ORIGINAL RESEARCH

Exploring the Interplay Between Glycosylated Hemoglobin and Dyslipidemia in Individuals with Type 2 Diabetes Mellitus

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ABSTRACT
Background: Individuals with both diabetes and concurrent dyslipidemia are frequently vulnerable to cardiovascular disease and increased mortality. Early interventions targeting the normalization of circulating lipids have demonstrated efficacy in reducing cardiovascular morbidity and mortality. Therefore, the objective of this study is to investigate the correlation between dyslipidemia and glycemic status in individuals diagnosed with type 2 diabetes. **Methods**: This cross-sectional and prospective study spanned a duration of one year, involving a cohort of 140 patients diagnosed with type 2 diabetes (T2DM) and concomitant dyslipidemia. The assessment encompassed the evaluation of various parameters, including fasting blood glucose (FBG), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglyceride (TG), and glycosylated hemoglobin (HbA1c) levels. **Results**: The distribution of Glucose Triad results, comprising Fasting Blood Sugar (FBS), Postprandial Blood Sugar (PPBS), and Hemoglobin A1c (HbA1c) levels in patients, is presented as Mean± SD. The mean FBS was 170.48±36.64, mean PPBS was 230.49±94.39, and mean HbA1c was 7.48±0.63. Additionally, the mean total cholesterol was 220.53±16.53, mean total triglyceride was 210.83±20.65, mean HDL was 30.63±3.96, mean LDL was 140.14±7.63, and VLDL was 40.46±3.69. HbA1c exhibited a positive correlation with the mentioned parameters. **Conclusion**: The findings of the study highlight the utility of HbA1c as an effective marker for lipid profile, suggesting its potential role in screening diabetic patients at a heightened risk of developing cardiovascular diseases.

Keywords: diabetes mellitus, Dyslipidemia, lipid profile

INTRODUCTION
Diabetes mellitus (DM) looms large on the global public health landscape, presenting a multifaceted metabolic challenge rooted in the intricate dysfunction of the pancreas—either in its failure to secrete insulin adequately, the malfunction of insulin itself, or a combination of both factors.[1] This metabolic turmoil, particularly evident in chronic uncontrolled type 2 diabetes (T2DM), sets the stage for a cascade of complications that extend far beyond mere glucose dysregulation. The repercussions encompass a spectrum of issues, including atherosclerosis, diabetic nephropathy, neuropathy, and retinopathy, collectively contributing to the complex clinical profile of individuals with diabetes.The pervasive rise of diabetes mellitus as a global epidemic transcends geographic and economic boundaries, affecting both developing and developed nations.[2] Its prevalence is characterized by a disturbing surge, underscored by metabolic irregularities that lay the foundation for long-term complications affecting both micro and macrovascular systems. Understanding the nuanced interplay of these factors becomes crucial in addressing the challenges posed by diabetes on both

an individual and public health scale.One striking consequence of diabetes, particularly in the context of type 2 diabetes, is the heightened susceptibility to coronary artery disease (CAD). The confluence of diabetes and metabolic syndrome amplifies this risk, weaving a complex tapestry of health challenges that necessitate a holistic and integrated approach to management. The intricate connections between these conditions underscore the need for comprehensive strategies that not only target glycemic control but also address the broader cardiovascular and metabolic implications.[3]In the realm of diabetes management, HbA1c has emerged as a cornerstone, established through the rigorous standards set by the Diabetes Complications and Control Trial (DCCT). Beyond its role as a glycemic marker, HbA1c plays a pivotal role in guiding therapeutic interventions and shaping preventive strategies against the complications associated with diabetes mellitus. As the global burden of diabetes continues its inexorable rise, unraveling the complexities of this metabolic web becomes paramount for effective public health initiatives and the delivery of personalized care to individuals navigating the intricate landscape of diabetes and its complications.Diabetes, a prevalent and challenging health concern, heightens the vulnerability of affected individuals to the development of dyslipidemia, particularly the atherogenic subtype. This dyslipidemic state is not only associated with macrovascular diseases like heart diseases and stroke but also extends its impact to microvascular complications, including neuropathy and nephropathy. Atherogenic dyslipidemia, characterized by elevated triglyceride (TG) levels, reduced high-density lipoprotein (HDL) levels, and increased low-density lipoprotein (LDL) levels in the serum, adds a layer of complexity to the management of diabetes and its associated cardiovascular risks.

