between HbA1c and TC, LDL and HDL. In various studies, HbA1c level was eminent as showing positive correlation with TC, LDL and TG in diabetic patients [21]. HDL was shown to be the stronger predictor of CVD in diabetic population by 'The Strong Heart Study' (data evaluated by Liu et al), with hazard ratios of 2.23 and 1.80 respectively in male and female [22]. This study showed that increasing HDL cholesterol concentrations had significant, curvilinear relationships with CVD and CHD risk. Moreover, NCEP ATPIII has recommended using HDL cholesterol in assessing CVD risk in patients with diabetes.

The measurement of HDL is simple which can be conducted even in non-fasting state of patients and can be determined regardless of TG concentration. Hence, HDL cholesterol can be of great value in determining dyslipidaemia in diabetic subjects. Risk ratio showed the strongest correlation with HbA1c in our study. In the prospective cohort study with inclusion of 418 Type 2 diabetic individuals with follow-up until the appearance of a cardiovascular event, Reddy AS et al, showed that the main lipid predictor of vascular events was mean TC/HDL-C ratio with hazard ratio (HR) of 1.46. In the same study, the predictive power of the TC/HDL ratio was found to be higher than that of HDL cholesterol and study concluded that TC/HDL-C can be used as a treatment guides for diabetic dyslipidemia [23]. Total number of apo-B containing particles and small LDL-C Particles are increased in diabetes and these metabolic abnormalities are better reflected by TC/HDL ratio and

Non-HDL than LDL alone [24]. Significant association of HbA1c with various lipid parameters such as TC, HDL, LDL in present study suggests the importance of glycaemic control in order to control dyslipidaemia

According to, Diabetes complications and control trial (DCCT) established HbA1c as the gold standard of glycaemic control. The level of HbA1c value ≤7.0% was said to be appropriate for reducing the risk of cardiovascular complications [25]. In the present study, we divided diabetic patients into 2 groups as per the HbA1c cutoff of 7.0%. The diabetic patients with HbA1c value > 7.0% exhibited a significant increase in TC, TG, LDL, VLDL and without any significant alteration in HDL in comparison to patients with HbA1c value ≤7.0%. According to Parveen K et al showed the impact of glycaemic control on various lipid parameters in which the diabetic patients were categorized into 3 groups according to their HbA1c levels: group 1, good glycaemic control (HbA1c 6%–9%) and group 3, worst glycaemic control (HbA1c>9%). Poor and worst glycemic control is considered as risk factor for complications in diabetes. Strict glycemic control lowers the risk of micro- and macrovascular complications of diabetes mellitus [26].

Severity of dyslipidaemia increases in patients with higher HbA1c value. As elevated HbA1c and dyslipidaemia are independent risk factors of CVD, diabetic patients with elevated HbA1c and dyslipidaemia can be considered as a very high-risk group for CVD. Improving glycaemic control can substantially reduce the risk of cardiovascular events in diabetics [27]. It has been estimated that reducing the HbA1c level by 0.2% could lower the mortality by 10% [28]. According to Memon FF et al. found a positive correlation between HbA1c and high triglycerides suggested that HbA1c can be used as a potent marker for dyslipidemia and mitigate the macro- and micro-vascular complications [29].

In this study, a significant correlation was observed between levels of glycosylated hemoglobin (HbA1c) and lipid profile. This may in turn help in predicting the lipid profile levels from the degree of glycemic control and therefore, identifying the patients with increased risk of diabetic complications. Lipid abnormalities are common in diabetic patients and frequently seen in patients with type-2 diabetic mellitus. The abnormal lipid profile observed in type 2 Diabetes mellitus is said to be related to insulin resistance as reported in previous studies, which leads to increased release of free fatty acids from fatty tissue, impaired insulin dependent muscle uptake of free fatty acids and increase fatty acid release to the hepatic tissue [30].

## CONCLUSION
Significant correlation between HbA1c and various circu-lating lipid parameters and significant difference of lipid parameters in two groups (≤7.0% and >7.0%) of glycated haemoglobin indicates that HbA1c can be used as a potential biomarker for predicting dyslipidaemia in type 2 diabetic patients in addition to glycaemic control hence early diagnosis can be accomplished through relatively inexpensive blood testing.

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