Diabetes, Metabolic Syndrome and Obesity

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ORIGINAL RESEARCH

Association Between Glycated Hemoglobin and the Lipid Profile at the Central Yunnan Plateau: A Retrospective Study

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Introduction: Dyslipidemia commonly complicates type 2 diabetes mellitus, yet the relationship between glycosylated hemoglobin and blood lipid levels remains uncertain.

Methods: This retrospective cross-sectional study included 27,158 participants from the People's Hospital of Yuxi. Statistical comparisons for continuous variables utilized analysis of variance (ANOVA), while chi-square analysis was employed for categorical variables. Boxplots assessed the concentration, dispersion, and deviation of total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL-C), and high-density lipoprotein (HDL-C) distribution. A linear regression analysis examined the association between HbA1c and lipid profile, complemented by a fitting curve to visualize trends.

Results: Participants who developed diabetes exhibited higher age and elevated Body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), TC, TG, LDL-C, and FPG levels compared to those without diabetes ($p < 0.001$). Linear regression analysis demonstrated significant associations between HbA1c values and TC, TG, LDL-C, and HDL-C ($p < 0.001$). The plotted curve indicated that as TC, TG, and LDL levels increased, HbA1c levels rose, while HDL levels decreased.

Conclusion: HbA1c was positively correlated with TC, TG, LDL-C, and negatively correlated with HDL-C in the population in the central Yunnan Plateau.

Keywords: dyslipidemia, HbA1c, lipid profile

Introduction

The prevalence of type 2 diabetes in China is escalating rapidly, posing a significant concern. China bears the highest burden of Type 2 Diabetes Mellitus (T2DM) globally, and this burden is expected to escalate, significantly straining disease control and prevention efforts.[1] A representative cross-sectional study conducted in mainland China revealed an estimated overall prevalence of diabetes was 12.4% and of prediabetes was 38.1%. Regional disparities in type 2 diabetes prevalence across China stem from diverse factors, including dietary habits, lifestyles, environmental influences, and genetic predisposition.[2]

Key causal factors of type 2 diabetes mellitus include aging, obesity, and dietary and lifestyle habits such as excessive consumption of simple sugars, high-calorie, and high-fat foods, along with inadequate exercise and sleep patterns.[3] The prevalence of high-fat, high-sugar, and high-calorie dietary habits in the central Yunnan Plateau heightens the risk of developing T2DM. When the blood sugar concentration is too high, the body cannot fully decompose or utilize these sugars in time, which leads to too much sugar being converted into blood lipids, which in turn leads to dyslipidemia. Dyslipidemia interacts with T2DM, impacting blood lipid metabolism and exacerbating the diabetic condition. Monitoring glycated hemoglobin (HbA1c) levels is a standard practice among diabetic patients to assess blood glucose control.[4] Dyslipidemia is a disorder of lipid metabolism characterized by abnormal serum lipoprotein or lipid levels,

Received: 19 May 2024
Accepted: 2 August 2024
Published: 9 August 2024

predominantly involving total cholesterol (TC), triglycerides (TG), low-density lipoprotein (LDL-C), and high-density lipoprotein (HDL-C).[5]

Current research indicates a correlation between HbA1c and blood lipid levels, although this relationship remains unclear, particularly in the central Yunnan Plateau. Investigating the correlation between glycated hemoglobin and blood lipid levels enables a more accurate assessment of the risk of dyslipidemia based on HbA1c levels, aiding in the identification of dyslipidemia indicators in diabetic patients. Thus, we initially examined the association between HbA1c levels and blood lipids in individuals residing in the central Yunnan Plateau.

Methods

Study Design and Participants

This retrospective study was conducted at the People's Hospital of Yuxi, Yunnan, China, involving 27,158 participants who underwent HbA1c testing. After excluding individuals aged < 18 years and those lacking follow-up data, the study included a total of 26,857 participants (Figure 1). This study received approval from the ethics committee of the Sixth Affiliated Hospital of Kunming Medical University (Approval No. 2024kmykdx6f003), adhering to the principles outlined in the Declaration of Helsinki. This retrospective analysis did not involve the collection of personal information from patients. Given that the exemption of informed consent would not adversely affect the rights or welfare of the subjects, we obtained approval for this exemption from the Ethics Committee.