The potential role of HbA1c as a predictive marker for dyslipidemia and heart disease has been a subject of interest in research. HbA1c, reflecting long-term glycemic control, is posited as a valuable tool for assessing the risk profile of diabetic patients.[4,5] Nevertheless, the landscape is nuanced, as conflicting evidence has emerged. While certain studies advocate for HbA1c as a reliable predictor, others question the strength of the association between HbA1c levels and dyslipidemia.In the context of Indian diabetic patients, specific studies have failed to establish a significant correlation between HbA1c levels and the lipid profile. This divergence in findings emphasizes the importance of considering population-specific factors in understanding the intricate interplay between glycemic control and lipid metabolism.The complexities inherent in this relationship underscore the need for further research to elucidate the mechanisms underlying the association between HbA1c and dyslipidemia.[6] Such insights are crucial for tailoring effective management strategies that not only focus on glycemic control but also address the multifaceted interactions between HbA1c and dyslipidemia. This tailored approach is particularly relevant in diverse populations, such as those observed among Indian diabetic patients, where variations in genetic, lifestyle, and environmental factors may contribute to the nuanced clinical presentation of these interrelated conditions.

In accordance with the guidelines provided by the American Diabetes Association (ADA) on diabetes management, maintaining an HbA1c level below 8% is emphasized as a pivotal measure to reduce the risk of both microvascular and macrovascular complications associated with diabetes. This includes a lowered risk of complications such as dyslipidemia and cardiovascular disease (CVD). The ADA further asserts that HbA1c levels serve as a predictive indicator for the risk of various diabetic complications, reinforcing the critical role of glycemic control in mitigating adverse health outcomes.The ADA estimates that the risk of diabetes-related mortality experiences a 25% increase for each 1% rise in HbA1c. This underscores the direct correlation between long-term glycemic control and the overall health outcomes for individuals with diabetes.[7] By setting a benchmark HbA1c level, the ADA aims to guide healthcare practitioners in their efforts to minimize the risk of complications and improve the quality of life for those living with diabetes.In the context of dyslipidemia in diabetes, characterized by elevated triglyceride levels and reduced high-density lipoprotein cholesterol (HDL), the guidelines acknowledge the significance of lipid profile management. Interestingly, among Indians, there is a distinctive lipid profile with relatively lower levels of lipids and lipoproteins, heightened triglycerides, and diminished HDL cholesterol. This unique lipid pattern, coupled with the prevalence of metabolic syndrome, is implicated in explaining a substantial portion of the excess burden of coronary artery disease (CAD) observed in this population.In summary, the ADA guidelines highlight the pivotal role of maintaining HbA1c levels below 8% in reducing the risk of complications associated with diabetes, including dyslipidemia and cardiovascular disease.[8] Understanding and addressing the specific lipid profile characteristics in diverse populations, such as among Indians, is crucial for tailoring effective preventive and management strategies in the context of diabetes-related cardiovascular risks.

MATERIALS AND METHODS

In the course of this prospective study conducted over a one-year period, a cohort comprising 140 individuals diagnosed with Type 2 Diabetes Mellitus (T2DM) and coexisting dyslipidemia was investigated. The study aimed to shed light on the relationship between dyslipidemia and glycemic status in these patients.

INCLUSION CRITERIA

- Adults aged 32 years and above.
- Diagnosis of Type 2 Diabetes Mellitus with concurrent dyslipidemia.

EXCLUSION CRITERIA

- Patients below the age of 32 years.
- Individuals undergoing multivitamin supplementation or receiving treatment with lipid-lowering drugs.
- Patients presenting with hepatic, renal, or metabolic bone disorders, including parathyroid-related issues.
- Individuals with a documented history of hemoglobinopathies were excluded from participation in the study.

These inclusion and exclusion criteria were carefully designed to ensure the homogeneity of the study population, allowing for a focused investigation into the interplay between dyslipidemia and glycemic control specifically in adults diagnosed with Type 2 Diabetes Mellitus. The exclusion of certain comorbidities and medication regimens aims to reduce confounding factors, enhancing the study's ability to draw meaningful conclusions regarding the relationship between dyslipidemia and glycemic status in this particular patient population.

