
The status of apoproteins b100 and a1 in type 2 diabetes in Erbil city

Received: 12/06/2025

Accepted: 31/07/2025

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Abstract

Background and objective: Type 2 diabetes mellitus (T2DM) originates from the body's incapacity to react to insulin. Hypoglycemic medications and lifestyle modifications can help control it. The aim of this study was to compare the serum Apolipoprotein B100/Apolipoprotein A1 Ratio (ApoB100/ApoA1) between T2DM patients and controls.

Methods: This case-control study was conducted in the Galiawa Teaching Center for Diabetes and Endocrinology in Erbil City from October to December 2024. The blood samples were taken from 45 patients with T2DM and 45 healthy control subjects. Two types of tubes were used to collect blood samples: one for serum separation (gel tube) and another for plasma (tri-potassium ethylene diamine tetra acetic acid) (K3EDTA) tube. The samples have been left at room temperature for fifteen minutes and then put in a centrifuge for ten minutes at 4000 rpm to get the serum of the blood. The separated serum was subjected to laboratory analysis to analyze the biochemical tests (ApoA1, ApoB100, fasting serum glucose, hemoglobin A1C (HbA1C), and lipid profile).

Results: Based on the research findings, diabetic patients had substantially higher levels of serum glucose, HbA1C, lipid profiles, and ApoB100/ApoA1 ratio than the healthy individuals. The case group had a mean serum ratio ApoB100/ApoA1 of (0.84 ± 0.06) , while the control group had a ratio of (0.66 ± 0.02) g/L ($P = 0.037$). While HbA1C and serum glucose with all lipid profile results were significantly higher in T2DM than the control group, high-density lipoprotein (HDL) was lower in T2DM.

Conclusion: The study found that patients with T2DM had a high ApoB100/ApoA1 ratio. Compared to the control group.

Keywords: Type 2 Diabetes Mellitus, Apolipoprotein A1, Apolipoprotein B100, Lipid Profile, ApoB100/ApoA1 Ratio.

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Introduction

Diabetes mellitus is a condition characterized by insufficient or inadequate insulin activity. There are two basic forms of diabetes mellitus: Type 1 diabetes mellitus (T1DM) and T2DM. The autoimmune disease that leads to T1DM happens when immune cells attack the pancreatic β cells that generate insulin (1).

Systemic metabolic dysfunctions cause T2DM to develop later in life. Individuals with a genetic predisposition to T2DM are more likely to have bad eating habits and sedentary lifestyles. Diabetes mellitus isn't only about elevated blood sugar levels. Diabetic retinopathy is one of the many complications that diabetic patients face; other complications may arise later in the course of the disease or may be evident at the time of diagnosis. Among these effects are malfunctions in several of the body's essential organs, especially the kidney, heart, retina, and nervous system. Pulmonary fibrosis, liver fibrosis, and cognitive decline are all developing as new conditions linked to diabetes mellitus (1).

T2DM is primarily prevalent in adults, due to obesity, physical inactivity, and bad eating habits. The combination of lifestyle, high blood uric acid levels, smoking, depression, cardiovascular disease, dyslipidemia, hypertension, age, ethnicity, and family history of diabetes mellitus may increase the risk

of T2DM, these are samples of psychosocial and demographic peril factors (2).

Since diabetes mellitus and dyslipidemia are known cardiovascular risk factors with therapeutic advantages, they are significant in clinical medicine. Dyslipidemia is common in persons with T2DM and is believed to play a part in moderating the disease's related cardiovascular risk. As a result, conversations concerning the connection between glucose and lipid metabolism have mostly focused on diabetic dyslipidemia. But the connection between lipid metabolism and glucose is far more intricate. It is commonly known that people with diabetes mellitus often exhibit dyslipidemia, which is defined by high triglycerides, low HDL-C (high density lipoprotein cholesterol), and a preponderance of small-dense LD (3).

Lipids are transported throughout the body by protein-lipid complexes called lipoproteins. Lipoproteins are the main factors that determine the plasma's lipid fractions. The protein component of lipoproteins, apolipoproteins, are necessary for lipoprotein assembly, solubilization of lipid fractions into lipoproteins, receptor interaction, and the activation of enzymes involved in lipoprotein metabolism and lipid transport (4). Numerous illnesses, such as metabolic syndrome, atherosclerosis, autoimmune diseases, cancer, T2DM,

and neurological issues, have been connected to anomalies in apolipoprotein glycosylation. Congenital glycosylation abnormalities can cause hyperlipidemia, development delays, mobility impairments, hepatic steatosis, and hepatosplenomegaly by disrupting the glycosylation of apolipoproteins. Overall, these investigations indicate that alterations in apolipoprotein glycosylation cause illness consequences (5).