Anthropometric and Biochemical Measurements

The data analyzed in this study were obtained from annual medical examinations conducted on healthy Chinese employees between 2011 and 2016. The dataset included demographic information, biomarkers, and follow-up data. Participant height and weight were measured with individuals wearing light clothing and no shoes, and recorded. Blood pressure measurements were taken after a 5-minute rest in a seated position using a standard sphygmomanometer. Body mass index (BMI) was calculated by dividing weight in kilograms by the square of height in meters. Additionally, comprehensive medical histories, including details of diseases and surgeries, were compiled. Laboratory tests, including blood counts and comprehensive metabolic panels, were conducted on fresh samples using a Roche automatic biochemical analyzer (Cobas 8000) and its associated reagents at the People's Hospital of Yuxi.

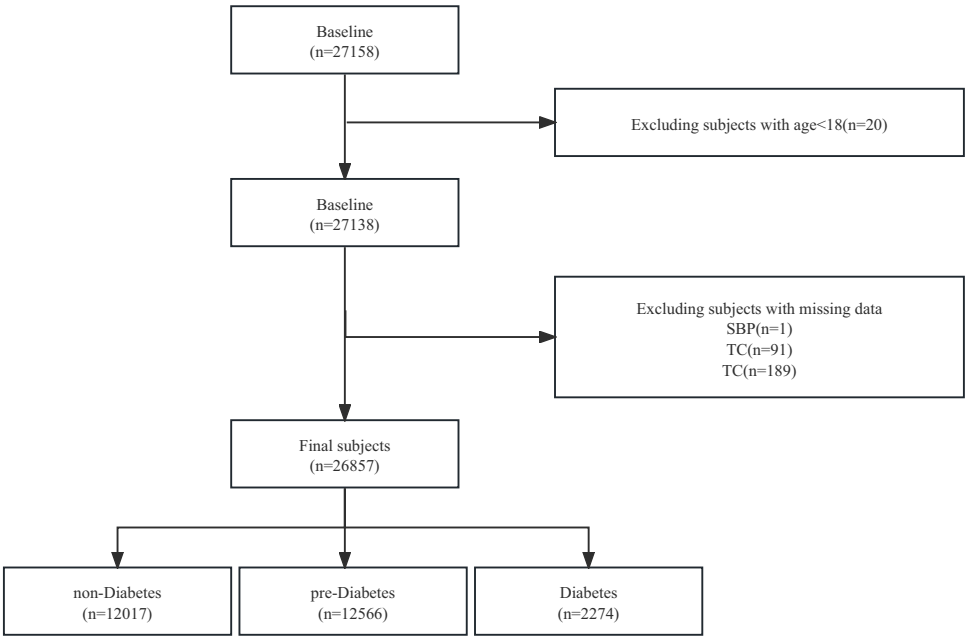

Figure 1 Flow chart of the study participants.

Definitions of Diabetes and Pre-Diabetes

According to The American Diabetes Association (ADA) 2024 diagnostic criteria, Diabetes was diagnosed based on fasting blood glucose levels ≥ 7.0 mmol/L, HbA1c levels ≥ 6.5%, or a documented history of diabetes diagnosis.[6] Pre-diabetes was characterized by fasting blood glucose levels between ≥ 5.6 mmol/L and < 7.0 mmol/L, or HbA1c levels between ≥ 5.7% and < 6.5%.[7]

Statistical Analysis

Normality of data was assessed using the Shapiro–Wilk test. Continuous variables were reported as mean ± standard deviation (SD), while categorical variables were expressed as numbers and percentages. Analysis of variance (ANOVA) was employed for statistical comparisons of continuous variables, and chi-square analysis was utilized for categorical variables. Boxplots were used to compare the concentration trend, dispersion degree, and deviation degree of TC, TG, LDL-C, and HDL-C distribution. A linear regression test was conducted to assess the association between HbA1c and the lipid profile. Additionally, a fitting curve was plotted to visualize the relationship between HbA1c and the lipid profile and observe the overall trend of the data. $P < 0.05$ was considered significant. All the analyses were performed with the statistical software packages R (http://www.R-project.org, The R Foundation).

Results

Baseline Characteristics

The cohort study included 26,857 participants, with a male-to-female ratio of 61.6% to 38.4% and a mean age of 45.7 ± 13.0 years. Among them, 12,017 were non-diabetic, 12,566 were pre-diabetic, and 2274 had diabetes. Individuals who developed incident diabetes showed higher age and elevated levels of BMI, systolic blood pressure (SBP), diastolic blood pressure (DBP), TC, TG, LDL-C, and FPG compared to those without diabetes ($P < 0.001$) (Table 1).

