American Journal of Bioscience and Clinical Integrity
https://biojournals.us/index.php/AJBCI
ISSN: 2997-7347

# Effect of CETP Gene Taq1.B Polymorphism on Lipid Profile Abnormalities in Iraqi Type 2 Diabetic Patients

**Abduqader W. Rasheid**
**Iraq /Ministry of Education/ The Open Educational College. Salah eldin.**
chemistbird2@gmail.com

**Received:** 2024, 25, Dec
**Accepted:** 2025, 10, Jan
**Published:** 2025, 31, Jan



**Abstract:** Previous studies have evaluated the associations between the cholesteryl ester transfer protein (CETP) TaqIB polymorphism, the risk of developing diabetes mellitus. The objective of this study was to investigate whether a relationship exists between CETP gene on lipid profile abnormalities in Iraqi diabetic patients. A meta-analysis of was conducted to clarify the associations of the CETP TaqIB polymorphism with HDL-C concentration and the diabetes mellitus. In this study 160 Iraqi subject were enlist, 90 patients with DM and 70 as a control. Table (1) shows serum lipid results of the population study , (TC , TG, LDL-C, and VLDL-C) were significantly higher (P<0.0001) except HDL-C was lower in the pa¬tient group compared to the control group (P<0.0001). There were more male (75.55%) than female (24.4%) with T2DM in this study. The high proportion of males in this study may be due to the nature of population admitting to this hospital in that more of them seek medical attention than women under favor of having more free time because most of them were retired. included in the association between the CETP TaqIB polymorphism and the concentration of HDL-C. Various single nucleotide polymorphisms have been depicted in the CETP gene. It has been accounted for that the rs708272 Taq1 B (g.5454G>A) polymorphism impacts HDL-C focus. Subsequently, the point of

this assessment was to evaluation the polymorphism of CETP gene at Taq1B site and its impact on serum lipid in Iraqi patients with lipid issue. We chose CETP Taq1 B polymorphism since a couple of assessments itemized its relationship to the HDL level and considering the way that we didn't find any Iraqi examination discussing this polymorphism of the CETP gene.

**Keywords:** CETP Taq1B gene, diabetes, cholesterol, triglyceride, polymorphisim.

## Introduction

Diabetes mellitus (DM) is a global epidemic disease that affects more than 150 million people worldwide. It is estimated that global number of adults suffering from all forms of diabetes will reach 439 million in 2030, most of them type 2 DM cases [(1)]. The term DM describes a metabolic disorder of multiple etiologies characterized by chronic hyperglycemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both [(2)]. Cholesteryl ester transfer protein (CETP) a hydrophobic glycoprotein, which has an important role in transporting of cholesterol from the peripheral tissues to the liver for elimination through exchanging triglycerides of VLDL and LDL against cholesteryl esters of HDL [(3)]. The removal of cholesterol from tissues and its delivery to the liver for excretion constitute the process of reverse transport [(4)]. Cholesterol is lipid or fatty substance and the precursor of all steroids hormone in the body, bile acid, and vitamin D, and it's an essential structural component of mammalian cell membranes and is required to establish proper membrane permeability and fluidity[(5,6)]. High levels of cholesterol in the blood have been linked to damage to arteries and cardiovascular disease[(7)]. A common strategy to examine the CETP function in humans has relied on assessing the clinical phenotype associated with variations in its gene[(8)]. plasma CETP is a highly hydrophobic glycoprotein consisting of 476 amino acids and 4 N-linked glycosylation sites and human CETP gene contains 16 exons, encompassing 25 kbp genomic DNA, and is located on the long arm of chromosome 16 near the lecithin cholesterol acyltransferase (LCAT) gene[(9)]. Several polymorphisms at the CETP locus have been identified Genetic variation in the CETP gene has been extensively studied for association with variation in HDL-C in different population[(10)]. More recently, GWAS studies reported the association of the rs3764261 SNP with higher HDL-C in Caucasians and this has been confirmed in several large studies including different ethnic groups [(11,12)]. However, most of this evidence has accumulated from association studies and little is known about whether diet modulates those associations[(13)]. As we previously mentioned, diet is a major determinant in the development of diabetes mellitus, given that factors such as HDL-C and TG can be susceptible to lifestyle behavior modification, and for this reason, it is essential to recognize the importance of gene edit interactions[(14,15)]. Interestingly, environmental factors have been shown to contribute to the association strength between these SNPs of the CETP gene and HDL-c concentrations [(16,17)]. One of the most frequent SNPs in the CETP gene is that located at the 227th nucleotide in its first intron (rs708272 or Taq1B, NG_008952.1:g.5454G>A) This SNP results in the disruption of a restriction site for the restriction enzyme Taq1 (B2 allele)[(18)]. The heterozygous B1B2 genotype is the most frequent in most populations. The Taq1B polymorphism is characterized by a silent base change from a G (designed as B1) to an A (designed as B2) nucleotide, at the 277th nucleotide in the intron 1 of the CETP gene, and possesses a restriction site for the endonuclease Taq1. The B2 allele of this SNP (absence of restriction site) has been associated with decreased CETP mass, increased HDL-c concentrations and decreased cardiovascular risk and metabolic syndrome Therefore, the Taq1B polymorphism of the CETP gene is likely to have an impact on lipid profile and thus determine CVD risk in T2DM patients[(19)]. CETP inhibitors as novel drugs have been progress to scale HDL-C concentrations and contrive HDL function in patients with diabetes mellitus, although the effect and inviolability still need to be chronic and many mutations in the CETP gene have been determine as a result in of CETP deficiency and change of HDL-C levels[(20)]. The aims of this study was to determine the levels of lipid profile (TC, TG, HDL-c, LDL-C, VLDL) in diabetic patient and control group, and also, to find polymorphism of (CETP) gene in patients and control that may be predict prone to diabetes mellitus.

