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Association between TCF_7L_2 (rs7903146) and $KCNQ_1$ (rs2237895 & rs2237892) genetic variants and risk of developing type 2 diabetes (T_2D) in Egyptian populations

Mahmoud A. Alshenawy[1]*, Moustafa A. Sakr[2], Mohammed F. Elshal[1], Shahira Elshafie[3] and Mohamed Y. Nasr[1]

1- Molecular Biology Department, Genetic Engineering and Biotechnology Institute (GEBRI), University of Sadat City, Sadat City, Egypt
2- Molecular Diagnostics and Therapeutics Department, Genetic Engineering and Biotechnology Research Institute (GEBRI), University of Sadat City, Egypt
3- Department of Clinical Pathology, Faculty of Medicine, Fayoum University, Egypt
*Corresponding author E-mail: mahmoud.abdelhamid.stu@gebri.usc.edu.eg
Co-authors E-mail: Mostafa.sakr@gebri.usc.edu.eg
mohamed.younis@gebri.usc.edu.eg

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ABSTRACT

Diabetes mellitus "simply diabetes" is a serious case in which blood glucose levels rise because bodies of patients are unable to produce any or enough insulin, or because they are unable to use the insulin produced efficiently. It is the most prevalent type of diabetes, affecting nearly 90% of all diabetes worldwide. In patient of type 2 diabetes (T_2D), his muscle, fat and liver cells can respond inappropriately to insulin, which means they can't efficiently take up glucose from blood or store it. This is known as insulin resistance. To compensate, the pancreas initially produces extra insulin. Over time, the pancreas is unable to keep up and produces insufficient insulin to maintain normal blood glucose levels.

In this study, we investigate whether the two single nucleotide polymorphisms (SNPs) in the transcription factor 7-like 2 gene (TCF_7L_2) and $KCNQ_1$ gene are associated with risk of developing T_2D in Egyptian populations. PCR-RFLP analysis was carried out for $KCNQ_1$ (rs2237892 and rs2237895) and TCF_7L_2 (rs7903146) genes for 66 T_2D patients and 34 control healthy. In $KCNQ_1$ (rs2237892) and TCF_7L_2 (rs7903146) for diabetic patients has a relatively high risk for diabetes, however, $KCNQ_1$ (rs2237895) showed no statistical significant differences between the diabetic patients and the healthy group. In conclusion the TCF_7L_2 (rs7903146) and $KCNQ_1$ (rs2237892) are the most unambiguous genetic factors influencing type 2 diabetes in Egypt.

Keywords: T_2D, TCF_7L_2, $KCNQ_1$, PCR-RFLP.

INTRODUCTION

The body doesn't use insulin properly in T_2D, this is referred to as insulin resistance, to compensate the pancreas produces extra insulin at first. Over time, the pancreas is incapable to keep up and produces deficient insulin to maintain normal blood glucose levels (Ericson *et al*., 2018). T_2D is also known as non-insulin-dependent diabetes mellitus (NIDDM), consideration more than 95 percent of diabetics. Its prevalence is increasing worldwide, but the most noticeable changes are now being seen in low and middle-income countries. T_2D is asymptomatic for many years and thus goes unnoticed in nearly half of those affected by the disease (Holt *et al*., 2017). A variety of factors can

contribute to T_2D. Although the exact causes are unknown, there is no b-cell autoimmune destruction, and none of the other known causes of diabetes are present in the patients (American Diabetes Association, 2021).

The Transcription factor 7-like 2 gene (TCF_7L_2), also known as TCF_4, is certainly the gene with the most significant effect on T_2D that has been identified to date (Holck *et al*., 2009). Because of its effects on pro- insulin processing and production, TCF_7L_2 is also regarded as a master regulator of glucose homeostasis (Liu *et al.*, 2017). The in cretin hormone glucagon-like peptide 1" is an important player in glucose homeostasis "GLP-1 which is produced in the small intestine by enteroendocrine L-cells and has a variety of beneficial effects on blood glucose control. TCF_7L_2 was discovered to be a transcription factor involved in the canonical Wnt signaling pathway before being discovered to be a T_2D gene. Wnt signals play a role in many essential cellular processes, including embryonic development, cell fate, stem cell maintenance, cell proliferation, tumor suppression, cell migration, and oncogenesis (Holck *et al.*, 2009).