Analysis of the lipid profile boxplot revealed that the median values of TC, TG, LDL-C, and HDL-C were clustered around the center line, indicating a concentrated distribution, but numerous outliers were observed (Figure 2).

Association Between HbA1c and the Lipid Profile

The linear regression analysis revealed significant associations between HbA1c values and TC, TG, LDL-C, and HDL-C ($P < 0.001$). TC, TG and LDL-C increased with the increase of HbA1c, while HDL-C showed a downward trend (Table 2). Plotting the fitted curve illustrated that HbA1c levels increased with rising TC, TG, and LDL, while decreasing with increasing HDL (Figure 3).

Table 1 Comparison of Baseline Characteristics

Variables	Total (n = 26857)	Non-Diabetes (n = 12017)	Pre-Diabetes (n = 12566)	Diabetes (n = 2274)	P
Gender, n (%)					< 0.001
Male	16545 (61.6)	7065 (58.8)	7837 (62.4)	1643 (72.3)	
Female	10312 (38.4)	4952 (41.2)	4729 (37.6)	631 (27.7)	
Age (years)	45.7 ± 13.0	42.3 ± 11.9	47.1 ± 12.9	55.3 ± 12.7	< 0.001
BMI (kg/m^2)	23.8 ± 3.4	23.2 ± 3.3	24.1 ± 3.4	25.8 ± 3.4	< 0.001
SBP (mmHg)	117.4 ± 16.7	114.9 ± 15.7	118.0 ± 16.7	127.4 ± 17.3	< 0.001
DBP (mmHg)	78.0 ± 10.5	77.0 ± 10.5	78.3 ± 10.4	81.7 ± 10.6	< 0.001
TC (mmol/L)	5.0 ± 1.0	4.9 ± 1.0	5.1 ± 1.0	5.3 ± 1.2	< 0.001
TG (mmol/L)	2.1 ± 1.8	1.9 ± 1.8	2.1 ± 1.7	2.7 ± 2.5	< 0.001
HDL-C (mmol/L)	1.4 ± 0.4	1.4 ± 0.4	1.4 ± 0.4	1.3 ± 0.3	< 0.001
LDL-C (mmol/L)	2.7 ± 0.8	2.6 ± 0.8	2.8 ± 0.8	2.8 ± 0.9	< 0.001
FPG (mmol/L)	5.3 ± 1.3	5.0 ± 0.5	5.2 ± 0.6	8.0 ± 3.0	< 0.001

Abbreviations: BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, Total cholesterol; TG, triglycerides; HDL-C, high density lipoprotein; LDL-C, low-density lipoprotein; FPG, fasting plasma glucose.

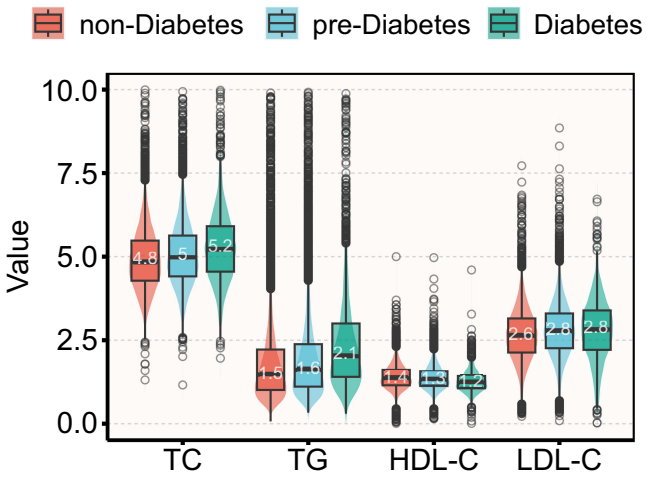

Figure 2 The boxplot of the lipid profile.

Discussion

Our study revealed a significant correlation between HbA1c levels and the lipid profile in the Central Yunnan Plateau. We observed positive correlations of HbA1c with TC, TG, and LDL-C, while noting a negative correlation with HDL-C. Elevated HbA1c levels often coincide with abnormal blood lipid levels, potentially leading to disturbed lipid metabolism and increased risk of atherosclerosis and cardiovascular disease.[8] Therefore, for patients with T2DM, it is imperative to monitor not only blood glucose but also lipid levels closely to maintain comprehensive metabolic stability. Recognizing this relationship underscores the importance of considering changes in both HbA1c and lipid profiles in the prevention and management of diabetes and associated complications, guiding the development of targeted control measures and treatment strategies.