During the course of this study, overnight fasting venous blood samples were systematically collected from the enrolled patients, adhering to a standardized protocol and utilizing specialized equipment. The collected samples were strategically divided into two distinct specimens for comprehensive analysis.The first sample comprised whole blood and was designated for the measurement of Hemoglobin A1c (HbA1c). This particular glycosylatedhemoglobin parameter serves as a valuable indicator of long-term glycemic control in individuals with diabetes.Concurrently, the second specimen, consisting of plasma, was utilized to assess fasting blood glucose (FBG) levels and the lipid profile. The lipid profile encompassed crucial components such as total cholesterol, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), and triglycerides. The choice of obtaining blood samples after an overnight fasting period is standard practice in clinical research, as it provides a baseline measurement free from the influence of recent dietary intake.Importantly, the calculation of LDL-cholesterol levels was executed using the Friedewald formula. This formula is a widely accepted and established method for estimating LDL-C levels and involves the subtraction of high-density lipoprotein cholesterol and one-fifth of the triglyceride level from the total cholesterol value.The meticulous adherence to standardized protocols and the use of advanced equipment ensure the reliability and consistency of the data collected, thereby enhancing the validity of the study's findings.

RESULTS

In our investigation, a total of 140 individuals diagnosed with Type 2 diabetes were enrolled, forming the cohort under scrutiny. Among these participants, there were 82 males and 58 females, providing a gender distribution within the study population. This composition allows for a gender-stratified analysis, which may be beneficial in exploring potential variations or trends in the relationship between dyslipidemia and glycemic status within the context of Type 2 diabetes. The inclusion of both male and female participants contributes to the overall representativeness of the study and enhances the generalizability of the findings to diverse populations affected by Type 2 diabetes.

Table 1: Gender Distribution of study population

	Total	Males	Females
No. of patients	140	82	58
Percentage	100	58.5	41.4

Figure1: Gender Distribution of study population

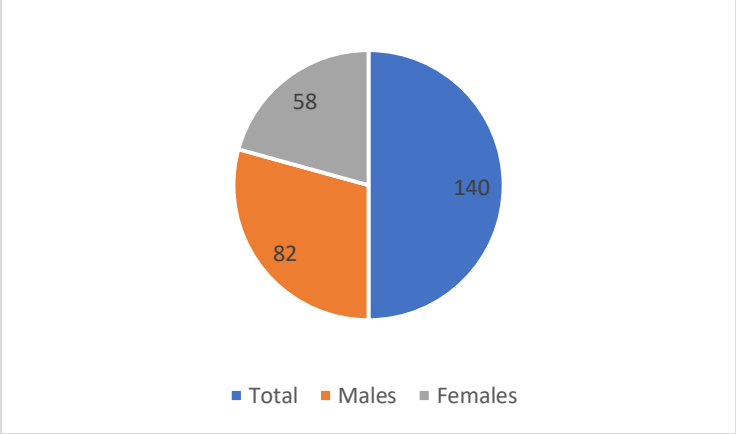

Table 2: Distribution of Glucose Triad

Parameters	Mean ± SD
FBS	170.48±36.64
PPBS	230.49±94.49
HbA1C	7.48±0.63

The mean values along with their standard deviations for various parameters are reported as follows. The fasting blood sugar (FBS) level is recorded at 170.48 with a standard deviation of 36.64. Postprandial blood sugar (PPBS) is measured at a mean of 230.49, accompanied by a standard deviation of 94.49. Hemoglobin A1C (HbA1C) is reported with a mean of 7.48 and a standard deviation of 0.63. These values provide insights into the central tendencies and variability of the respective parameters, reflecting important indicators related to blood glucose levels.

Table 3: Distribution of Lipid Profile and HbA1c

Parameters	Mean ± SD
Total cholesterol	220.53 ± 16.53
Triglycerides	210.83 ± 20.65
Mean HDL	30.63 ± 3.96
Mean LDL	140.14 ± 7.63
Mean VLDL	40.46 ± 3.69

The table presents mean values along with their standard deviations for various lipid profile parameters. The total cholesterol level is reported as 220.53 with a standard deviation of 16.53. Triglycerides are recorded at 210.83 with a standard deviation of 20.65. The mean high-density lipoprotein (HDL) cholesterol is 30.63 with a standard deviation of 3.96, while the mean low-density lipoprotein (LDL) cholesterol is 140.14 with a standard deviation of 7.63. Additionally, the mean very-low-density lipoprotein (VLDL) cholesterol is 40.46 with a standard deviation of 3.69. These values offer insights into the average levels and variability of key lipid components, providing important information for assessing cardiovascular health.