The potassium voltage-gated channel KQT-like subfamily, member 1 ($KCNQ_1$) is a gene that associated with T_2D and there was an evidence that the potassium voltage-gated channel (GWAS) can identify this gene and therefore can be used as disease management targets. $KCNQ_1$ gene encodes proteins that belong to the cell potassium channel family, which is important for insulin secretion and is targeted by sulfonylurea derivatives, which are already broadly used anti-diabetic drugs. SNP selection and genotyping were carried out on two $KCNQ_1$ SNPs (rs2237892 and rs2237895) which had previously been linked to type 2 diabetes in other studies (Yu *et al.*, 2012). The excess risk of T2D associated with $KCNQ_1$ SNPs is most likely due to a decrease in insulin secretion, increased "FBS" levels, or "HbA1c", implying that $KCNQ_1$ variants may play an important physiological role in the metabolism also dynamic balance of blood glucose. In addition to their inconsistent association with T_2D, $KCNQ_1$ is linked to plasma lipid parameters..

This work aims to define at the relationship between TCF_7L_2 (rs7903146) and KCNQ1 (rs2237895 & rs2237892) gene polymorphisms with T_2D in Egyptian patients with potential impact on disease prediction, prevention and therapy response studies. TCF_7L_2 and $KCNQ_1$ were denimreted genotyped using the polymerase chain reaction method.

SUBJECTS AND METHODS

1. Study design and population

In this study, a total of 100 persons, including 66 T_2D patients and 34 non-diabetic of ethnicity selected population over the period from December 2019 to October 2020, to investigate some gene polymorphisms in T_2D among Egyptians populations. Routine laboratory investigations included FBS, HbA1c, CHO, TG, HDL, LDL, urea, Cr, GPT, GOT and CBC in addition to detection of TCF_7L_2 (rs7903146) gene in addition to two "SNPs in $KCNQ_1$, (rs2237892, & rs2237895) by using Polymerase Chain Reaction-Restriction Fragment Length Polymorphism (PCR-RFLP).

2. Sample collection & preparation

Samples were obtained from Omar Bin Al Khattab Hospital (Cairo), Arab Contractors Medical Center (Cairo), Al Seddiq Medical Clinics (Cairo) and Octa Lab (Giza). Verbal approval of participants had been obtained. All blood samples were collected. Venous blood samples (5 ml) were taken from fasting participants from 9 to 12 hr. and were divided by sodium

fluoride tube, EDTA tube and serum separator gel tube.

3. Routine laboratory investigations:

Fasting blood sugar (FBS)", HbA1c, cholesterol (CHO), "high density lipoprotein (HDL), low density lipoprotein (LDL), triglycerides (TG), creatinine (Cr), urea, glutamic oxaloacetic transaminase (GOT), glutamic pyruvic transaminase (GPT), were performed on a spectrophotometer (ADALTIS S.r.l. UM-PCHM01 and Clini-Chem 1 ES1022008PN281 Biomed) using (Spectrum and Biomed diagnostics kits) Egypt and complete blood count "CBC" was carried out on"3 part differential automated cell counter (Genrui auto hematology analyzer KT-6400)".

