Lack of association between *IGF2BP2* genes (rs4402960 and rs11705701) polymorphism and type two diabetes mellitus.

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Abstract

Background: The most frequent illness in the world is chronic disease. Diabetes type 2 is mostly caused by autoimmune disease, -cell dysfunction, and obesity. IGF2BP2 is one of the genes related to T2DM identified through GWAS (Genome-Wide Association Studies), and it has been confirmed in a range of ethnic groups.

Material and methods : The samples were collected from AL Sadder Hospital's core medical city in Najaf. rs 4402960 and 11705701 of IGF2BP2 Allele-specific polymerase chain reaction T-ARMS-PCR was utilized to measure polymorphism in patients and controls (case_ control study). The statistical analysis was carried out using SPSS software.

Results : There is no difference between patients and control subjects in the genotyping of (rs4402960) in the IGF2BP2 gene (p>0.05), and there is no difference between patients and control in the genotyping of (rs11705701) in the IGF2BP2 gene (p>0.05).

Conclusion : Our results showed no association between The IGF2BP2 gene Polymorphisms (rs4402960 G/T and rs11705701 G/A) and T2DM patients.

Keywords: Polymorphisms in IGF2BP2, Diabetes Mellitus type 2.

Introduction

Diabetes Mellitus is a chronic disease that arises when the pancreas fail to produce enough insulin or when insulin production is insufficient [1]. Regular checkups and effective health management could prove capable to mitigate these consequences [2].

Diabetes patients who do not take treatment suffer serious serious risks that include cardiovascular disease, chronic renal failure, stroke, foot ulcers, and vision lack [3]. Because hyperglycemia develops gradually, 90% to 95% of patients with type 2 diabetes are obese or have been obese for years without receiving a diagnosis [4].

Home health care (HHC) is crucial for older adults with type 2 diabetes since they may require continuing care and nursing at home, according to the American Diabetes Association's (ADA) new initiatives for 2019 [5]. When the cells in the pancreas are damaged by an autoimmune illness, insulin production is reduced or halted, resulting in Type 1 diabetes. Diabetes mellitus type 2 occurs primarily by decreased insulin secretion and insulin resistance, both of which decrease the body's ability to use insulin [6].

Type 2 diabetes is caused by two variables: insufficient insulin production and decreased tissue sensitivity to insulin response [7].

Insulin, a polypeptide hormone with a molecular weight of (5808) Dalton, is produced by Langerhans pancreatic -cells. The islets are made up of four distinguish hormone-producing cells, in addition to PP-cells, which establish glucagon, insulin, somatostatin, and pancreatic polypeptide [8]. Diabetes history is linked to a variety of metabolic conditions and is a significant risk factor of developing type 2 diabetes (T2DM) [9].Although genetic and common environmental factors among family members are likely to play a role in this increased risk of T2DM, the precise causes of this risk increase are unknown. T2DM risk factors includes anthropometric and lifestyle factors such as BMI, waist circumference, and physical inactivity. [10]. Advances in molecular biology allowed the effective finding of many single nucleotide polymorphisms (SNPs) related to diabetes susceptibility [11]. IGF2BP2 refers to the mRNA-binding protein family, which aids in the location, stability, and

translation of RNA [12]. IGF2BP2 is a crucial growth and insulin signaling protein related to lower insulin production, which contributes to T2DM. assist maintain glucose homeostasis, it advances peripheral glucose absorption in many tissues while inhibits hepatic gluconeogenesis and lipolysis [13].

Materials and methods

The individuals in this study were separated into two groups. The first group included 60 males who were clinically diagnosed with type 2 diabetes in the Najaf Center at Medical City of AL Sadder hospital. Their ages ranged from (35- 60) years, with an average age of 52.2 7.13. The healthy control group included of (60) males ranged in age between (35-60) years, with an average age of 51.5 6.7. A syringe (5 ml) was utilized to obtain venous blood samples from both controls and patients. Two milliliters of blood were obtained from every person through venipuncture, and the two milliliters were placed in EDTA tubes and maintained at - 20 C (deep freeze) to be utilized later in the genetic part of the study.

Inclusion criteria:

1. A patient with diabetes.

2.Individuals who have type 2 diabetes lack chronic complications2.

3. All subscribers must be at least 35 years old.

Ethical Issues Before collecting samples, all participants in this study were informed and verbal consent was obtained from each of them. The study protocol, as well as the subject information and approval form, were evaluated and approved by a local ethics committee according to document number 14 in 06/07/2022.