## Materials and Methods

### Subjects selection

A total number of the study sample was 170 subjects, 100 individuals were patients with DM and 70 individuals were healthy have been selected as a control, age ranged from 18 to 60 years and sex were matched in both groups, volunteers were recruited by private clinic from Iraqi population.

### Sample collection

At the time of clinical examination, 5 ml of blood samples were collected from each subject and divided into two parts: In the first part 1 ml of blood has been collected in EDTA tubes for DNA extraction, while in the second part 4 ml was taken in a normal test for separation of the serum.

**Laboratory measurements**

Serum "lipid profile TC, HDL-C and TG levels were measured by enzymatic colorimetric methods [21], and the LDL and VLDL was estimated by Friedewald" formula[22].

**Determination of CETP Taq1B gene polymorphism**

Extraction of genomic DNA was perform by using [23] method. The purity and integrity of genomic DNA was systematic by the absorbance ratio of 260 nm to 280 nm (A260/A280) and the high molecular weight and better quality of the electrophoresis of agarose gel reciprocally. Polymerase chain reaction restriction fragment length polymorphism (PCR-RFLP) technique was used to determine the genotype of the CETP Taq1 B gene according to[24]. The following primers forward 5-CAC TAG CCC AGA GAG AGG AGT GCC-3 and reverse 5-CTG AGC CCA GCC GCA CAC TAA C-3 were used to amplify a fragment of 535 bp from intron 1 of the CETP gene. PCR amplification was performed in a total volume of 20 µL including 10 µL of 2X Go Taq green master mix supplied by Promega company (USA), 4 µL of genomic DNA, 1 µL of each primer in addition to 4 µL of DNase/RNase free water. PCR cycling was carried out according to the following program: one cycle for 5 minutes at 95 °C followed by 30 cycles, each cycle includes 95 °C for 30 seconds, 63 °C for 30 seconds and 72 °C for 45 seconds with one cycle of 5 minutes at 72 °C for a final extension. The resulting of PCR product (535 bp) was determined by using a 2% agarose gel electrophoresis stained with red safe. Ten units of the Taq I restriction enzyme (New England, BioLabs, Inc.) was added to 5 µl of the PCR product and incubated at 65 °C for 1 hour. The digest fragments were visualized on 2% agarose gel electrophoresis stained with red safe in the presence of 100 bp DNA ladder (Biolabs-England). Three types of bands were shown, single fragment (535 bp) as a B2B2 homozygous indicate the absence of the TaqI restriction site, 2 fragments (361 and 174 bp) as a B1B1 homozygous indicate the presence of the restriction site and 3 fragments (535, 361,174 bp) as the B1B2 heterozygous.

**Statistical analysis :**

SPSS version 20 PC programming were applied to statistical analyses. Hardy Weinberg equilibrium and recurrence of alleles and genotypes intuition odds ratios (OR) and their 95% confidence intervals (CI) of the patients, and control group were determined utilizing Pearson's chi-square test: $P<0.05$ was viewed as significant and ($P<0.05$) as high significant. One-way ANOVA and student's t-test were applied for the comparison of mean ± standard deviation (SD) of lipid parameters among healthy, patients group, and between the genotypes of CETP Taq1 B polymorphism.

