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Relationship Between Glycosylated Haemoglobin and Dyslipidaemia in Individuals Exposed to COVID-19: A Cross Sectional Study in North Indian Population

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Abstract

Objective: To investigate the correlation between Glycosylated Hemoglobin and dyslipidemia in individuals exposed to COVID-19 in the Delhi/NCR region. **Method:** In the Delhi/NCR region, a total of 521 patient fasting blood samples were gathered from a NABL Accredited labs. These samples, collected between July 2020 and March 2022, consisted of 334 males and 187 females. HbA1C and lipid profile tests for the patients were conducted using conventional methods at a laboratory located in Gurugram. **Findings:** Among diabetic patients below 40 years of age, the mean HDL levels decreased to 40.3% compared to 42 mg/dl in non-diabetics. Increased glycosylated hemoglobin [more than 7%] with dyslipidemia noted in males 114 compared to females 64. A significant decrease in HDL levels were observed in diabetic patients above 40 years of age, with the mean level of HDL dropping to 33 mg/dl. The dyslipidemia was present in 80.9% of male diabetic patients and 88.6% of female diabetic patients. In diabetic male patients, a correlation between increasing triglyceride levels and the decreased HDL levels found. The mean triglyceride level in diabetic patients was 199 mg/dl, while the mean HDL level was 42 mg/dl. On the other hand, non-diabetic individuals had a mean triglyceride level of 105 mg/dl and an HDL level of 44 mg/dl. **Novelty:** Dyslipidemia is significantly associated with poorly controlled HbAa1c in T2DM than non-diabetic subjects after covid exposure. This observation points towards a U-shaped correlation between HDL and glycated haemoglobin in diabetic patients.

Keywords: Glycosylated haemoglobin; Dyslipidemia; Cardivascular disease; High density lipoprotein Diabetes mellitus (DM); coronary heart disease (CHD)

1 Introduction

Diabetes mellitus (DM), coronary heart disease (CHD), and dyslipidemia are ailments intricately woven with lifestyle choices, and their prevalence has surged to epidemic proportions in India. These conditions also stand as prominent global contributors to illness and mortality[1–3]. Presently, DM and CHD jointly constitute 21.9 percent of total deaths, a figure that is anticipated to escalate to 26.3 percent by 2030[4]. Within the Indian context, DM coupled with CHD manifests at a prevalence rate of 7.8 percent. Alarming differentials emerge, as CHD patients grappling with diabetes experience mortality rates two to four times higher than their non-diabetic counterparts[5,6]. This hazardous synergy culminates in a heightened 20.2 percent risk of myocardial infarction for individuals burdened by both diseases[7]. A panoramic view across eleven observational studies unveils a landscape of stability. The meta-analysis casts its verdict, revealing no significant fluctuations in HbA1c levels [weighted mean difference (WMD), 0.06 [95% CI −0.12 to 0.24)] and body mass index (BMI) [0.15 (95% CI −0.24 to 0.53)] between the pre-pandemic and pandemic epochs[8]. In a counterpoint, a Spanish study illuminates an intriguing facet. During the COVID-19 pandemic, the occurrence of high blood sugar decreases, but people dealing with type 2 diabetes face worsening blood sugar levels. This requires an increase in the use of medications to manage the situation[9]. Dyslipidemia maintains its grip, hovering at 23.5 percent prevalence in 2019 and 2020, inching upwards to 24.5 percent in 2021[9]. Meanwhile, an investigation in South India charts a different trajectory, as the lockdown's influence on overall glycemic control remains marginal[10]. In the Arabian region, a study saw a new development: a six-week lockdown doesn't affect blood sugar control for people with type 1 diabetes who don't use telemedicine[11].