4. DNA extraction & molecular genotyping

DNA was extracted from whole blood (EDTA tubes), and 100 patients (66 T_2D patients and 34 healthy) were genotyped by PCR-RFLP for TCF7L2 (rs7903146). The TCF_7L_2 (C/T) polymorphism was genotyped using the primers listed following: Forward "5'-AAG AGA AGA TTC CTT TTT AAA TGG TG-3'", Reverse "5'-CCT CAT ACG GCA ATT AAA TTA TAC A-3'"and positive amplicons digested with Hpy-CH4III "Thermo Fisher Scientific Inc, Waltham, MA, USA" restriction enzyme at 37°C overnight. Two SNPs in KCNQ1 (rs2237892 & rs2237895), one primer set forward primer: "5'-GCTGCAGCCCGTGTTCCT-3'"; reverse primer: "5'-CGCATTCCGGGGGCTTCC-3'" were designed to amply DNA segment containing rs2237892 diverse in $KCNQ_1$. The second primer set for "rs2237895"diverse was "5'-TGGGGCAGGGGTGTCTTTA-3'"(forward primer) and "5' TCTGCCTCTTGGTCTCATCTTTAC-3'" (reverse primer). Cfr9I"Xma I" was used to digest both PCR products. Thermo Fisher Scientific Inc, Waltham, MA, USA at 37 °C for 4 h. A total reaction volume of 18 μL for the PCR-RFLP was designated, which contained 2 μL of genomic DNA, 1 μL of each primer, 2 μL PCR buffer, 10 μL PCR master mix "Thermo Fisher Scientific Inc, Waltham, MA, USA". The PCR-RFLP was carried out on AmpiliSeq Thermal Cycler under the following cases: "95°C for 15 min, then 34 cycles of 95°C for 30 sec, 58°C for 30 sec, 72°C for 30 sec and a final extension of 72°C for 9 min. Digested products were loaded on a 3% agarose gel electrophoresis at 100 V for 30 minute stained with "ethidium bromide&" photographed in investigated by Gel-Doc Imaging System (E-Box VILBER, France).

5. Statistical analysis:

The information was entered into a computer and analysed using "IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp)" to describe qualitative data, numbers & percentages were used. The Kolmogorov-Smirnov test" was used to confirm the distribution's normality. Range min and max, standard deviation, mean, median and interquartile range (IQR) were used to describe quantitative data. The significance of the gained results was determined at the 5% level.

RESULTS

Clinical characteristics:

In this study,a total of 100 persons and were categorizedinto 2 groups; (66 patient group) with median age of 58 years old (30 were males (45.5%) and 36 were females (54.5%) and (34 healthy group) individuals with median age of 45.5 years old (15 males (44.1%) and 19 females (55.9%)). There were no discernible differences in sex between T_2D patients and healthy. But age significant was between

patients with T_2D and control. The results indicated that the values of FBS, HBA1C, Urea, and Creatinine were increased significantly in T_2D patients than controls individuals (P<0.001). The hematological parameters showed that, the values of the RBCs, Hb, Platelets and WBCs were not different significantly among the two groups (P>0.05). Also the CHO, TG, HDL, LDL, GPT and GOT levels were not significantly varied between the two groups "(P>0.05) (Table 1).

Genotypic characteristics:

The Genotype distributions of all "$KCNQ_1$ polymorphisms were conformed to the Hardy-Weinberg equilibrium in all studied groups. In KCNQ1 (rs2237892) for diabetic patients, frequencies for the "CC", "CT", and "TT" genotypes were 24.2%, 60.6% and 15.2%, respectively. In controls, these distributions were 29.4%, 35.3% and 35.3%, respectively. Compared to TT genotypes, CT genotypes has a relatively high risk for diabetes (p = 0.016) (Table 2). PCR-RFLP analysis of the "$KCNQ_1$ (rs2237892) locus revealed two bands of "220 bp "and "67 bp" in the "CC homozygote genotype", one band of "287 bp" in the "TT" homozygote, and three bands of "287 bp", "220 bp", "&67 bp" in the "CT heterozygote genotype (Fig. 1).