DISCUSSION

The escalating incidence of type 2 diabetes represents a formidable and growing public health challenge in India, mirroring a global trend. Over recent decades, the prevalence of this metabolic disorder has surged, solidifying its status as a leading health concern. In tandem with this rise, the intricate interplay between diabetes and lipid abnormalities has garnered increasing attention. Type 2 diabetes patients, in particular, frequently exhibit lipid irregularities, contributing significantly to the multifaceted landscape of their health complications.[9]The complex relationship between diabetes and dyslipidemia is underscored by a constellation of risk factors commonly found in individuals with type 2 diabetes. These risk factors, including dyslipidemia itself, obesity, hypertension, advanced age, sleep apnea, anemia, chronic kidney disease, and coronary heart diseases, collectively amplify the susceptibility to cardiovascular issues. It is noteworthy that hyperglycemia, a hallmark of diabetes, further heightens the risk of heart failure in individuals with type 2 diabetes, adding another layer of complexity to their health profile.In the specific context of the current study, which delved into diabetic patients grappling with dyslipidemia (n = 140), an intriguing observation emerged. The severity of dyslipidemia exhibited an upward trajectory in patients with elevated levels of glycated hemoglobin (HbA1c > 7%). This finding aligns with similar observations reported by researchers like Habiba NM et al. and corroborates trends noted in diverse regions across India.

Exploring the intricate web of associations within the lipid profile and glycosylated hemoglobin, researchers such as Nanaware M et al. have discerned significant correlations. These correlations not only validate the findings of the present study but also underscore the interconnected nature of metabolic markers in individuals with diabetes and dyslipidemia.[10]Moreover, a broader review of literature reveals consistent patterns in studies conducted by Maharjan et al., Babik et al., Juet al., and Devkar et al. These studies collectively highlight substantial correlations between glycosylated hemoglobin and various lipid parameters, including triglycerides, total cholesterol, low-density lipoprotein, and high-density lipoprotein. The convergence of evidence from diverse studies further solidifies the understanding that glycosylated hemoglobin serves as a valuable indicator of lipid profile variations in the diabetic population.Delving into the underlying mechanisms, the pathogenesis of diabetic dyslipidemia emerges as a nuanced interplay involving insulin resistance. Indeed, insulin resistance assumes a central role in shaping the aberrant lipid metabolism seen in diabetes. Specifically, the heightened release of free fatty acids from insulin-resistant fat cells emerges as a key driver of diabetic dyslipidemia, providing a mechanistic insight into the observed lipid abnormalities.[11]In summation, the current study, in the broader context of existing

literature, contributes to a deeper understanding of the intricate relationships between diabetes, dyslipidemia, and associated risk factors. As the prevalence of type 2 diabetes continues to rise globally, unraveling these complexities becomes paramount for effective intervention and management strategies, with potential implications for public health policies and clinical practices.

The heightened risk of cardiovascular disease (CVD) in individuals with type 2 diabetes mellitus (T2DM) is intricately linked to alterations in the lipid profile that often accompany this metabolic disorder. Numerous investigations have delved into the relationship between glycated hemoglobin (HbA1c) and various lipid profile parameters in T2DM patients, with some proposing HbA1c as a potential biomarker for discerning abnormal lipid profiles and identifying those at risk of CVD.[12] The results of our study align with this body of research, revealing a noteworthy positive correlation between HbA1c and triglycerides, as well as between HbA1c and total cholesterol. These findings corroborate similar observations in previous studies, underlining the crucial connection between glycemic control and dyslipidemia in individuals with T2DM.The association between HbA1c and lipid abnormalities further suggests that HbA1c may serve as a direct indicator of dyslipidemia in T2DM patients. This insight not only contributes to understanding the intricate interplay of metabolic markers but also implies that monitoring HbA1c levels could indirectly assist in assessing the risk of both micro- and macrovascular complications in individuals with T2DM. The recognized cause of dyslipidemia in T2DM patients is insulin resistance, wherein insufficient insulin secretion or function is linked to elevated triglyceride (TG) levels through various mechanisms.In our study, the correlation between HbA1c and low-density lipoprotein cholesterol (LDL-c) was identified as weak-positive and statistically insignificant, and no correlation was observed between HbA1c and high-density lipoprotein cholesterol (HDL-c). These results align with earlier studies that reported inconsistent or no correlations between HbA1c and these specific lipid parameters.[13] The complexity of these relationships underscores the multifactorial nature of lipid metabolism in T2DM, where various factors may contribute to the observed variations.Additionally, our study revealed a significant and positive association between the age of diabetic patients and total cholesterol levels, consistent with previous research that reported a positive significant association between LDL-c and age. This suggests that age may be a contributing factor to lipid profile alterations in individuals with T2DM.Furthermore, our findings indicated a significant and positive correlation between diastolic blood pressure in T2DM patients and their blood cholesterol and triglyceride levels. This association emphasizes the potential interplay between blood pressure and lipid abnormalities in the context of T2DM, highlighting the need for comprehensive cardiovascular risk assessment in diabetic patients.In conclusion, the intricate relationships between HbA1c, lipid profile parameters, age, and blood pressure underscore the complexity of cardiovascular risk in individuals with T2DM. While HbA1c emerges as a potential marker for dyslipidemia, the multifactorial nature of these associations emphasizes the importance of considering various factors in assessing cardiovascular risk in this population. These insights contribute to the ongoing efforts to refine risk stratification and develop targeted interventions for individuals with T2DM to mitigate the risk of cardiovascular complications.[14,15]