**Results:**

**Serum lipid results of the population study**

In this study 160 Iraqi subject were enlist, 90 patients with DM and 70 as a control. Table ( 1) shows serum lipid results of the population study , (TC , TG, LDL-C, and VLDL-C) were significantly higher ($P<0.0001$) except HDL-C was lower in the patient group compared to the control group ($P<0.0001$). The resulted shown abnormalities of lipoprotein metabolism are the one of factors contributing to dyslipidemia risk in patients with type 2 DM, and diabetic dyslipidemia includes not only quantitative but also qualitative and kinetic lipoprotein abnormalities that are inherently atherogenic [17]. The primary (characteristic) quantitative abnormalities are

hypertriglyceridemia, accompanied by prolonged postprandial hyperlipidemia and increased levels of remnant particles (related to the increased production of triacylglycerol-rich lipoproteins and a reduction in the rate of catabolism of triacylglycerol-rich lipoproteins), and decreased HDL-cholesterol levels secondary to an increased rate of HDL catabolism [18]. The most frequent qualitative abnormalities, which are potentially atherogenic, include an increase in large VLDL particle size (VLDL1); a greater proportion of small, dense LDL particles; an augmented susceptibility of LDLs to oxidation; an increase in triacylglycerol content of both LDL and HDL; and glycation of Apo lipoproteins [19]. Although levels of LDL may be normal in patients with type 2 DM, LDL plasma residence time is increased due to a slower turnover rate, and this may infer the promotion of lipid deposition within artery walls. Some factors, such as insulin resistance and possibly some adipokines (e.g. adiponectin) and hyperglycemia, are involved in the pathophysiology of diabetic dyslipidemia [20].

**Table (1) : comparison between lipid levels of patients and control group**

| Parameter | Patients (No. 90) | Control (No. 70) Mean ± SD | *P* value |
|---|---|---|---|
| **HDL-C (mg/dL)** | 43.237 ± 11.824 | 51.7 ± 8.377 | 0.001** |
| **TC (mg/dL)** | 169.501 ± 5.456 | 148.3 ± 2.249 | 0.001** |
| **LDL-C (mg/dL)** | 103.025 ± 5.374 | 71.3 ± 9.822 | 0.001** |
| **VLDL-C (mg/dL)** | 27.409 ± 9.510 | 32.285 ± 5.538 | 0.002** |
| **TG (mg/dL)** | 137.479 ± 7.302 | 74.7 ± 10.703 | 0.001** |

**Genotypes and alleles frequency:**

By PCR-RFLP analysis of the CETP Taq1 B polymorphism, three types of genotypes (B1B1, B1B2, B2B2) have been obtained as show in (Fig 2).

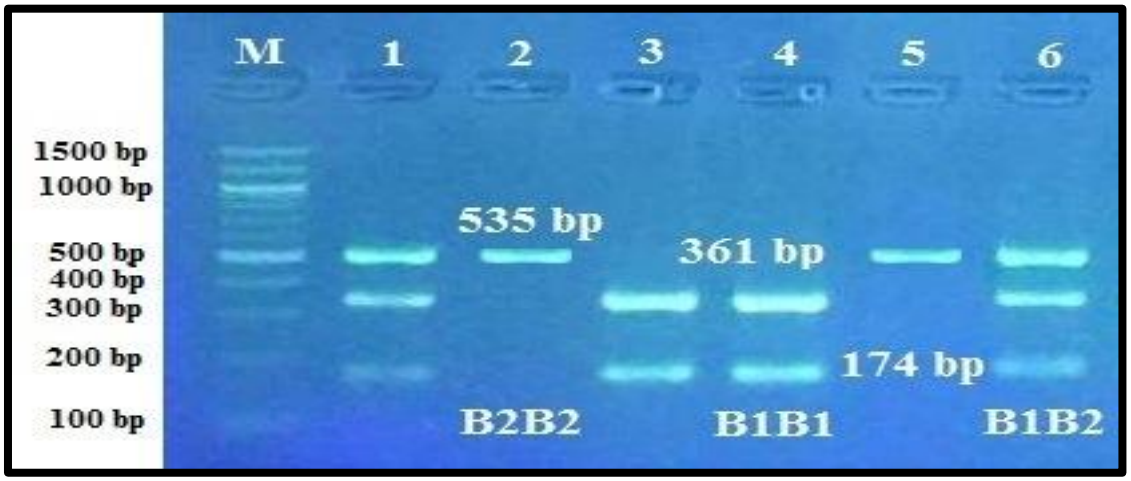


**Figure 2: Showing CETP Taq1 B gene polymorphism of PCR-RFLP products. lane (M) 100 bp DNA ladder, lane (3 & 4) B1B1 homozygote (361 & 174 bands), lane (1 & 6) B1B2 heterozygote (535, 361 & 174 bp bands), lane (2 & 5) B2B2 homozygote (535 bp band).**

There were more male (75.55%) than female (24.4%) with T2DM in this study. The high

proportion of males in this study may be due to the nature of population admitting to this hospital in that more of them seek medical attention than women under favor of having more free time because most of them were retired.