While our study has generated significant findings, there remains a paucity of research on the association between HbA1c and the lipid profile, and consensus has not yet been reached. For example, a study[9] in Afghani T2DM patients suggests a significant positive association between TC, TG, and LDL-C, but HDL-C showed a statistically nonsignificant negative correlation. In contrast, another study[10] found a positive correlation only between HbA1c and TC. Similarly, research[11] in South Africa demonstrated a significant positive correlation between HbA1c and TG, while another study[12] reported no correlation between HbA1c and TG.

The causal relationship between HbA1c and blood lipids remains unclear, hindering full comprehension of the underlying pathological mechanism concerning the interaction between T2DM and dyslipidemia. In type 2 diabetes, patients typically experience insulin resistance and insufficient insulin secretion.[13] Insulin plays a crucial role in promoting glucose absorption and utilization, inhibiting fat breakdown, and fostering fat synthesis.[14] Insulin resistance and insufficiency diminish the adipose tissue's responsiveness to insulin, resulting in increased lipolysis and elevated blood lipid levels.[15] Concurrently, dyslipidemia can incite inflammation, particularly within adipose tissue, disrupting the

Table 2 Association of Glycated Hemoglobin with Lipid Profile

Variables	β (95% CI)	P
TC (mmol/L)	0.12 (0.11,0.13)	< 0.001
TG (mmol/L)	0.06 (0.05,0.07)	< 0.001
HDL-C (mmol/L)	−0.22 (−0.25,-0.19)	< 0.001
LDL-C (mmol/L)	0.07 (0.06,0.08)	< 0.001

Abbreviations: TC, Total cholesterol; TG, triglycerides; HDL-C, high density lipoprotein; LDL-C, low-density lipoprotein.

