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Molecular Genetic Investigation of ANGPTL8 Gene in Type I Diabetic Patients and Its Relationship with Some Serum Lipid Profile.

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Abstract

Diabetes is characterized by hyperglycemia due to various metabolic disorders of carbohydrates, proteins, lipids, water and electrolytes due to relative or absolute lack of insulin excretion from pancreatic beta cells, disturbance in the mechanism of action of insulin or both. The existing study was carried out to explore the near of ANGPTL8 gene in diabetic patients and its relationship with lipid profile. One hundred blood samples were collected from diabetic and normal men aged 50 to 65 years at the hospital in Al-Diwaneyah city, Al-Qadisiyah, Iraq, for ANGPTL8 gene expression and assessment of HbA1c, lipid profiles (TG, LDL and HDL) and betatrophin. The results revealed significant elevation of serum TG, LDL, HbA1c and betatrophin concentrations as well as blood *ANGPTL8* gene expression level and significant decline of serum HDL concentration in diabetic patients than normal men.

Key words: Diabetes Mellitus, LDL, HDL, ANGPTL8.

INTRODUCTION

The prevalence of diabetes is an epidemic with an increasing number of persons pretentious by each variety 1 diabetes (T1D) produced by insulin lack or variety 2 diabetes (T2D) produced by insulin conflict [1,2]. The renaissance of beta cells in equally species was considered to be the crucial objective that could progress or substitute the treatment of diabetes for both illnesses [3]. Factors such as glucagon-derived gut hormones such as peptide 1 (GLP1) plus glucose-reliant on insulin-dependent peptides have been exposed to rise insuline excretion and rise beta cell propagation [4]. Petatrofen too baptized the protein ANGPTL8 because of its similarity with members of the angiopoietin family (ANGPTL) [5,6]. It has been exposed to mark beta cell propagation and has been proposed as a potential board for beta cell revival [4,7]. ANGPTL8 has been exposed to interrelate with ANGPTL3 plus regulates triglycerides (TG) and greasy acid breakdown. Renn et al. [8] It was explained that ANGPTL8 was stimulated throughout the stage of primary rat lipid and human lipid cells in addition to 3T3 L1 adipogenesis. A lessening in betatrophin was too related with minor adipogensis which was pigeonholed by minor TG [8]. Likewise, mice that lacked betatrophin had a similar TG near in abstaining equaled to desolate type and minor TG near after lactation, abortive to hoard fatty acids properly in adipose matter and displayed gentler heaviness advance equaled with desolate lymphocytes [8] . However, they prepared not expression slightly variations in glucos balance in mices nursed on food or great-fat diets. In persons, it has remained exposed that betatrophin has amplified in T1D. ANGPTL8, which is accountable for the amino caustic changes in the R59W-prearranged protein, was found to be concomitant with low serum LDL and HDL cholesterol in Hispanic and Hispanic Americans in the Dallas Heart Reading [7]. The racial variability in MAF was observed for this modified and its connotation with LDL and HDL. The Europeans had fewer MAF and no association between R59W, LDL, and HDL was observed in the Dallas Heart Reading [7]. To reading the conclusion of the ANGPTL8 serial sequences in Iraqis, we used the Sanger categorisation to determine the new ANGPTL8 alternatives. We used Iraqi material from the sample sample to determine categorization differences in ANGPTL8 and to reading its connotation with the equal of ANGPTL8 and other metabolic danger influences, especially FBG, TG, LDL, and HDL.

MATERIALS AND METHODS

Samples collection: One hundred blood samples were collected from both men with diabetes and normal age between 50 and 65 years in hospital in Diwaniyah, Qadisiya, Iraq. Blood samples were divided into two parts, one for the purpose of gene expression and the other was used to separate the serum for the purpose of biochemical tests.

Laboratory measurements: Blood samples were obtained after fasting for at least 10 hours. Blood serum was obtained and analyzed for HbA1c and lipids including TG, LDL and HDL, using Seimens Dimension RXL (Diamonde Diagnostices, Hollieston, MA). HbA1c was resolute using the VariantTM device (BioRade, Herecules, CA). The Elisa test was used to determine betatrophin.

Molecular analysis: Total RNA was isolated from blood examples conferring to the procedure labelled by the TRIzol® component constructer (Promegae co. USA). After separation, the quantity (ng/µL) plus the excellence of aggregate RNA was resolute using Nanodrop UV/VIS spectrophotometer (OPTIZEN POP. MECASYS, Korea). The single-stranded cDNA was renewed into second-strand cDNA which was used as a prototype for transcription rejoinder. qRTPCR was achieved using AccuPower® Greenstar™ qPCR PreMix component kit (Bioneer, Korea) and Exicycler™ 96 Real-Time Quantitative Thermal Block (Bioneer, Korea). After completion of response, data analysis has been achieved, where the housework gene (*GapdH*) was epitomized as a regulate gene that can be charity for intention of the virtual gene expression or fold variation in mark gene (ANGPTL8 gene).

Statistical Analysis: The results were articulated as cruel standard deviation. A assessment was made between groups using a t-test for students. The variances were careful important at P <0.05. Arithmetical exploration was achieved using GraphPade Priesm (SAS Instietute, Inc., USA).

RESULTS

Serum lipid profile: As shown in Table (1), a significant increase (P <0.05) of TG concentrations and serum LDL was reported (P <0.05) of serum HDL concentration in diabetic patients compared with normal people.