Statistical analysis

In order to do the statistical analysis, SPSS version 20.0 was used. Mean and standard deviation are used to represent continuous variables. The analysis of variance student t test was used to compare the patient and control groups,

and a change was judged significant if P 0.05. The ANOVA test was used to compare the means of three or more groups.

Results

Table 1 shows the demographic characteristics of the 120 participants studied, 60 of whom had type 2 diabetes and 60 of whom did not. Patients in this study ranged in age from 35 to 60 years old, with a mean SD of 52.27.13 years. The control group ranged in age from 35 to 60 years old, with a mean SD of 51.5 6.7 years.

Table 1: Means and standard deviation of age and BMI in patients and control Patients in this study ranged in age from 35 to 60 years old, with a mean SD of 52.27.13 years. The control group ranged in age from 35 to 60 years old, with a mean SD of 51.5 6.7 years.

Parameter	Patient (50) Mean ± SD	Control (50) Mean ± SD	P-value
Age	52.2± 7.13	51.5 ± 6.7	0.82
BMI	25.31 ± 2.59	23.7 ± 1.11	0.1

*P < 0.05 is consider significant, SD = standard deviation, NS = not significant

Detection of Genes Polymorphisms

Distribution of Allele Frequency of (rs4402960) SNP in Diabetes Mellitus Type 2 Patients and Control Group.

As shown in Table 2, there is no significant difference in allele frequency (P>0.05) between sick and healthy control. One of the alleles demonstrated is a risk factor for Diabetes mellitus.
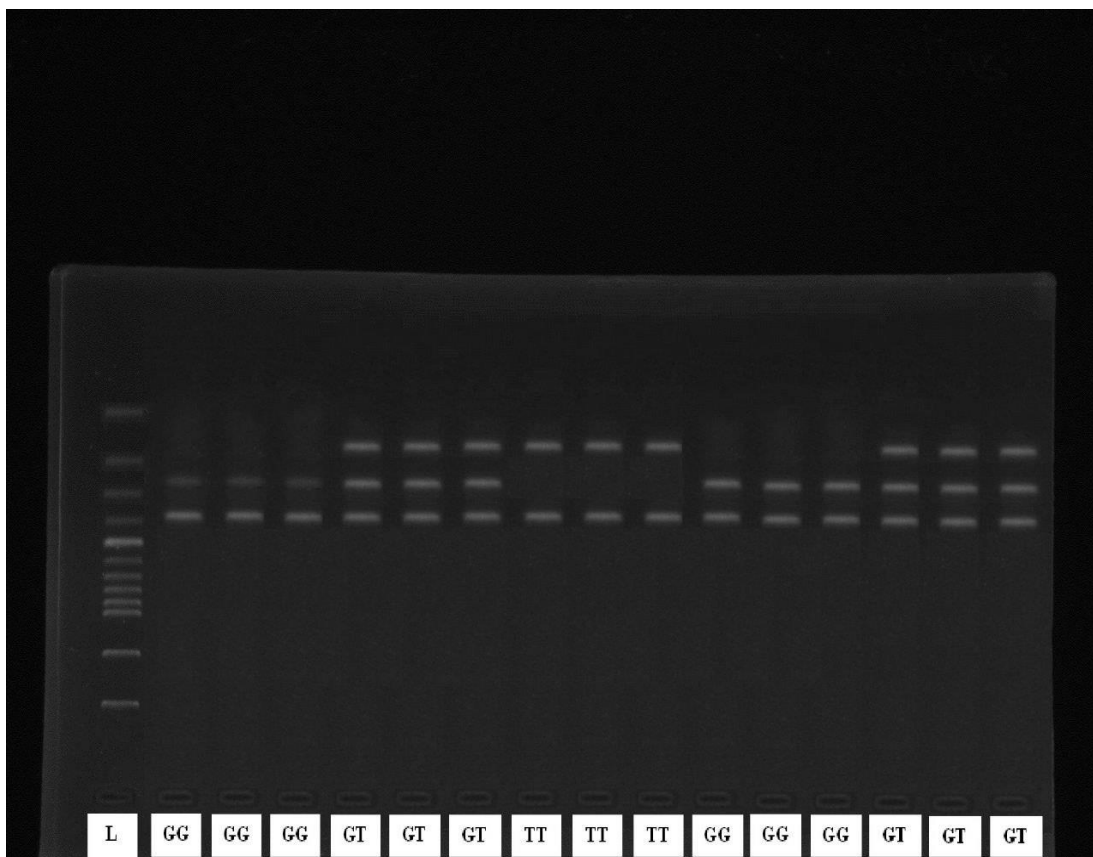
Table 2 : Genotypes Distribution and Frequency of IGF2BP2Gene (rs4402960 G/T)SNP in patient with T2DM, and control Groups.