In patients with diabetes, many studies have clearly established that complications are mainly due to chronic hyperglycemia that exerts its injurious to health effects through several mechanisms: dyslipidemia, platelet activation, and altered endothelial metabolism and Both lipid profile and diabetes have been shown to be the important predictors for metabolic disturbances including dyslipidemia[24]. Lipids play a vital role in the pathogenesis of diabetes mellitus. Dyslipidemia as a metabolic abnormality is frequently associated with diabetes mellitus. Abnormalities in lipid metabolism have been reported in patients with diabetes mellitus accompanied by the risk of cardiovascular arteriosclerosis, but in the present study, significantly higher mean serum levels of total cholesterol, triglycerides and LDL cholesterol were noted in patients with diabetes[25]. In diabetes many factors may affect blood lipid levels, because of interrelationship between carbohydrates and lipid metabolism. Therefore, any disorder in carbohydrate metabolism leads to disorder in lipid metabolism and vice versa. Insulin resistance is a primary defect in the majority of patients with T2DM. In non-diabetic individuals insulin resistance in combination with hyperinsulinemia has a strong predictive value for future development for type 2 diabetes [26]. Several studies showed that insulin affects the liver apolipoprotein production and regulates the enzymatic activity of lipoprotein lipase and cholesterol ester transport protein, which causes dyslipidemia in diabetes mellitus. Moreover, insulin deficiency reduces the activity of hepatic lipase and several steps in the production of biologically active lipoprotein lipase and Hypertriglyceridemia usually accompanies decreased HDL cholesterol, which is also a prominent feature of plasma lipid abnormalities seen in individuals with diabetes [27]. The cluster of lipid abnormalities associated with T2DM is defined by a high concentration of TG and small dense LDL and a low concentration of HDL cholesterol. The association between reduced HDL cholesterol levels and increased risk of heart disease is, on the other hand, well established, independently of TG levels and other risk factors[28]. The possible mechanism responsible for hypertriglyceridemia may be due to increased hepatic secretion of very low density lipoprotein (VLDL) and delayed clearance of triglyceride rich lipoproteins, which is predominantly due to increased levels of substrates for triglyceride production, free fatty acids and glucose[29]. Abnormal glucose reading is the commonest metabolic abnormality in people with T2DM accompanied by lower HDL levels, elevated LDL, hypercholesterolemia, and hypertriglyceridemia. Poor glycemic control and hypertriglyceridemia are significant biochemical abnormalities in patients with T2DM. Dyslipidemia management in people with diabetes mellitus, just like in any other individual, starts with a flawless evaluation that aims to identify secondary causes that might contribute to the abnormal lipid profile [30]. Although obesity and T2DM commonly co-exist[31], mean BMI in our study was in the overweight range. Subjects enrolled in the study were the patients who have diagnose of their diabetes for averagely 3 years. They were under control of a dietitian since the

date of diagnose. This might be the cause that patients in our study were mostly overweight, but not obese. Lifestyle changes, including increased physical activity and dietary modifications, are the milestones of management. There is need for increased efforts by family members, community and healthcare professionals towards preventive based approach in the management of diabetes. This can be achieved through increased emphasis on lifestyle modification strategies such as exercise, increased dietary restrictions and weight control strategies especially for those with impaired fasting glucose. Monitoring of lipid profile by blood tests done in regular intervals in primary healthcare also might play an important role to detect and take care of lipid abnormalities both in diabetics and non-diabetics.

