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Evaluation Of Apolipoprotein B In Type Ii Diabetes Mellitus Patients

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Abstract

According to statistics about 415 million people in the world suffer from this dangerous disease, Type 2 DM accounts for over 90% of DM cases. So, we evaluated some parameters that may affect T2DM. The aim of the present study is to find the relation of Apo B, with the T2DM condition and to evaluate how apo B change affects the T2DM. In case-control study the 180 serum and whole blood sample which collected from non-diabetic (n = 60) and T2DM (n = 120) persons were estimated for Apo B by the use of ELISA technique and the lipid profile was estimated by using mindray BS-430 and HbA1c by GH-900 Plus device. Whole blood was collected via vein puncture. We were collecting 180 sample of whole blood and serum from the diabetes center which divided into two groups 60 non diabetic and 120 diabetic persons. In present study showed significantly ($P<0.001$) increase in T2DM group compare to non-diabetic group in serum Apo B and HbA1c, FBS, TG, Cholesterol, LDL. This study was showed a significant ($P<0.05$) positive correlation between Apo B, HbA1c and lipid profile. From this study can be concluded that Apo B and lipid profile changes affect insulin resistance and as a result T2DM. And can be concluded that Apo B can be regarded as a marker of T2DM.

Keywords

ApoB, lipid profile, HbA1c, T2DM.

The core pathogenesis of T2DM involves islet β-cell and α-cell dysfunctions, Pancreatic islet β-cell dysfunction of T2DM is presented with blunted insulin sensitivity and/or abnormal insulin secretion. Type 2 diabetes Mellitus (T2DM) is characterized by a state of insulin resistance, which leads to metabolic alterations that aggravate the state of health of people. In the early stages of hyperglycemia, T2DM may developed gradually with mask symptoms of hyperglycemia and it usually stays untreated for years, T2DM risk rises with age, obesity, lack of physical activity, hypertension or dyslipidemia, a family history of diabetes among first-degree relatives (more than type 1 diabetes) (Mana et al., 2022).

The significant symptoms of diabetes blurred vision, Polyphagia(excessive hunger), Polydipsia(excessive thirst), and Polyuria(excessive urination), The long-term presence of uncontrolled diabetes may lead to loss of vision, nephropathy, sexual dysfunction, cardiovascular diseases and neuropathy (Pathan et al., 2020). insulin binding to its receptors leads to enhanced glucose transport into skeletal muscle, adipose tissue, and the heart, mainly facilitated by an acute translocation of GLUT4 transporter vesicles to the plasma membrane and, in addition, to an inhibition of hepatic gluconeogenesis (Chadt and Al- Hasani, 2020).

Insulin resistance is a result of dysfunction of insulin signaling pathway in multiple organs including the liver, skeletal muscle, and adipose

tissue, in which insulin inhibits glucose production and stimulates glucose utilization, Insulin resistance reduces the insulin activities leading to disorder in the glucose production by liver and glucose utilization in the skeletal muscle and adipose tissue (Liu et al., 2022). Obesity is a serious, preventable chronic disease that affects millions of people worldwide, and its prevalence continues to increase, Obesity is defined as having a BMI greater than or equal to 30 kg/m2, whereas overweight is defined as having a BMI greater than or equal to 25 kg/m2, The underlying cause of overweight or obesity is generally due to an energy imbalance, which may lead to weight gain (Wesling and D'Souza 2022). Apolipoprotein B exists in two forms: apo B-100 and apo B-48. In the fasting state, most of the apo B in plasma is apo B-100, Apo B-100, a single polypeptide of more than 4500 amino acids, is the full-length translation product of the APOB gene, In humans, apo B-100 is made in the liver and is secreted into plasma as part of VLDL, IDL, or LDL show (Rifai, 2017). (ApoB) is a structural component of lipoproteins that facilitates the LDL receptor binding and contributes to the cellular uptake of cholesterol from cholesterol-rich lipoproteins (Naeini, 2023).

Because the apoB effects on risk of type 2 diabetes might be confounded by adiposity and fat distribution, evidence of association between apoB and type 2 diabetes, implicate apoB in several major diseases, including heart disease, stroke, and diabetes, patients with hypertriglyceridemia, which is very frequent in T2DM patients, may present falsely lower LDL-c concentrations, However, these patients still have a high atherogenic risk, since ApoB levels remain elevated, even with decreased LDL-c levels (Fonseca et al., 2020).

Materials And Methods

This study was conducted in the Imam Al Hasan Center for the endocrins and diabetes in Karbala Province, Iraq, during the period from 1 Nov. 2022 to 31 Mar. 2023. Blood specimens were collected from T2DM patients in addition to control group that attended to Imam Al Hasan Center. 180 sample was collected from that 120 was T2DM and 60 normal persons. Average age of patients is (50±9.5) years.

Blood collection

Blood samples were collected by vein puncture technique obtain 5 ml of blood from both diabetic patient and control. 2ml for EDTA tube for HbA1c was estimated by GH-900 plus device, and 3 ml After that hold the blood at room temperature so as to clot then centrifuge it in 5000 rounds for 5 minutes to obtain serum which by using ELISA technique was estimate the concentration of apolipoprotein B, and by using mindray BS-430 was estimate the concentration of lipid profile.