Chylomicron remnants, an essential HDL protein component with immunomodulatory and anti-inflammatory properties, are rich in ApoA1. ApoA1, in particular, is associated with lipoprotein (a) particles and the protective effect of HDL (4).

The main structural proteins present in lipoprotein particles are apolipoproteins. The primary apolipoprotein for HDL cholesterol is ApoA1, whereas the fundamental apolipoprotein for LDL cholesterol is ApoB. Consequently, the ApoB100/ApoA1 ratio could suggest that these atherogenic and antiatherogenic lipid particles' cholesterol equilibrium. A high ApoB to ApoA1 ratio has been shown in several previous studies to be a more powerful predictor of metabolic disorders, such as T2DM (6). However, also make the assumption that there is a linear relationship between T2DM risk and the ApoB to ApoA1 ratio, which has

hardly ever been examined in published research (4). The goal of the current investigation was to assess the connection between T2DM and the ApoB to ApoA1 ratio (7).

Apolipoproteins are essential for the metabolism of blood glucose and lipoproteins (4). Two main types of apolipoproteins that have been thoroughly investigated are ApoA1 and ApoB. The main lipoprotein associated with HDL-C is ApoA1. ApoB is just one of the molecules found in lipoproteins with low, intermediate, and extremely low densities. ApoA1 and ApoB increased insulin levels, which in turn improved fasting blood glucose (FBG) levels, according to study conducted in vitro and on animals (8). Several studies have examined the relationship between FBG levels and ApoA1, ApoB, and the ApoB100/A1 ratio; they have shown that ApoB and the ApoB100/A1 ratio are positively correlated (4), while ApoA1 is inversely correlated (9, 10). Notably, the study found a reversal association between ApoA1 and T2D presence (11), as well as a positive correlation between ApoB and the ApoB100/A1 ratio and T2D presence (12). Based on these findings, the pathogenic mechanisms behind FBG and T2D may depend critically on ApoA1, ApoB, and the ApoB100/A1 ratio (4). The aim of this study is to assess the serum levels of ApoA1, ApoB100 and ApoB100/ApoA1 ratio in individuals

with T2DM to compare with control group.

Methods

From October through December 2024, samples of patients and controls were collected at the Galiawa Teaching Center for Diabetes and Endocrinology in Erbil City as part of a case-control study. Ninety individuals participated in the study (45 cases and 45 controls). Each group consisted of 22 men and 23 women, ages 33 to 76. An expert doctor (endocrinologist) has already determined that the case participants have T2DM. The research made use of a specially designed questionnaire. The questionnaire's first section asked for demographic data, such as age, gender, marital status, occupation, and educational attainment. There were height (m) assessment questions in the second section. Additionally, body mass index (BMI) is calculated as follows: $BMI = kg/m^2 = Mass\ kg / (Height(m))^2$, to compare the weight between two groups. The last portion asked questions about diet, exercise, and smoking, among other lifestyle-related topics. T2DM duration, family history, monitoring, and control were all covered in the fourth portion of the questionnaire. In this study included T2DM while excluded T1DM.

Ethical considerations

The Hawler Medical University- College of Health Science ethics committee approved the experimental design.

The patients gave informed verbal permissions.

Specimen Collection

Standard phlebotomy techniques were used to obtain blood samples. A disposable needle was used to draw five milliliters of blood, which was then divided between two tubes: an EDTA tube for HbA1C assessment as well as a gel tube for biochemical investigation (lipid profile, glucose, ApoA1, ApoB100). To extract the serum, the gel tube was centrifuged for 10 minutes at 4000 rpm following a 10-minute incubation period at room temperature. After that, the serum was placed in Eppendorf tubes and stored at -20°C. The biochemical parameters were evaluated using the Cobas C 501.

Statistical Analysis

Data entry and analysis were conducted using SPSS version 26, a statistical software for social science. Descriptive statistics were employed in the first approach to ascertain frequencies and percentages, whereas the unpaired t-test was employed in the second technique (analytic statistics) to compare two means. A value of $P \leq 0.05$ is considered statistically significant.