**Table 2: Serum lipid levels of the patients according to gender**

| Parameter | Male (No. 68) | Female (No. 22) Mean ± SD | *P* value |
|---|---|---|---|
| **HDL-C (mg/dL)** | 31.6069 ± 10.833 | 37.409 ± 10.751 | 0.031** |
| **TC (mg/dL)** | 163.580 ± 5.704 | 188.045 ± 42.777 | 0.049** |
| **LDL-C (mg/dL)** | 93.436 ± 5.127 | 132.663 ± 8.893 | 0.001** |
| **VLDL-C (mg/dL)** | 40.767 ± 4.91 | 27.8364 ± 5.507 | 0.003** |
| **TG (mg/dL)** | 136.929 ± 5.889 | 139.181 ± 5.535 | 0.847 |

The result of this study showed significant increase in the levels of total cholesterol (p=0.888) in diabetic patients compared to non-diabetic subjects, this increase it may be due to an increase in the plasma concentration of VLDL and LDL, which may be due to increase hepatic production of VLDL or decreased removal of VLDL and LDL from the circulation13. The study suggest significant increased level of LDL (p=0775) in diabetic patients and higher level of triglycerides (p=0 .327) in diabetic patients may due to overproduction of VLDL lead to increased plasma levels of triglyceride which, via an exchange process mediated by cholesterol ester transfer protein (CETP), result in lower levels of high density lipoprotein HDL-cholesterol, also may be due to insulin deficiency which results faulty glucose utilization causes hyperglycemia and mobilization of fatty acids from adipose tissue. In diabetes blood glucose is not utilized by tissue resulting in hyperglycemia. The fatty acids from adipose tissue are mobilized for energy purpose and excess fatty acid is accumulated in the liver, which are converted to triglyceride15. The most frequent alterations of lipid profile were combination of elevated TGs (VLDL-TG), decreased clearance of TG-rich lipoproteins and decreased high-density lipoproteins HDL [(29)].

**Table (3): Serum lipid levels of the patients and control according to CETP Taq1 B polymorphism**

| Parameter | B1B1 (No. 47) Mean ± SD | B1B2 (No. 26) Mean ± SD | B2B2 (No. 17) Mean ± SD | *P* value |
|---|---|---|---|---|

| | | | | |
|---|---|---|---|---|
| **HDL-C (mg/dL)** | 32.999 ± 4.486 | 34.2631±11.94 | 31.227 ±11.633 | 0.682 |
| **TC (mg/dL)** | 166.973 ± 5.966 | 169.988 ± 4.903 | 174.023 ± 5.347 | 0.888 |
| **LDL-C (mg/dL)** | 105.325 ± 5.844 | 96.720 ± 5.926 | 105.965 ± 9.628 | 0.775 |
| **VLDL-C (mg/dL)** | 35.656 ± 3.704 | 40.366 ± 6.612 | 38.682 ± 5.848 | 0.417 |
| **TG (mg/dL)** | 139.658 ± 7.761 | 143.3012 ± 5.267 | 122.246 ± 3.125 | 0.327 |

Table 4 shows results of the genotype and allelic frequencies in (%) and number of patients having each genotype of study population. The distribution of genotype in case and control group was conducted in the Hardy-Weinberg equilibrium. The results show that there is a significant differences (p value 0.001) between frequency of genotypes and alleles of CETP Taq1 B polymorphism in the patient and control groups. Patients with B2B2 genotype (22.86%) were significantly lower while both the B1B1 (8.57%) and B1B2 (68.57%) genotypes were higher compared with the control. Also we observed that there is an increasing in the B1 allele frequency on the contrary B2 allele in the patient compared to the control group (p value 0.002).

**Table (4): Distribution of genotypes and alleles frequency of the patients and controls group**

| **Genotypes** | **Patients No. (90)** | | **Control No. (70)** | | ***P* value** | **OR** | **(95% CI)** |
|---|---|---|---|---|---|---|---|
| | **No.** | **%** | **No.** | **%** | | | |
| **B1B1** | 47 | 47 | 6 | 8.57 | | 7.37 | 2.48-21.93 |
| **B1B2** | 26 | 26 | 48 | 68.57 | **0.0001**** | 0.51 | 0.22-1.17 |
| **B2B2** | 17 | 17 | 16 | 22.86 | | 1 Ref. | - |
| **Alleles** | **No.** | **%** | **No.** | **%** | ***P* value** | | |
| **B1** | 120 | 66.66 | 60 | 42.85 | | 2.666 | 1.689 to 4.208 |
| **B2** | 60 | 33.34 | 80 | 57.15 | **0.0002**** | 1 Ref. | - |