The Diabetes Control and Complications Trial (DCCT), orchestrated by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) in the United States, stands as a landmark investigation that has significantly shaped our comprehension of glycemic control in the context of diabetes. A cornerstone finding of the DCCT was the unequivocal designation of glycated hemoglobin (HbA1c) as the gold standard for the assessment and monitoring of glycemic control in individuals grappling with diabetes. The trial's revelations underscored the critical importance of maintaining HbA1c levels at or below 7.0%, establishing it as a pivotal clinical target to mitigate the risk of cardiovascular complications—a pressing concern in the management of diabetes.Your study, building upon the foundations laid by the DCCT, further substantiates the intricate relationship between HbA1c and key lipid profile parameters in diabetic patients.[16] Specifically, the positive correlation observed between HbA1c and total cholesterol, low-density lipoprotein (LDL) cholesterol, and triglycerides reinforces the complex interplay between glycemic control and lipid metabolism. This correlation underscores that achieving optimal glycemic control not only contributes to diabetes management but also plays a vital role in modulating lipid profiles, thereby impacting cardiovascular risk.However, it is crucial to acknowledge the inherent limitations of the present study. The small sample size, while providing valuable insights, may limit the generalizability of the findings. Studies with larger cohorts often offer increased statistical power and enhance the reliability of results. Additionally, the study did not delve into critical factors that can significantly influence both glycemic control and lipid profiles. The absence of information on patients' dietary habits, lifestyle patterns, duration since the diagnosis of diabetes, and the extent of regular physical activity introduces variables that could contribute to the observed variability in glycemic and lipid parameters.[17,18] Recognizing these factors is pivotal for a comprehensive understanding of the intricate relationship between glycemic control and cardiovascular risk in diabetes.Despite these

limitations, the present study adds valuable pieces to the intricate puzzle of diabetes management. It underscores the need for further research endeavors that encompass larger and more diverse populations, accounting for a spectrum of lifestyle and clinical variables. Such comprehensive investigations will contribute to refining our understanding of the nuanced connections between glycemic control, lipid profiles, and cardiovascular risk in individuals with diabetes. These insights, coupled with the foundational knowledge provided by groundbreaking trials like the DCCT, propel ongoing efforts to optimize diabetes management strategies and enhance overall patient outcomes.

CONCLUSIONS

Your study has made a noteworthy contribution by establishing a direct and significant correlation between glycated hemoglobin (HbA1c) and various components of the lipid profile, including total cholesterol, triglycerides, very-low-density lipoprotein (VLDL), and low-density lipoprotein (LDL). This finding adds a valuable dimension to our understanding of the relationships between glycemic control and lipid metabolism in individuals with diabetes.The significant positive correlation observed in your study implies that HbA1c may not only serve as a reliable marker for glycemic control but also as a predictor for dyslipidemia. This dual role underscores the potential utility of HbA1c in assessing not only blood glucose management but also the risk of lipid abnormalities in individuals with diabetes. The identification of HbA1c as a predictor for dyslipidemia could have clinical implications for healthcare professionals, providing an additional tool for risk assessment and preventive measures to curb complications associated with dyslipidemia.This expanded role of HbA1c aligns with the growing recognition of its multifaceted utility beyond glycemic control alone. Integrating HbA1c as an indicator of both glycemic status and potential lipid-related risks could streamline monitoring strategies and contribute to a more comprehensive approach in managing individuals with diabetes. It also underscores the interconnected nature of metabolic parameters and the need for a holistic assessment to address the broader spectrum of diabetes-related complications.In summary, your study's findings highlight the dual significance of HbA1c, not only as a gauge for glycemic control but also as a potential predictor for dyslipidemia. This expanded understanding has implications for clinical practice, emphasizing the importance of comprehensive assessments and preventive measures to mitigate the risk of complications associated with both elevated blood glucose and lipid levels in individuals with diabetes.

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