On the other hand, the genotype and allele distributions of $KCNQ_1$ (rs2237895) polymorphism showed no statistically significant between the diabetic patients and the healthy group as (p value > 0.05) (Table 2). PCR-RFLP analysis of the $KCNQ_1$ (rs2237895) site revealed two bands of "294 bp" and " 191 bp" in the "CC homozygote genotype", one band of "485 bp" in the "AA homozygote", and three bands of "484 bp", "294 bp", "&191 bp" in the "AC heterozygote genotype (Fig. 2).

Regarding the genotype and allele distributions of TCF_7L_2 (rs7903146), in comparison with the healthy patients, the diabetic patients had a higher frequency of CC genotype (21.2% vs 5.9%, P=0.034)". TC & TT genotypes frequency were not significantly variant between the two groups (37.9% vs 38.2%, 40.9% vs 55.9%, respectively) (Table 2). PCR-RFLP analysis of the TCF7L2 (rs7903146) site revealed two bands of "112 bp" and "24 bp" in the "TT homozygote genotype", one band of "136 bp" in the "CC homozygote", and three bands of "136 bp", "172 bp", and "24 bp" in the "CT heterozygote genotype (Fig. 3).

The common T_2D clinical pathological features including FBS, CHO, TG, HDL, LDL, Urea, Creatinine, GPT, GOT, Hb, RBCs, WBCs and Platelets. No significant relation was observed between the $KCNQ_1$ (rs2237892 and rs2237895) and TCF_7L_2 (rs7903146) gene polymorphisms and all clinic-pathologic status and markers. Only HbA1c was significant with $KCNQ_1$ (rs2237892) gene (p=0.016) (Tables 3, 4, 5).

Diabetic patients had significantly higher "C allele genotypic" frequencies than the healthy group. (P=0.020). Collectively, these data suggested that, $KCNQ_1$ (rs2237892) CT genotype and TCF_7L_2 (rs7903146) CC genotypes may be considered as risk factors for the diabetes among Egyptian populations.

DISCUSSION

The present findings indicated that the SNPs $KCNQ_1$ (rs2237892), and TCF_7L_2 (rs7903146) may be considered as risk factors for T_2D among Egyptian patients, but SNPs (rs2237895) may be not considered as risk factors for the T_2D among Egyptian patients. In Icelandic, Asian Indian, Danish, and US samples, the SNP TCF_7L_2 (rs7903146) had the strongest association with T_2D (Bodhini *et al.*, 2007; Grant *et al.*, 2006). TCF_7L_2 gene variants have been replicated in a variety of ethnic groups and have been linked to T_2D (Cauchi *et al.*,

2007), including Caucasians(Van Vliet-Ostaptchouk *et al*., 2007), Ghanaians (Danquah *et al.*, 2013), Europeans (Helgason *et al.*, 2007), Indians (Chandak *et al*., 2007), Africans (Humphries *et al*., 2006), and East Asians (Ng *et al*., 2007; Hayashi *et al*., 2007). Among which, TCF_7L_2 (rs7903146) SNPs had the strongest relationship with disease susceptibility (Cauchi *et al*., 2007; Humphries *et al*., 2006; Ng *et al.*, 2007; Hayashi *et al*., 2007). The association between TCF_7L_2 and T_2D varied in Arab region, and it was strong in Tunisians (Ezzidi *et al*., 2009), Moroccans (Cauchi *et al.*, 2007), Omanis (Al-Sinani, 2015) and Palestinians (Ereqat *et al.*, 2010), In the United Arab Emirates or Saudi Arabia, there was a weak or no significant association (Saadi *et al*., 2008; Alsmadi *et al*., 2008).

TCF_7L_2 (rs7903146) gene polymorphism was discovered to be associated with T_2D patients (Bahaaeldin *et al*., 2020). The $KCNQ_1$ SNPs (rs2237892 and rs2237895) showed strong associations with T_2D in Chinese population (Qi *et al*., 2009; Yu *et al*., 2012).