A compelling connection emerges between dyslipidemic obesity and HbA1c, but this bond is specific to the realm of type 2 diabetes mellitus (T2DM)[12]. Beyond its role in glycemic regulation, HbA1c unfurls its predictive capabilities for lipid profiles[13]. A recent study noticed a complex dance happening, where glycated Hb and triglycerides (TGs) move together smoothly. At the same time, age, body mass index (BMI), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and fasting plasma glucose (FPG) dance together in a subtler rhythm[14]. After COVID-19, some people are dealing with new health issues like diabetes, high blood pressure, and cholesterol problems. These ongoing changes in blood sugar, blood pressure, and cholesterol levels highlight the importance of including diabetes, high blood pressure, and cholesterol issues in the overall diagnosis for post-COVID situations. This strengthens the basis for providing medical care based on solid evidence[15]. While HbA1c's reliability as a predictor of lipid profiles resonates, the studies cited above introduce a contrarian note. As COVID-19's narrative shifts from pandemic to endemic, an expanding multitude faces its impact, recognizing the potential for enduring consequences akin to other viral infections. In the wake of the COVID-19 pandemic, a glaring void remains—North India's inquiry into the interplay between HbA1c and dyslipidemia stands absent. Thus, the present exposition embarks on a journey, aiming to unearth potential correlations between HbA1c and dyslipidemia, post-COVID-19, within the tapestry of western India. As echoes of the pandemic persist and the terrain continues to evolve, this study adds its voice to the chorus of understanding.

2 Methodology

2.1 Study Design

This prospective study was designed as a post covid 19 screening test and was conducted at a NABL Accredited lab in the Delhi NCR region. The study included both diabetic and non-diabetic patients.

2.2 Sample Size

A total of 521 patient blood samples were collected from the NABL Accredited lab in the Delhi NCR region. The samples included 334 males and 187 females.

2.3 Ethical Approval and Patient Consent

Ethical approval for this study was obtained from the relevant authorities prior to its initiation. Additionally, written informed consent was obtained from all study participants before the study commenced.

2.4 Study Eligibility Criteria

- **Inclusion Criteria**

The study includes both diabetic and non-diabetic patients of any gender, aged between 30 and 75 years. Participants must have fasting blood sugar levels above 126 mg/dl, postprandial blood sugar levels above 190 mg/dl, and HbA1c levels above 6.2%. Individuals who are willing to participate and capable of providing valid written informed consent were enrolled in the study.

- **Exclusion Criteria**

Patients with the following clinical history were excluded from the study: blood pressure higher than 180/110 mmHg, diabetic patients with foot wounds, patients undergoing dialysis, and pregnant women. Additionally, individuals below the age of 30 and above the age of 75 were also excluded. Patients who were unwilling or unable to provide valid written consent were not included in the study.

The study commenced by screening individuals with diabetes and without diabetes, and enrolling them based on the eligibility criteria. A total of 521 participants from the Delhi NCR region were screened for this study, spanning from July 2020 to March 2022. Among the 621 initially assessed patients, 100 were excluded from the study. Of these, 80 subjects did not meet the inclusion criteria entirely, while 20 subjects declined to provide consent. Ultimately, 521 patients who met all the study's eligibility criteria and agreed to participate were recruited. These patients were then divided into two groups: the diabetic [DM+] group and the non-diabetic [non-DM] group.

Patient blood samples were collected from a NABL Accredited lab in the Delhi NCR region, comprising 334 males and 187 females. Biochemical testing was conducted following a standard protocol for various parameters, including Glycosylated Haemoglobin, serum cholesterol, serum triglycerides, High-Density Lipoproteins, Low-Density Lipoproteins, and Very Low-Density Lipoproteins. Samples with incomplete or missing data for any biochemical parameters were excluded from the analysis.

Biochemical Analysis: Glycosylated Haemoglobin was measured using the Direct Photometric method. Triglycerides and cholesterol levels were estimated using the GPO PAP and CHOD PAP methods, respectively. HDL estimation was conducted using an enzymatic method. All tests were performed on the Humastar-200 fully automated biochemistry instrument.

Statistical Analysis: All the data was statistically analyzed using the SPSS software. The data was categorized into different groups based on factors such as gender, age group, lipid profile, diabetic and non-diabetic status, and glycated haemoglobin measurements. The statistical analysis employed the one-way ANOVA parametric test to calculate the F-value and p-value.

3 Results and Discussion

This study involved 521 patients, with 178 of them being diabetic and 343 non-diabetic. Further analysis was conducted specifically on the 178 diabetic patients, revealing a higher prevalence of glycosylated hemoglobin (more than 7%) with dyslipidemia noted in males [114] compared to females [64].