Geno-Type	T2DM N=60	control N=60	OR	(95% CI)	P-value
GG	30 50%	32 53.3%	Refe	Refe	Refe
GT	21 35%	18 30 %	0.803	(0.36-1.79)	0.59
TT	9 15%	10 16.6%	1.04	(0.37-2.91)	0.93

GG: Wild genotype,   GT: Heterozygous and TT : Homozygous genotype

Table 3: Allele Distribution of (rs4402960) SNP of IGF2BP2 gene Polymorphism.

IGF2BP2 rs4402960	Patient N=60	Control N= 60	P-value	OR	95% CI
G	40	41			
T	20	19	0.89	0.96	(0.55-1.65)

Genotype Distribution and Allele Frequency of rs 11705701.

There is no results of **rs 11705701** as shown in table 3

Table 3: Show the wild genotype (G/G) (rs11705701 G/A) for Patients and Control .

Genotype	rs11705701 G/A			P- value
	Case (n=60)	**Control(n=60)**	**OR(95% CI)**	
GG Wild type	60 (100%)	60 (100%)	Reference	
GA Mutant heterozygous	0	0	1(0.019-51.38)	1.000
AA Mutant homozygous	0	0	1(0.019-51.38)	

Discussion

Although the etiology of T2DM is complex and causes more study, genetic factors have been identified as a major cause, with an increasing number of candidate genes being identified in recent years. The investigation of believe genes associated with the onset and progression of T2DM will throw light on the disease's core molecular mechanisms [14].

IGF2BP2 is found on chromosome 3q27. IGF2BP2 is a member of the insulin-like growth factor 2 (IGF2) mRNA-binding protein family, which is involved in normal embryonic growth and development [15]. It is particularly abundant in pancreatic islets.

Variants in IGF2BP2 have been showed to influence first-phase insulin production and the hyperglycemic clamp disposition index [16].

The IGF2BP2 delivers target m-RNAs to the mitochondrial surface, and thus inhibits the assembly and activation of mitochondrial respiratory complexes I and IV. A few studies indicates IGF2BP2 serves a role in mitochondrial assembly, metabolism, and activity. IGF2BP2 is required for embryonic development and differentiation of neurons at the physiological level. IGF2BP2 dysregulation is linked to a number of diseases, including diabetes of the type 2 [17].

In animal models, IGF2BP2 is a signaling protein that is required for insulin action and growth and has an effect on pancreas development. In addition, higher levels of FPG and serum insulin were discovered. The diacylglycerol kinase g-1 (DGKG) gene, which is similar to IGF2BP2, has been related to insulin secretion control [18]. As a result, more functional research into IGF2BP2 pathophysiological pathways is needed. IGF2BP2 is one of the genes related to T2DM found through GWAS (Genome-Wide Association Studies), and it has been confirmed in a range of ethnic groups. The polymorphisms rs4402960 G/A and rs11705701 G/A received the greatest attention Many

studies have confirmed the link [19]. Other studies [20] found no correlation. Furthermore, replication studies in other populations yielded results that were unclear [21].

The association of rs4402960 and rs11705701 in the IGF2BP2 gene with the development of T2DM in the Iraqi population was studied in this study. We also evaluated the significance of these single nucleotide polymorphisms (SNPs) in a variety of medical characteristics associated with Type 2 diabetes. Our findings showed an association between the rs4402960 SNP and T2DM but not with the rs11705701 SNP. A prior investigation in the Lebanese Arab population[22] discovered that both IGF2BP2 changes were common T2DM susceptibility genes, with rs4402960 having the greatest relationship.

Several previous studies in the Chinese Han population discovered that rs11705701 G/A mutant variants were inversely correlated with T2DM susceptibility, with GA and AA genotypes having lower frequencies in T2DM patients compared to healthy controls [23].

Referance

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