Estimation of serum Apolipoprotein B

Apolipoprotein B tested for All samples (case and control) by ELISA instrument, The procedure of Apo B (Catalog No : E-EL-H0464;) was measured according to the standards required by the manufacturer company

Results And Discussion

The levels of the parameters in current study are different in patients compared healthy group, the results showed high levels in patients of most parameters compared control group. Mean level of ApoB (1.78±0.57) in patient group was highly significant (p-value 0.0001) increase than in control (1.16±0.18). Then, the mean level of LDL (139.97±30.58) in patient group was high significant (p-value 0.0001) increase than in control group, The mean HbA1c % value was significantly higher in the diabetes group than in the non-diabetic group (Son, 2019). The results as shown in table 1. significant increase in T2DM group compare to control group in ApoB, lipid profile, HbA1c,FBS.

Table 1: Comparison of demographic and biochemical parameters in TDM2 patients and control studied groups.

Variables	Patients N=120	Control N=60	p-value
BMI (kg/m^2)	27.98±3.49	26.54±4.09	0.014 *
FBS (mg/dl)	213.3±55.76	90.33±9.57	0.0001 **
HbA1c (%)	8.88±1.94	4.52±0.57	0.0001 **
Cho. (mg/dl)	192.18±39.09	161.28±33.65	0.0001 **
TG (mg/dl)	188.83±62.78	120.71±26.32	0.0001 **
HDL (mg/dl)	39.23±5.58	45.19±6.67	0.002 *
LDL (mg/dl)	139.97±30.58	106.62±24.57	0.0001 **
Apo-B (mg/dl)	1.78±0.57	1.16±0.18	0.0001 **

* Significant at p-value <0.05, ** <0.00. NS: non-significant. Data expressed as mean ±SD (standard division).

Biochemical markers

Apolipoprotien B with T2DM

Increased concentrations of apolipoprotein B (ApoB)- containing particles, is often present in individuals with type 2 diabetes mellitus (T2DM) (Lorenzatti et al., 2021). As shown in figure 1 The result showed strong correlated between Apolipoprotein B and T2DM with (P = 0.0001). In the state of IR, insulin is unable to bind to insulin receptors, thereby suppressing intracellular signals. In turn, it activates the hormone sensitive lipase(HSL), which hydrolyse TGs to glycerol and FFAs, which are released into the circulation towards the liver, Elevated free fatty acids can directly disrupt the activity of lipoprotein lipase by causing it to detach from the endothelial surface, Consequently, the increased hepatic availability of free fatty acids leads to decreased degradation of apoB. ApoB is a component of very low-density lipoprotein (VLDL), increased flux of free fatty acids promotes hepatic TG production, which subsequently induces apoB and VLDL secretion (Shetty and Kumari, 2021; Haile et al., 2020).

Increased FFA and saturated fats can harm beta-cell through cytokine-induced inflammation with progressive weakening of beta-cell function leading to beta-cell death. Proinflammatory cytokines cause beta cell death due to mitochondrial stress leading to beta-cell destruction. Furthermore, saturated fatty acid encourages islet inflammation and proliferates cytokines expression in beta cells thus making beta-cell dysfunction. Beta-cell hypertrophy (decreased beta-cell size) and hyperplasia (increased beta cell number) arise during beta-cell compensation to increase beta-cell mass in response to hyperglycemia. loss of beta-cell function leading to increased blood glucose levels, Slowly rising HbA1c (Salami et al., 2021).

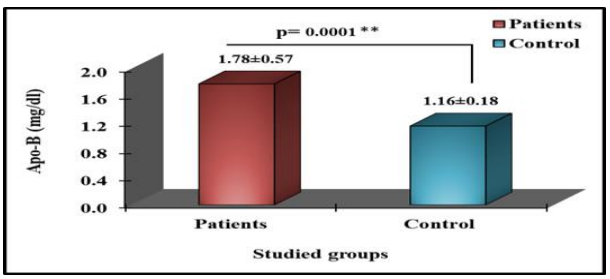

Figure 1: Concentration of Apolipoprotein B levels among patients and controls.

Correlation between Apolipoprotein B and HbA1c

The mean concentrations of HbA1c, serum Apo B are significantly increased in type 2 diabetic cases when compared with healthy controls. HbA1c concentration is significantly positively correlated with serum Apo B in type 2 diabetic cases (Namani and Laxmi, 2022). As shown in Figure 2. positive Pearson correlation between Apo B and HbA1c. (P=0.032)

Elevated plasma FFA levels significantly decreased the insulin-stimulated glucose uptake and reduced the plasma membrane levels of the glucose transporter GLUT4. Skeletal muscle tissue accounts for nearly 75−80% of the postprandial insulin-mediated glucose uptake, elevated levels of FFAs lead to skeletal muscle insulin resistance, by dysregulating the steps in the insulin signaling cascade muscle tissue plays a paramount role in maintaining glucose homeostasis, Impairments in insulin-mediated muscle glucose uptake lead to reduced glucose tolerance and T2DM, FFAs significantly impair the insulin signaling. GLUT4 expression was probably reduced by the presence of excessive lipids and free fatty acids, GLUT4 are mainly involved in glucose transport (Lackner et al., 2020).