**Discussion:**

Various single nucleotide polymorphisms have been depicted in the CETP gene. It has been accounted for that the rs708272 Taq1 B (g.5454G>A) polymorphism impacts HDL-C focus. Subsequently, the point of this assessment was to evaluation the polymorphism of CETP gene at Taq1B site and its impact on serum lipid in Iraqi patients with lipid issue. We chose CETP Taq1 B polymorphism since a couple of assessments itemized its relationship to the HDL level and considering the way that we didn't find any Iraqi examination discussing this polymorphism of the CETP gene. Results in table 1 shows high significant differences (P<0.01) of serum lipid (TC , TG, , LDL-C, and VLDL-C) except HDL-C was lower in the patient group compared to the control group (P<0.01). The assessment of recurrence course of Taq1B polymorphism showed a basic differentiation between patients with lipid issue and the solid gathering. The B2B2 genotype was altogether higher (26 %) in the control bunch than in the patients gathering (68.57 %), demonstrating a possible cautious occupation of this genotype. Despite what might be expected,

we note a high recurrence of B1B1 genotype (47 %) in the patients gathering contrasted and the solid gathering (8.57 %). This can demonstrate the probability of this genotype being related with the hereditary inclination of the lipid issue, particularly that the recurrence of allele B1 was (66.66 %) and the chances proportion esteem (2.6) of the patients contrasted with recurrence (42.85 %) in the solid gathering. These outcomes were conflict with Ahmed AI et al, 2011(20) whose found some differences in the frequency of alleles and genotypes between patients and healthy groups but not significant, this may because the small sample size used. CEPT establishes the key component of cholesterol turn around exchange – the defensive framework against the improvement of atherosclerosis. Based on a few studies, it is conceivable to express that polymorphism Taq1B of the CETP gene is the determinant of the CEPT level [(32)]. What's more, when we surveyed the impact of polymorphism Tag1 B of quality CETP on the convergence of serum lipid profile in the investigation populace. As indicated by genotype we found that the comparative HDL-C levels in patients (B1B1 32.999 ± 4.486, B1B2 34.2631±11.94and B2B2 31.227 ±11.63) and this can be ascribed to the way of life and the earth of the members and notwithstanding their low number in the investigation which may weaken the measurable power of potential associations between CETP Taq1 B polymorphism and the serum lipid parameters. Then again, in the patients gathering, the nearness of the B1B1 genotype was seen as related with high TC and TG levels despite the fact that not measurably critical (P<0. 05), thus, B1B1 genotype might be considered as a hazard factor for lipid issue in Iraqi society. The aftereffects of this investigation were steady with the discoveries of Yilmaz H, et al, 2004 indicating the high level of TG levels with the B1B1 genotype of the group of type 2 diabetes patients in Turkish society[(30)]. Taking everything into account, our outcomes demonstrate that CETP Taq1 B polymorphism was huge relationship with Iraqi patients with diabetes mellitus contrasted with controls. The genotype B1B1 and B1 allele can be considered as a marker of hereditary inclination to bring down HDL-C levels and higher TC and TG levels in the Iraqi populace and lead to expanded helplessness of the diabetes mellitus . Different examinations ought to be directed utilizing a bigger number of tests in various areas of Iraq to affirm these result.

## Conclusion

This study evaluated the CETP Taq1B polymorphism's impact on serum lipid profiles and its role in lipid abnormalities among Iraqi diabetic patients. The findings contribute to understanding the genetic basis of dyslipidemia in T2DM and highlight the importance of investigating population-specific genetic variations**.** It is evident that there is a strong relationship between Taq1B gene polymorphism and diabetes mellitus among Iraqi people. This association was more a binding with triglyceride than other lipid profile.

## Acknowledgment

To everyone who contributed, directly or indirectly, to the completion of this work, I extend my deepest thanks and appreciation.

## References

1. Alberti, K.; Aschner, A.; Javerlana. Definition, Diagnosis and Classification of Diabetes Mellitus and its Complications. World Health Organization WHO Department of Noncommunicable Disease Surveillance Geneva.1:(2012). Online available fromhttps://www.staff.ncl.ac.uk/philip.home/who_dmc.

2. Ali A, Iqbal F, Taj A, Iqbal Z, Amin MJ, Iqbal QZ. Prevalence of microvascular complications in newly diagnosed patients with type 2 diabetes. Pakistan journal of medical sciences. 2013 Jul;29(4):899.

3. Ridker PM, Pare G, Parker AN, Zee RY, Miletich JP, Chasman DI. Polymorphism in the CETP gene region, HDL cholesterol, and risk of future myocardial infarction: Genomewide analysis among 18 245 initially healthy women from the Women's Genome Health Study. Circulation: Cardiovascular Genetics. 2009 Feb;2(1):26-33.