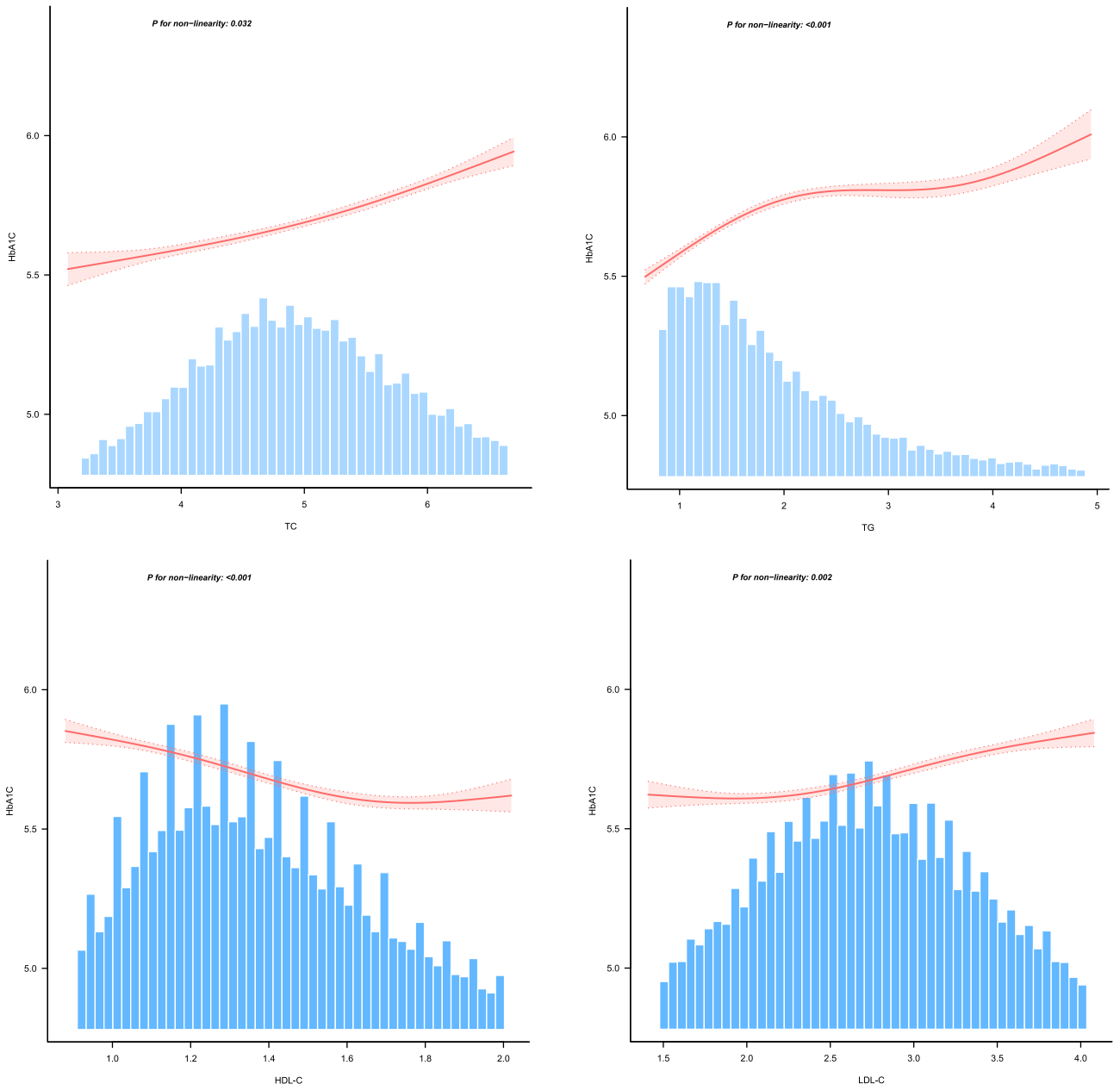

Figure 3 Fitted curves between the lipid profile and HbA1c.

insulin signaling pathway and fostering insulin resistance and aberrant glucose metabolism.[16] Dyslipidemia induces hormonal imbalance in adipose tissue, such as adiponectin and adrenaline,[17] and generates metabolites like fatty acids and triglycerides,[18] which negatively impact insulin secretion and function, further affecting glucose metabolism. Hyperglycemia escalates the production of glycation end products, triggering non-enzymatic glycation of proteins and excessive generation of glucose oxidation products,[19] thus damaging the vascular wall and promoting atherosclerosis, consequently impacting lipid metabolism.[20] In summary, a close interplay exists between T2DM and dyslipidemia. Dyslipidemia influences the insulin signaling pathway, insulin secretion, and glucose metabolism, elevating the risk of T2DM. Conversely, T2DM can also disturb blood lipid metabolism, inducing dyslipidemia. Therefore, diligent monitoring of both blood sugar and blood lipid levels is crucial for diabetic patients. Comprehensive management and control of both blood sugar and dyslipidemia not only help prevent complications but also enhance patients' quality of life.

However, most previous studies have focused on individuals with T2DM, whereas our research includes individuals undergoing normal physical examinations. This represents a significant advantage of our study. As T2DM is a chronic condition that develops gradually over time, changes in TC, TG, and LDL-C tend to correspond with increases in glycosylated hemoglobin, while HDL-C levels typically decrease. In our investigation, we introduced the concept of pre-diabetes. Interestingly, we observed that the alterations in these indices during the transition from normoglycemia to pre-diabetes are much more pronounced than those from pre-diabetes to diabetes. This underscores the importance of closely monitoring HbA1c and blood lipid levels during the pre-diabetic stage. Timely detection and intervention for hyperglycemia and dyslipidemia at this early phase may offer opportunities for diabetes prevention. Understanding the relationship between glycosylated hemoglobin and blood lipids is crucial for early identification of diabetes and its associated cardiovascular risks. This knowledge can also inform personalized treatment programs for diabetic patients, leading to improved blood sugar control and blood lipid management. This constitutes another significant strength of our study.

Nonetheless, our study possesses several limitations. Firstly, it remains an observational study, distinct from a prospective cohort study. Moreover, all participants were recruited from a single region, predominantly sharing similar professional backgrounds. Hence, the generalizability of our findings to a broader, multi-ethnic population in China is uncertain. This limitation raises questions about establishing a causal relationship between type 2 diabetes and dyslipidemia. Secondly, both blood pressure and glycated hemoglobin are assessed based on single measurements, and the presence of numerous outliers in the blood lipid boxplot suggests further data screening is warranted to ensure reliability. Lastly, the absence of logistic regression analysis prevents the derivation of the risk ratio, which remains a direction for future research.

Conclusion

In the population of the central Yunnan Plateau, HbA1c exhibited positive correlations with TC, TG, and LDL-C, while showing a negative correlation with HDL-C. Thus, individuals in this region, particularly those with T2DM, should prioritize monitoring and adjusting their blood lipid levels alongside their blood glucose levels. Through our research on the relationship between glycosylated hemoglobin and blood lipids in the plateau of central Yunnan, we can also provide more personalized treatment programs for diabetic patients in this area, and reduce the incidence of diabetes and its complications in this area through early intervention.

Disclosure

The authors report no conflicts of interest in this work.

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