Higher FFA levels cause insulin resistance by interfering with insulin signaling and inhibiting insulin-stimulated glucose uptake, oxidation, and glycogen synthesis in liver and skeletal muscle, increased FFA levels lead to glucose homeostasis disturbances by causing insulin resistance in liver and skeletal muscle, and impaired pancreatic β-cell function, The deleterious role of FFA in type 2 diabetes is most evident in obese patients because obesity is associated with elevated levels of circulating FFA, due to expanded adipose tissue mass and decreased FFA clearance (Li et al., 2021).

FFAs causing dysregulating of insulin signaling, reduced GLUT4 expression, reduce glucose uptake lead to reduced glucose tolerance, all that's leading to hyperglycemia and increase glycation of hemoglobin A1 (increase HbA1c levels). (Pohanka, 2021) .

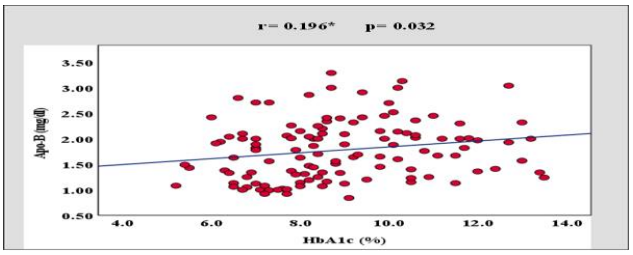

Figure 2: Positive significance between Apo B and HbA1c in T2DM patients than in the control group.

Correlation between Apolipoprotein B and lipid profile

The results of the present study showed positive Pearson correlation between Apo B and

TG(P=0.014). Dyslipidemia associated with T2DM have been attributed to increased free fatty acid (FFA) flux from adipocytes to insulin resistance and hepatic esterification of FFA to triglyceride (TG). This, in turn, augments very low density lipoprotein (VLDL) and apolipoprotein B (apoB) 100 synthesis. (Pelham et al., 2019). The net effect is an increased availability of apo B resulting in increased VLL-C and non-HDL-C secretion, dyslipidemia in T2D is characterized by elevated apo B concentration (reduced clearance and increased synthesis). Multiple studies thus far have shown elevated apo B levels in obesity, metabolic syndrome, and T2D, i.e., conditions with mixed dyslipidemia (Sunil and Ashraf, 2020).

Apolipoprotein B and BMI

As shown in Figure 3. The current study showed positive correlation between Apo B and BMI (P=0.001). Adipose tissues grow through a process known as adipogenesis, which can be defined as the ability of preadipocytes to multiply and to differentiate into mature adipocytes. During the development of obesity as a result of chronic positive energy balance, adipose tissue volume increases via 2 main processes: adipocyte hypertrophy (increase in Fat cell size) and hyperplasia (increase in fat cell number) (Ye et al., 2022).TAG is the main lipid form in the fat body, which is synthesized from dietary carbohydrates, fatty acids or proteins and is stored in intracellular lipid droplets (Parra-Peralbo et al., 2021). The triglycerides carried in VLDL are metabolized in muscle and adipose tissue by lipoprotein lipase releasing free fatty acids and IDL are formed. The IDL are further metabolized to LDL, which are taken up by the LDL receptor in numerous tissues including the liver (Feingold, 2021).

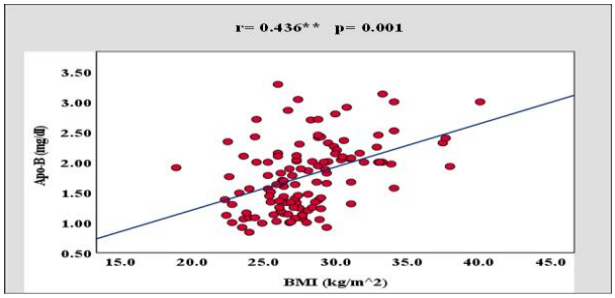

Figure 3: Positive significance between Apo B and BMI in T2DM patients than in the control group

The lipid abnormalities seen in patients who are obese include elevated triglyceride, VLDL, Apo B, and non-HDL-C levels, The increase in serum triglycerides is due to increased hepatic production of VLDL particles and a decrease in the clearance of triglyceride rich lipoproteins, The greater the increase in BMI the greater the abnormalities in lipid levels. Approximately 60-70% of patients who are obese are dyslipidemic while 50-60% of patients who are overweight are dyslipidemic. (Feingold, 2020).

Conclusion

This study showed that Apo B and lipid profile increase affects insulin resistance and as a result occurs diabetic type 2. However, Apo B can be regarded as a marker of T2DM. Therefore, this study recommended on importance of performing the Apo B test for a person who suffering from metabolic disordered along with HbA1c and the lipid profile as biochemical markers for T2DM.

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