Additionally, it was observed that male diabetic patients had higher lipid levels [Figure 1].

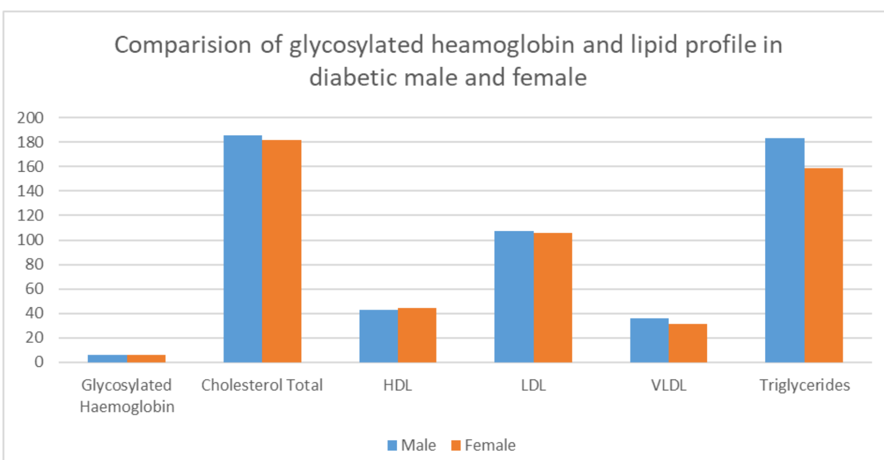

Fig 1. Comparison of glycosylated haemoglobin and lipid profile in Diabetic male and females

Diabetic females have higher HDL and lower cholesterol and triglycerides levels than male diabetics. In diabetic male patients, present study revealed a correlation between increasing triglyceride levels and the decreased HDL levels. The mean

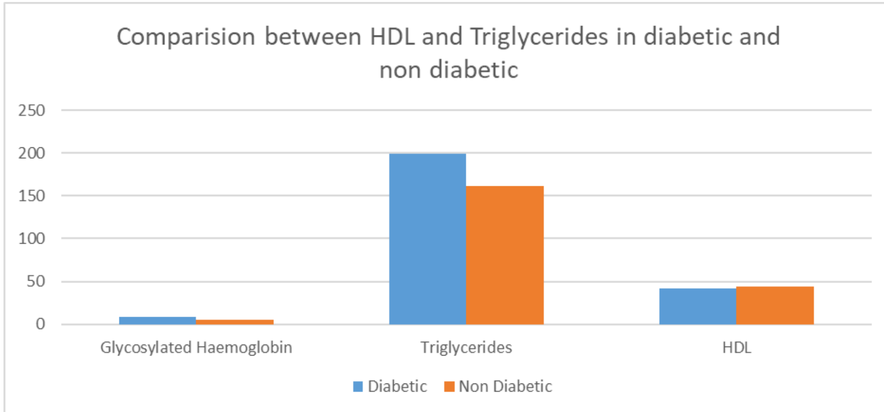

Fig 2. Reverse relationship between triglycerides and HDL in diabetic and non-diabetic patients

triglyceride level in diabetic patients was 199 mg/dl, while the mean HDL level was 42 mg/dl. On the other hand, non-diabetic individuals had a mean triglyceride level of 105 mg/dl and an HDL level of 44 mg/dl [Figure 2].

The relationship between glycated hemoglobin [HbA1C] and HDL levels in non-diabetic individuals was examined. It was found that the mean HDL levels in non-diabetic patients remained consistent, regardless of their age. The average HbA1C level was 5.5%, while the average HDL level was 44 mg/dl. The population was divided into two groups based on age, with individuals categorized as either above or below 40 years old, and similar results were observed in both groups.

Among diabetic patients below 40 years of age, the mean HDL levels decreased to 40.3% compared to 42 mg/dl in non-diabetics. However, a significant decrease in HDL levels was observed in diabetic patients above 40 years of age, with the mean level of HDL dropping to 33 mg/dl. These findings led us to conclude that a U-shaped relationship exists between HDL and glycated hemoglobin in diabetic patients, regardless of their gender [Figure 3].