Results

Type 2 Diabetes mellitus Patients' and Healthy Controls' Demographics

Ninety people of both sexes participated in the study. Those with T2DM were the case group, while the

control group consisted of healthy individuals. Each group had 45 participants, including 23 females and 22 males, respectively. Approximately 26 diabetes mellitus patients had a family history of T2DM, while control group only 4 of them have family history with T2D. The findings of this investigation indicated that the serum mean levels of serum Glucose in T2D patient was (196.91±12.32) mg/dL, while in the control group was (95.10±0.97) mg/dL with P value was (0.001), The findings of this investigation indicated that the plasma mean level of HbA1C in T2D patient was (8.92±0.26), while in the control group was (5.45±0.05) with P value was (0.0001), The results of the study showed that, compared to the control group, patients with diabetes mellitus had significantly higher mean levels of fasting blood glucose and HbA1C (Table 1).

Comparison of levels serum ApoA1 and ApoB100 and the ratio of ApoB100/ApoA1 in the control and case groups

The findings of this investigation indicated that the mean level of serum APOA1 in T2D patient was (1.35±0.04) g/L, while in the control group was (1.32±0.03) g/L with P value was (0.424). The mean level of serum APOB100 in T2D was (1.09±0.05) g/L, while in the control group was (0.86±0.02) g/L with P-value was (0.005) and the ratio of ApoB100/ApoA1 in T2D patients was (0.84±0.06), while in the control group was (0.66±0.02) with P-value was (0.037). These results indicate that the mean concentration value of (APOA1, APOB100, and APOB100/APOA1) ratio in the diabetic patient were non significantly higher than that of the control, as shown in (Table 2).

Table 1. Comparison of fasting serum glucose level and plasma HbA1C in diabetes mellitus patients with those of the control group

Parameters	Control	Case	F-Test	P-Value
Glucose (mg/dL)	95.10±0.97	196.91±12.32	78.71	0.001
HbA1C (%)	5.45±0.05	8.92±0.26	60.68	0.001

Note: F-Test is statistical test to compare between two groups.

Table 2. The study compared the serum ApoA1 and ApoB100 also the ratio of ApoB100/ApoA1 levels of diabetes mellitus patients to those of the control group

Parameters	Control	Case	F-Test	P-Value
ApoA1 (g/L)	1.32±0.03	1.35±0.04	0.645	0.424
ApoB100 (g/L)	0.86±0.02	1.09±0.05	8.175	0.005
ApoB100/ApoA1	0.66±0.02	0.84±0.06	4.471	0.037

Differentiation of levels serum lipid profile in the control and case groups

Referring to the study's findings, the average serum levels of cholesterol (Chol) in people with T2DM were (195.02 ± 7.11) mg/dL, while in the control group were (160.10 ± 4.32) mg/dL, the P-value was (0.003). The serum means level of serum Triglyceride (TG) in T2D was (204.15 ± 24.07) mg/dL, while in the control group was (90.90 ± 4.44) mg/dL, the P-value was (0.001). The mean level of serum High Density Lipoprotein (HDL) in T2D was (44.31 ± 1.82) mg/dL, while in the control group was (49.47 ± 1.49) mg/dL, the P-value was (0.84). The mean level of serum Low Density Lipoprotein (LDL) in T2D was (114.41 ± 6.37) mg/dL, while in the control group was (98.48 ± 3.75) mg/dL, the P-value was (0.005). The mean level of serum Very Low-Density Lipoprotein (VLDL) in T2D was

(40.83 ± 4.81) mg/dL, while in the control group was (18.18 ± 0.89) mg/dL, the P-value was (0.001). The result of this study showed that all lipid profile parameters in T2D (CHOL, TG, LDL, VLDL) - except HDL – are significantly higher than controls. HDL in T2D patients non significantly higher than controls, all found in (Table 3).

Comparison of serum LDL/HDL ratio and atherogenic index of plasma (AIP) in the control and case groups

Results showed that serum mean levels of LDL/HDL ratio were 2.83 ± 0.27 in T2D and 2.04 ± 0.08 in the control group, with a P value of 0.005. Similarly, serum mean levels of AIP were 0.59 ± 0.05 in T2D and 0.25 ± 0.03 in the control group, with a P value of 0.001. The findings of these studies demonstrated that the AIP and LDL/HDL ratio were significantly greater in patients than in controls, as appears in (Table 4).