4. Thompson A, Di Angelantonio E, Sarwar N, Erqou S, Saleheen D, Dullaart RP, Keavney B, Ye Z, Danesh J. Association of cholesteryl ester transfer protein genotypes with CETP mass and activity, lipid levels, and coronary risk. Jama. 2008 Jun 18;299(23):2777-88.

5. Clifford AJ, Rincon G, Owens JE, Medrano JF, Moshfegh AJ, Baer DJ, Novotny JA. Single nucleotide polymorphisms in CETP, SLC46A1, SLC19A1, CD36, BCMO1, APOA5, and ABCA1 are significant predictors of plasma HDL in healthy adults. Lipids in health and disease. 2013 Dec;12(1):66.

6. Hanukoglu I. Steroidogenic enzymes: structure, function, and role in regulation of steroid hormone biosynthesis. The Journal of steroid biochemistry and molecular biology. 1992 Dec 1;43(8):779-804.

7. Schwartz CC, VandenBroek JM, Cooper PS. Lipoprotein cholesterol ester production, transfer, and output in vivo in humans. Journal of lipid research. 2004 Sep 1;45(9):1594-607.

8. Padmaja N, Kumar MR, Soya SS, Adithan C. Common variants of Cholesteryl ester transfer protein gene and their association with lipid parameters in healthy volunteers of Tamilian population. Clinica chimica acta. 2007 Jan 1;375(1-2):140-6.

9. Yamashita S, Hirano K, Sakai N, et al. Molecular biology and pathophysiological aspects of plasma cholesteryl ester transfer protein. Biochim Biophys Acta. 2000;1529:257–75 Hegele RA. Plasma lipoproteins: genetic influences and clinical implications. Nature Reviews Genetics. 2009 Feb;10(2):109.

10. Huggins GS, Papandonatos GD, Erar B, Belalcazar LM, Brautbar A, Ballantyne C, Kitabchi AE, Wagenknecht LE, Knowler WC, Pownall HJ, Wing RR. Do genetic modifiers of high-density lipoprotein cholesterol and triglyceride levels also modify their response to a lifestyle intervention in the setting of obesity and type-2 diabetes mellitus? The action for health in diabetes (Look AHEAD) Study. Circulation: Cardiovascular Genetics. 2013 Aug;6(4):391-9.

11. Radovica I, Fridmanis D, Vaivade I, Nikitina-Zake L, Klovins J. The association of common SNPs and haplotypes in CETP gene with HDL cholesterol levels in Latvian population. PLoS One. 2013 May 13;8(5):e64191.

12. Takeuchi F, Isono M, Katsuya T, Yokota M, Yamamoto K, Nabika T, Shimokawa K, Nakashima E, Sugiyama T, Rakugi H, Yamaguchi S. Association of genetic variants influencing

lipid levels with coronary artery disease in Japanese individuals. PLoS One. 2012 Sep 26;7(9):e46385.

13. Heidema AG, Feskens EJ, Doevendans PA, Ruven HJ, Van Houwelingen HC, Mariman EC, Boer JM. Analysis of multiple SNPs in genetic association studies: comparison of three multi-locus methods to prioritize and select SNPs. Genetic Epidemiology: The Official Publication of the International Genetic Epidemiology Society. 2007 Dec;31(8):910-21.

14. Corsetti JP, Ryan D, Rainwater DL, Moss AJ, Zareba W, Sparks CE. Cholesteryl ester transfer protein polymorphism (TaqIB) associates with risk in postinfarction patients with high C-reactive protein and high-density lipoprotein cholesterol levels. Arteriosclerosis, thrombosis, and vascular biology. 2010 Aug 1;30(8):1657-64.

15. Li Q, Huang P, He QC, Lin QZ, Wu J, Yin RX. Association between the CETP polymorphisms and the risk of Alzheimer's disease, carotid atherosclerosis, longevity, and the efficacy of statin therapy. Neurobiology of aging. 2014 Jun 1;35(6):1513-e13.

16. Maroufi NF, Farzaneh K, Alibabrdel M, Zarei L, Cheraghi O, Soltani S, et al. Taq1B Polymorphism of Cholesteryl Ester Transfer Protein (CETP) and Its Effects on the Serum Lipid Levels in Metabolic Syndrome Patients. Biochem Genet. Springer US; 2016;54(6):894–902.

17. Garcia-Rios A, Alcala-Diaz JF, Gomez-Delgado F, Delgado-Lista J, Marin C, Leon-Acuña A, Camargo A, Rodriguez-Cantalejo F, Blanco-Rojo R, Quintana-Navarro G, Ordovas JM. Beneficial effect of CETP gene polymorphism in combination with a Mediterranean diet influencing lipid metabolism in metabolic syndrome patients: CORDIOPREV study. Clinical Nutrition. 2018 Feb 1;37(1):229-34.