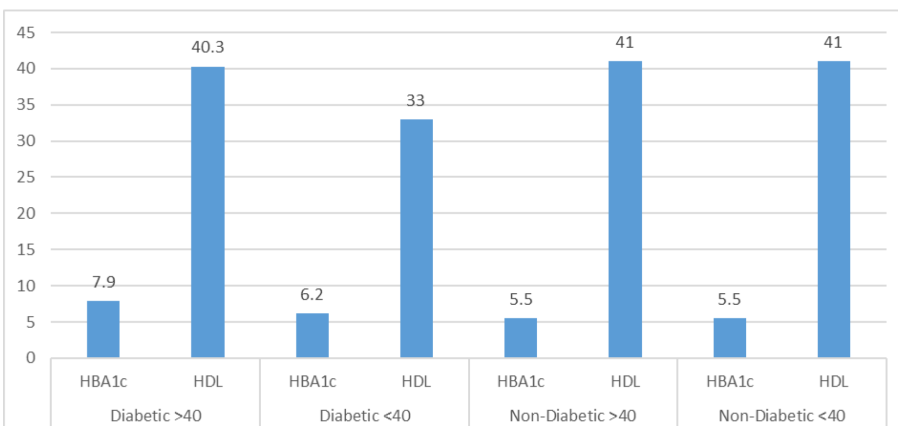

Fig 3. Depressed HDL levels in diabetic patients having age <40 yrs

A strong correlation was observed between glycated hemoglobin and HDL levels in diabetic females. More than 94% of diabetic females exhibited HDL levels below 50 mg/dl. On the other hand, in diabetic males, the levels of triglycerides were more prominently increased compared to other parameters. All the results were subjected to statistical analysis using the SPSS software, revealing a p-value of less than .00001. This indicates that the obtained result is highly significant, with a significance level of $p<0.5$.

Several studies have established a link between glycated hemoglobin and dyslipidemia, although a few reports contradict this association. In a prospective study by Sheth et al. conducted in urban western Indian population revealed, elevated triglyceride levels and low HDL levels are characteristic of diabetic dyslipidemia, and when considered together, they can serve as predictors of cardiovascular diseases, as these factors are interdependent. High prevalence of dyslipidemia and obesity in all subjects irrespective of their disease status in a Western Indian population. The dyslipidemic obese subjects had significant linear association with HbA1c in T2DM subjects.[12] In our present study the relationship between glycated hemoglobin and lipid profile in diabetic patients exhibited a range of 6.1% to 13.5% for glycosylated hemoglobin, with a mean of 7.7%. The lipid profile results indicated that the mean values for Total Cholesterol, HDL, LDL, VLDL, and Triglycerides were 189.1 mg/dl, 42.3 mg/dl, 110.9 mg/dl, 42.3 mg/dl, and 184.3 mg/dl, respectively. Therefore, our study revealed that there is no linear association with HbA1c and T2DM subjects. Our study demonstrated significant association of hyper-Triglycerides levels in T2DM subjects as compared to non-diabetic control subjects, contrary to the studies by Sheth et al. Dyslipidemia was seen in 50.27 % of the study population.[12]

In our study the dyslipidemia was 51.7% in study population. Saera Suhail et al., [2020] revealed that triglycerides were found significantly higher in females when compared with male patients and HbA1c provides valuable supplementary information about the extent of circulating lipids besides its primary role in monitoring long-term glycemic control.[13] In our present study, female diabetic patients, data revealed that female triglycerides and cholesterol levels are lower than male diabetic patients, for females, the mean values for glycosylated hemoglobin, total Cholesterol, HDL, LDL, VLDL, and Triglycerides were 7.4%, 195 mg/dl, 43 mg/dl, 120 mg/dl, 32 mg/dl, and 195 mg/dl. In our research, 51.7% of people have dyslipidemia in study population, while in the study by Seara and others, it's 57%[13]. Onthe other hand, male diabetic patients had mean values of 7.9% for glycosylated hemoglobin, 185 mg/dl for Total Cholesterol, 41 mg/dl for HDL, 105 mg/dl for LDL, 39 mg/dl for VLDL, and 197 mg/dl for Triglycerides.