Table 3. Displays each person's lipid profile (mg/dl) in the T2 DM and control groups

Parameters	Control	Case	F-Test	P-Value
Chol (mg/dL)	160.10 ± 4.32	195.02 ± 7.11	9.468	0.003
TG (mg/dL)	90.90 ± 4.44	204.15 ± 24.07	16.258	0.001
HDL (mg/dL)	49.47 ± 1.49	44.31 ± 1.82	0.042	0.839
LDL (mg/dL)	98.48 ± 3.75	114.41 ± 6.37	8.236	0.005
VLDL (mg/dL)	18.18 ± 0.89	40.83 ± 4.81	16.258	0.001

Table 4. Comparison of fasting serum LDL/HDL ratio and AIP in diabetes mellitus patients with those of the control group

Parameters	Control	Case	F-Test	P-Value
LDL/HDL Ratio	2.04 ± 0.08	2.83 ± 0.27	8.237	0.005
Atherogenic Index of plasm (AIP)	0.25 ± 0.03	0.59 ± 0.05	14.476	0.001

Discussion

Type 2 Diabetes Mellitus (T2DM) is a complex metabolic illness. The study conducted by (Ahmed S. and Ali R. 2023) indicates that uncontrolled T2DM is the principal cause of morbidity and mortality due to its consequences (13).

In our study the results show the ratio of ApoB100/ApoA1 were significantly higher in T2DM comparing to control group. Our study found a significant relationship between the ApoB100/ApoA1 ratio and the prevalence of T2DM, which is consistent with another research (7).

The association between T2D prevalence and blood levels of ApoA1 and ApoB, as well as the ApoB100/ApoA1 ratio, and FBG level has been assessed in the community. Cross-sectional investigation Serum ApoA1 levels were linked to a lower frequency of T2D, whereas ApoB levels and a higher prevalence were linked to the ApoB100/A1 ratio (14). In accordance with these results, we found no correlation between ApoA1 and FBG while positive relation between ApoB and the ApoB100/ApoA1 ratio. Additionally, ApoB and the ApoB100/ApoA1ratio achieved better results than ApoA1 in terms of predicting the happening of T2D. Our findings showed that ApoA1 and HDL-C had an inverse relationship with the T2D, Numerous studies demonstrated that relation between FBG levels to

serum ApoB and the ApoB100/ApoA1 ratio in T2DM patients (12, 14, 15). In a study of kidney transplant recipients, serum ApoB and the ApoB100/ApoA1 ratio were correlated of developing diabetes mellitus after the donation (12). ApoB concentration was found to be a more accurate indicator of T2DM than LDL-C levels (4).

The Apo B100/Apo A1 ratio revealed a significantly significant difference between healthy controls, controlled diabetics, and uncontrolled diabetics. There were notable favorable connections between the Apo B100/A1 ratio and both HbA1C and one another. As indicated by the HbA1C results, the Apo B100/Apo A1 ratio has a highly substantial positive correlation with the patients' glucose tolerance. The lower levels of these indicators seen in controlled diabetics compared to uncontrolled diabetics indicate that the levels of the Apo B100/Apo A1 ratio can be regulated if appropriate glycemic management is maintained (16).

ApoA1 has also been identified as an anti-inflammatory lipid protein in CVD. The relationship between APOB/ApoA1 and metabolic syndrome has been the subject of earlier research. According to a number of researches, APOB/ApoA1 was substantially linked to increased risks of insulin resistance and metabolic syndrome (17).

Conclusion

The results of this study concluded that higher ratio of ApoB100/ApoA1 in subjects with T2D mellitus as compared with group healthy subjects and useful as predictor for diabetic complications caused by increased LDL, ApoB100, Apo B100/Apo A ratio and decreased HDL with elevated atherogenic index (AIP), all are biomarkers of atherosclerosis.

Recommendations

The ratio APO A100/APO A1 is significantly increased in patients with T2DM and strongly correlated with both dyslipidemia and HbA1C. This ratio can serve as a sensitive marker for cardiovascular risk assessment and may be useful in routine clinical evaluation of T2DM patients.

Competing interest

The authors declare that they have no competing interests.