Blood HbA1c and betatrophin concentration: Blood concentrations of HbA1c and betatrophin were pointedly higher (P <0.05) in diabetic patients compared with control people (Table 2).

Relative quantification of blood *ANGPTL8* genes expression: In the current study, a important rise (P <0.05) of the level of blood gene expression ANGPTL8 (fold changes) was reported in diabetic patients compared to normal people (Figure 1).

Table (1): Serum lipid profile in normal and diabetic patients.

Parameters	Normal	Diabetic patients
TG	42.463±9.881	62.238±14.981 *
HDL	48.191±8.974 *	33.082±7.017
LDL	38.751±12.127	55.578±9.034 *

The values are expressed as M±SD
The stars signify important difference (p<0.05) between studied groups.

Table (2): Blood HbA1c and betatrophin concentrations in normal and diabetic patients.

Parameters	Normal	Diabetic patients
HbA1c (ng/L)	77.932±19.763	167.258±19.831 *
Betatrophin (ng/L)	6.7371±2.5157	13.6538±5.1073 *

The values are expressed as M±SD
The stars signify important difference (p<0.05) between studied groups.

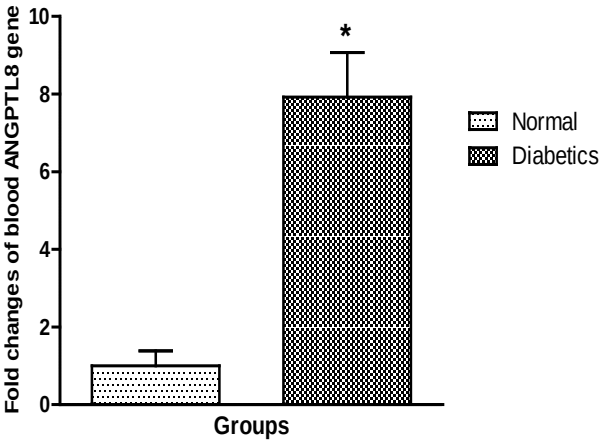

Figure (1): Gene expression levels (fold changes) of Blood *ANGPTL8* gene in normal and diabetic peoples.
The values are expressed as M±SD
The stars signify important difference (p<0.05) between studied groups.

DISCUSSION

ANGPTL8, as a newly recognised protein, has been exposed to piece a character in lipid breakdown. The successive arrangement of the ANGPTL8 gene is linked to the variable LDL and HDL level in persons [7]. This reading meant to study the levels of ANGPTL8 in persons and its connotation with metabolic hazard influences for diabetes. The ANGPTL8 gene is produced mainly in liver and fatty matter, which has been conventional as a watchdog of lipid metabolism, since successive sequences in betatrophin have been exposed to be related with low LDL-C and HDL-C [7]. In command to test the influence of ANGPTL8 on persons cells, Jiao et al. [9] NOD-Scid mice immunized with S961 to tempt insulin struggle, where a important increase in ANGPTL8 expression was reported in addition to β-cell replication in active mice as well as mice implanted ectopically under the renal lozenge. Conversely, dealing did not reason slightly rise in β cell propagation using persons carrots cultivated [9]. Moreover, Gusarova et al. [10]. Examine the knockout influence of ANGPTL8 on β cell propagation, and conveyed that β-cell response to insulin-induced insulin resistance or insulin receptor therapy S961. It also that augmented expression of ANGPTL8 did not rise the mass of Egypt cells or advance the glucose balance. However, they have also established that the TG level has abridged in knockout mice and has amplified the over-expression of ANGPTL8. Later, Yi et al. [11] displayed that they were unable to reproduce their original data and indicated a important alteration in the influence of ANGPTL8 injection on β cell propagation. Therefore, many researchers confirmed that the induction of ANGPTL8 for β cell propagation in mice was not replicable and its scoring did not disturb β cell propagation as previously proposed [12]. In relation to the role of ANGPTL8 insufficiency in β cell propagation was apart, where preliminary studies described on ANGPTL8 that it was due to insulin [11; 13]. Other persons studies have also exposed that ANGPTL8 was absolutely connected through insulin [14-16]. On the other hand, the serum near in diabetes was unhurried in multiple groups [15-19]. In persons, Espes et al. [17]. Displayed that the near of circulation of ANGPTL8 has amplified in T1D focuses. In another reading, the level of ANGPTL8 was augmented in focuses T2D [20-22]. The level of ANGPTL8 was connected with blood glucose, insulin, and insulin conflict as unhurried by the insulin struggle archetypal for the estimation of insulin (HOMA-IR) in non-pleasant substances only. No connexion was pragmatic with these factors in T2D focuses [14]. Furthermore, the near of ANGPTL8 has been exposed to be related with amplified C-peptide levels in non-x-rays but not in T2D focuses.

Their collective data displayed that the rise in ANGPTL8 in T2D did not rise insulin production in T2D [15]. On the other hand, other studies have exposed that ANGPTL8 did not rise in subject T2D and instead lessened [18, 23]. Recently, Lee et al. [24] The relationship between the ANGPTL8 and T2D level was achieved on the basis of a total of nine studies, where they found that the level of ANGPTL8 was suggestively higher in patients with T2D connected with non-diabetics. Equally, the near of

ANGPTL8 expression was amplified in people with gestational diabetes [25-26] and in persons with metabolic syndrome [27].

CONCLUSION

The current reading demonstrations that the ANGPTL8 gene alternative is connected with a higher near in diabetic illess than normal persons. The character of ANGPTL8 in glucose metabolism entails further research to ensure the focal purpose of ANGPTL8.

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