The investigation conducted by Seara et al., demonstrated an inverse correlation between HbA1c and high-density lipoprotein (HDL), a finding consistent with our current study. However, these observations are inconsistent with the outcomes reported by Sami Hamdan et al. in their 2019 study conducted in Saudi Arabia. In their research, glycated hemoglobin (Hb) exhibited an association with triglycerides (TGs), while no statistically significant relationship was observed with total cholesterol[14]. In contrast, our study identified a correlation between glycated Hb and total cholesterol.

This contradicts the study of Rocio Mateo-Gallego, that revealed overload of the health system caused by the COVID-19 pandemic has resulted in an under diagnosis of T2D that might have increased hyperglycermia including undiagnosed T2D.[9] However, our present study revealed that increased HbA1c is associated with low levels of HDL in Diabetic patients in both males and females. A strong correlation was observed between glycated hemoglobin and Cholesterol and HDL levels in diabetic females. More than 94% of diabetic females exhibited HDL levels below 50 mg/dl. In diabetic patients, we noticed a correlation between increasing triglyceride levels and the suppression of HDL levels in diabetic male patients. The mean triglyceride level in diabetic patients was 199 mg/dl, while the mean HDL level was 42 mg/dl. On the other hand, non-diabetic individuals had a mean triglyceride level of 105 mg/dl and an HDL level of 44 mg/dl.

A study conducted by, Maryasia et al. showed that the patients presented with altered glucose levels, blood pressure and lipid profiles several months after recovery from COVID-19 infection.[15] We observed that there is no significant increase in the number of diabetic patients after covid exposure but diabetic patients had elevated triglyceride levels compared to non-diabetic individuals. In diabetic patients, the range of triglycerides was 87.9-627.0 mg/dl, with a mean of 184 mg/dl. In contrast, non-diabetic individuals had triglyceride levels ranging from 82-658 mg/dl, with a mean of 165 mg/dl. Interestingly, patients with high triglyceride levels also exhibited surprisingly low levels of HDL in non-Diabetics. Diabetic females have higher HDL and lower cholesterol and triglycerides levels than male diabetics.

In the present study, diabetic males were found to exhibit low HDL values than females. Supporting this observation, Gomez Rosso et al. [2017] have demonstrated that inadequate glycemic control can affect the composition and function of HDL[16]. In a study by Rakesh showed that the Prevalence of dyslipidemia among diabetic patients at baseline was 85.5% among males and 97.8% among females[17], but our present study revealed the dyslipidemia is 80.9% of male diabetic patients and 88.6% of female diabetic patients. Our study suggests that HbA1c can serve as a marker for dyslipidemia in diabetic patients, aiding in the prediction of cardiovascular disease [CVD] risk. However, it appears to have limited value in non-diabetic populations. This dual biomarker capacity of HbA1c, serving as an indicator for both glycemic control and lipid profile, can be utilized to screen high-risk diabetic patients. Dyslipidemia in COVID-affected patients may be indicative of an underlying metabolic disorder. Further studies are warranted to elucidate the precise mechanisms involved in this association, shedding light on potential metabolic pathways affected by the viral infection.

4 Limitations

In our study, the sample size is limited. Consequently, it is essential to conduct larger-scale studies in various settings to either validate or challenge the conclusions drawn from our region's data. We recommend implementing early intervention measures, such as screening all diabetic patients with elevated HbA1c levels, to confirm the presence of dyslipidemia. Employing an aggressive treatment approach is advisable as it can potentially reduce cardiovascular morbidity and mortality among individuals with Type-2 diabetes.

5 Conclusion

This study indicates a higher prevalence of high glycosylated hemoglobin and dyslipidemia in males than females after covid infection. Diabetic females have higher HDL levels and lower cholesterol and triglycerides levels than male diabetics. Dyslipidemia is significantly associated with poorly controlled HbAa1c in T2DM than non-diabetic subjects after covid exposure. HbA1c can be a valuable diagnostic tool for assessing blood lipids, in addition to its primary function of monitoring long-term glycemic control, even after exposure to COVID-19. These findings led to conclude that a U-shaped relationship exists between HDL and glycated hemoglobin in diabetic patients. By implementing proactive intervention strategies to improve glycemic control, these individuals can significantly reduce or delay the risk of developing ischemic heart disease or other metabolic diseases, even if they have not yet developed these conditions.

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