18. Clifford AJ, Rincon G, Owens JE, Medrano JF, Moshfegh AJ, Baer DJ, Novotny JA. Single nucleotide polymorphisms in CETP, SLC46A1, SLC19A1, CD36, BCMO1, APOA5, and ABCA1 are significant predictors of plasma HDL in healthy adults. Lipids in health and disease. 2013 Dec;12(1):66.

19. Iwanicka J, Iwanicki T, Niemiec P, Balcerzyk A, Krauze J, Górczyńska-Kosiorz S, Ochalska-Tyka A, Grzeszczak W, Żak I. Relationship between CETP gene polymorphisms with diabetes mellitus in Polish population. Molecular biology reports. 2018 Dec 1;45(6):1929-35.

20. Ahmed AI, Helal MM, Kassem KF. Cholesteryl ester transfer protein Taq1B (g. 5454G> A) gene polymorphism in primary combined hyperlipidemia in the Egyptian population. Laboratory Medicine. 2011 Aug 1;42(8):482-6.

21. Naito H.K. Kaplan A et al. Cholesterol, Clin Chem The C.V. Mosby Co. St Louis. Toronto. Princeton ,(1984); 1194-11206 and 437.

22. Naito H K. Kaplan A et al., HDL Cholesterol, Clin Chem The C.V. Mosby Co. St Louis. Toronto. Princeton, (1984); 1207-1213 and 437.

23. Ali SM, Mahnaz S, Mahmood T. Rapid genomic DNA extraction (RGDE). Forensic Science International: Genetics Supplement Series. 2008 Aug 1;1(1):63-5.

24. Pac-Kożuchowska E, Krawiec P. Cholesterol ester transfer protein (CETP) gene polymorphism and selected parameters of lipid metabolism in children from families with history of cardiovascular system diseases. Medical science monitor: international medical journal of experimental and clinical research. 2013;19:818.

25. Manu Arora, Shyamal Koley, Sunil Gupta and J.S. Sandhu. A Study on Lipid Profile and Body Fat in Patients with Diabetes Mellitus.Anthropologist, 2007; 9(4): 295-298.

26. Sapna Smith,Alok M Lall. A Study on Lipid Profile Levels of Diabetics and Non-Diabetics Among Naini Region of Allahabad, India. Turk J Biochem 2008; 33 (4) ; 138–141.

27. Sattar N, Gill JM. Type 2 diabetes as a disease of ectopic fat?. BMC medicine. 2014 Dec;12(1):123.

28. Bruckert E, Pamphile R, McCoy F, André P. Defining the prevalence of low HDL-C in a European cohort of dyslipidaemic patients. European Heart Journal Supplements. 2005 Jul 1;7(suppl_F):F23-6.

29. Brown ML, Inazu A, Hesler CB, Agellon LB, Mann C, Whitlock ME, Marcel YL, Milne RW, Koizumi J, Mabuchi H, Takeda R. Molecular basis of lipid transfer protein deficiency in a family with increased high-density lipoproteins. Nature. 1989 Nov;342(6248):448.

30. Yilmaz H, Agachan B, Karaali ZE, Isbir T. Taq1B polymorphism of CETP gene on lipid abnormalities in patients with type II diabetes mellitus. International journal of molecular medicine. 2004 Jun 1;13(6):889-93.

31. Yaghootkar H, Scott RA, White CC, Zhang W, Speliotes E, Munroe PB, Ehret GB, Bis JC, Fox CS, Walker M, Borecki IB, Knowles JW, Yerges-Armstrong L, Ohlsson C, Perry JR, Chambers JC, Kooner JS, Franceschini N, Langenberg C, Hivert MF, Dastani Z, Richards JB, Semple RK, Frayling TM: Genetic evidence for a normal-weight “metabolically obese” phenotype linking insulin resistance, hypertension, coronary artery disease and type 2 diabetes.Diabetes 2014.

32. Corella, D.; Carrasco, P.; Amiano, P.; Arriola, L.; Chirlaque, M.D.; Huerta, J.M.; Martínez, C.; Martinez-Camblor, P.; Molina, E.; Navarro, C. Common cholesteryl ester transfer protein gene variation related to high-density lipoprotein cholesterol is not associated with increase glucose in diabetic patients after a 10-year follow-up in a Mediterranean cohort: Modulation by different agent consumption. 2010, 211, 531–538.