All genetic models revealed significant associations between different populations "Caucasian", "East Asian" and "South Asian populations" in the ethnicity-based stratified analysis, demonstrating that the “C alleles” of “rs2237892 and rs2237895” $KCNQ_1$ polymorphism are a risk factor for developing T_2D (Sun *et al*., 2012).

Regarding the genotype and allele distributions of TCF_7L_2 (rs7903146) compared with the control group, the diabetic patients had a higher frequency of "CC" genotype (21.2% vs 5.9%, P=0.034). TC and TT genotypes frequency were not significantly varied between the two groups (37.9% vs 38.2%, 40.9% vs 55.9%, respectively). C allele genotypic frequencies in diabetic patients had significantly higher levels than the healthy group (P=0.020). Collectively, these data suggested that, $KCNQ_1$ (rs2237892) CT, TT genotype and TCF_7L_2 (rs7903146) CC genotypes may be considered as risk factors for diabetes among Egyptian patients.

Conclusion:

TCF_7L_2 (rs7903146) and $KCNQ_1$ (rs2237892) are the most probable genetic factors influencing type 2 diabetes in Egyptian patients.

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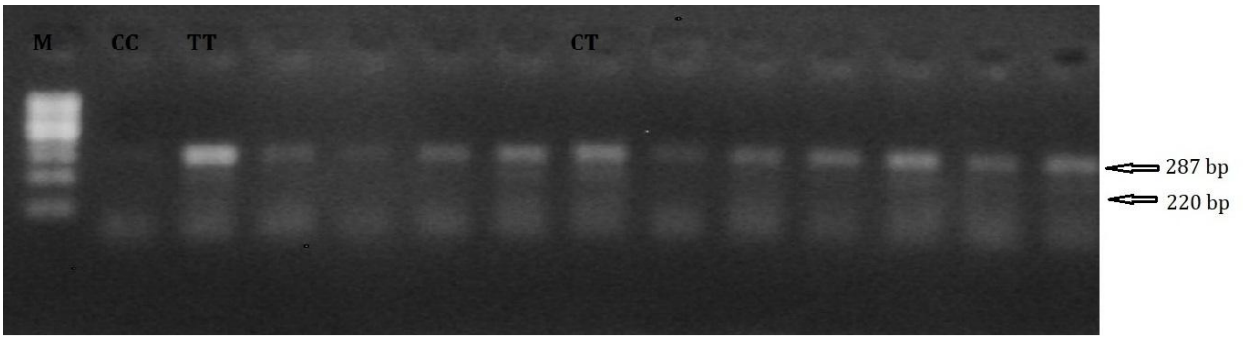

Fig. 1. PCR-RFLP analysis of the KCNQ1 rs2237892 locus revealed two bands of 220 bp and 67 bp in the CC homozygote genotype, one band of 287 bp in the TT homozygote, and three bands of 287 bp, 220 bp, and 67 bp in the CT heterozygote genotype. M = 100 bp ladder DNA marker.