References

1. Demir S, Nawroth PP, Herzig S, Ekim Ustunel B. Emerging Targets in Type 2 Diabetes and Diabetic Complications. *Adv Sci (Weinh)*. 2021;8(18):e2100275. <https://doi.org/10.1002/advs.202100275>
2. Ismail L, Materwala H, Al Kaabi J. Association of risk factors with type 2 diabetes: A systematic review. *Comput Struct Biotechnol J*. 2021;19:1759-85. <https://doi.org/10.1016/j.csbj.2021.03.003>
3. Parhofer KG. Interaction between Glucose and Lipid Metabolism: More than Diabetic Dyslipidemia. *Diabetes Metab J*. 2015;39(5):353-62. <https://doi.org/10.4093/dmj.2015.39.5.353>
4. Gao L, Zhang Y, Wang X, Dong H. Association of apolipoproteins A1 and B with type 2 diabetes and fasting blood glucose: a cross-sectional study. *BMC Endocr Disord*. 2021;21(1):59. <https://doi.org/10.1186/s12902-021-00726-5>
5. Subramanian SP, Gundry RL. The known unknowns of apolipoprotein glycosylation in health and disease. *iScience*. 2022;25(9):105031. <https://doi.org/10.1016/j.isci.2022.105031>
6. Janghorbani M, Amini M. Utility of serum lipid ratios for predicting incident type 2 diabetes: the Isfahan diabetes prevention study. *Diabetes/metabolism research and reviews*. 2016;32(6):572-80. <https://doi.org/10.1002/dmrr.2770>
7. Mao Y, Xu Y, Lu L. The nonlinear association between apolipoprotein B to apolipoprotein A1 ratio and type 2 diabetes. *Medicine (Baltimore)*. 2017;96(1):e5834. <http://dx.doi.org/10.1097/MD.00000000000005834>
8. Tang S, Tabet F, Cochran BJ, Cuesta Torres LF, Wu BJ, Barter PJ, et al. Apolipoprotein A-I enhances insulin-dependent and insulin-independent

- glucose uptake by skeletal muscle. *Sci Rep.* 2019;9(1):1350. <https://doi.org/10.1038/s41598-018-38014-3>
9. Domingo-Espin J, Nilsson O, Bernfur K, Del Giudice R, Lagerstedt JO. Site-specific glycation of apolipoprotein A-I lead to differentiated functional effects on lipid-binding and on glucose metabolism. *Biochim Biophys Acta Mol Basis Dis.* 2018;1864(9 Pt B):2822-34. <https://doi.org/10.1016/j.bbadis.2018.05.014>
10. Retnakaran R, Ye C, Connelly PW, Hanley AJ, Sermer M, Zinman B. Serum apoA1 (Apolipoprotein A-1), Insulin Resistance, and the Risk of Gestational Diabetes Mellitus in Human Pregnancy-Brief Report. *Arterioscler Thromb Vasc Biol.* 2019;39(10):2192-7. <https://doi.org/10.1161/ATVBAHA.119.313195>
11. Wu X, Yu Z, Su W, Isquith DA, Neradilek MB, Lu N, et al. Low levels of ApoA1 improve risk prediction of type 2 diabetes mellitus. *J Clin Lipidol.* 2017;11(2):362-8. <http://dx.doi.org/10.1016/j.jacl.2017.01.009>
12. Malyala R, Rapi L, Nash MM, Prasad GVR. Serum Apolipoprotein B and A1 Concentrations Predict Late-Onset Posttransplant Diabetes Mellitus in Prevalent Adult Kidney Transplant Recipients. *Can J Kidney Health Dis.* 2019;6:2054358119850536. <https://doi.org/10.1177/2054358119850536>
13. Ahmed S, Ali R. Atherogenic index of plasma as a biomarker of atherogenecity in type 2 diabetes mellitus in Erbil city. *Zanco J Med Sci.* 2023;27(1):1-5. <https://doi.org/10.15218/zjms.2023.001>
14. Mellor DD, Georgousopoulou EN, D'Cunha NM, Naumovski N, Chrysohoou C, Tousoulis D, et al. Association between lipids and apolipoproteins on type 2 diabetes risk; moderating effects of gender and polymorphisms; the ATTICA study. *Nutr Metab Cardiovasc Dis.* 2020;30(5):788-95. <https://doi.org/10.1016/j.numecd.2020.01.008>
15. Chou YC, You SL, Bai CH, Liao YC, Wei CY, Sun CA. Utility of apolipoprotein measurements in predicting incident type 2 diabetes: A Chinese cohort study. *J Formos Med Assoc.* 2020;119(1 Pt 1):51-8. <https://doi.org/10.1016/j.jfma.2019.03.001>
16. Patel VI, Patel KP, Makadia MG, Shah AD, Chaudhari KS, Nilayangode HN. Levels of Apolipoprotein A1, B100 and Lipoprotein (a) in Controlled and Uncontrolled Diabetic Patients and in Non-Diabetic Healthy People. *J Clin Diagn Res.* 2017;11(2):BC01-BC5. <https://doi.org/10.7860/JCDR/2017/22741.9258>

17. Wang W, Chen ZY, Guo XL, Tu M. Monocyte to High-Density lipoprotein and Apolipoprotein A1 Ratios: Novel Indicators for Metabolic Syndrome in Chinese Newly Diagnosed Type 2 Diabetes. Front Endocrinol (Lausanne). 2022;13:935776.
<https://doi.org/10.3389/fendo.2022.935776>