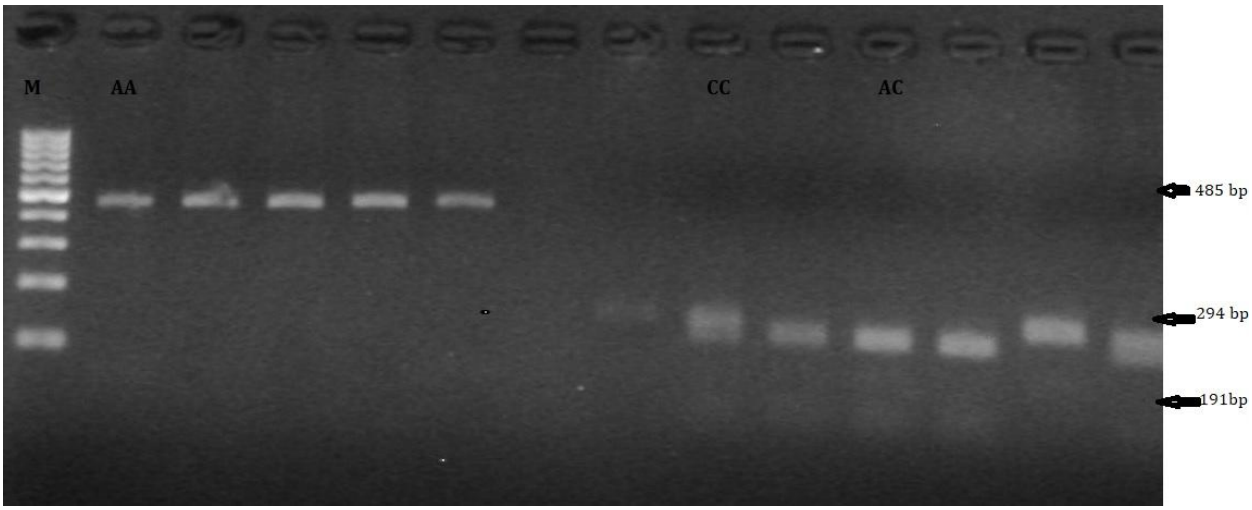

Fig. 2. PCR-RFLP analysis of the KCNQ1 rs2237895 locus revealed two bands of 294 bp and 191 bp in the CC homozygote genotype, one band of 485 bp in the AA homozygote, and three bands of 484 bp, 294 bp, and 191 bp in the AC heterozygote genotype. M = 100 bp ladder DNA marker.

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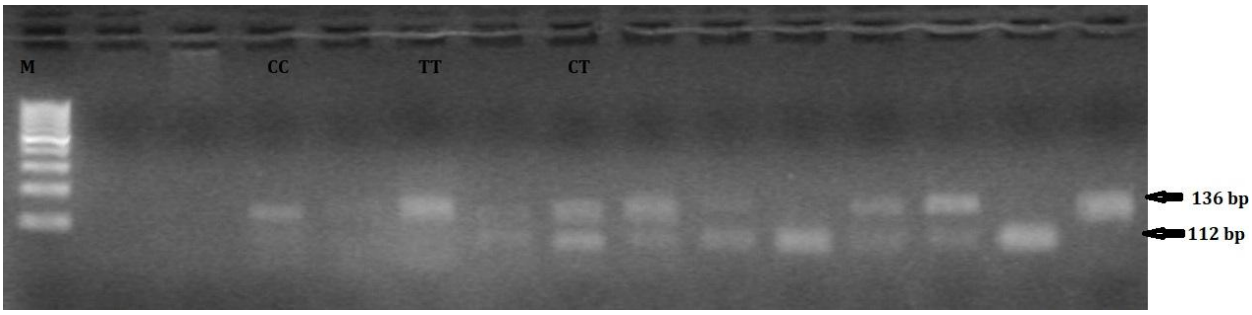

Fig. 3. PCR-RFLP analysis of the TCF7L2 (rs7903146) locus revealed two bands of 112 bp and 24 bp in the TT homozygote genotype, one band of 136 bp in the CC homozygote, and three bands of 136 bp, 172 bp, and 24 bp in the CT heterozygote genotype. M = 100 bp ladder DNA marker.

Table 1. Selected clinical and demographic characteristics of patients and controls.

Parameters	Diabetes (n =66) Mean ± SD	Non diabetes (n = 34) Mean ± SD	Test of Sig.	P
Demographic data				
Age (years)	56.44 ± 9.91	47.74 ± 9.78	t= 4.180*	<0.001*
Sex, n (%)	M, 30(45.5%)- F, 36(54.5%)	M, 15(44.1%)- F, 19(59.9%)	χ^2=0.016	0.899
Biochemical parameters				
FBS (mg/dl)	194.58 ± 106.15	92.32 ± 12.95	U=222.0*	<0.001*
HbA1c (%)	9.45 ± 3.11	5.52 ± 0.54	t=9.959*	<0.001*
Total cholesterol (mg/dl)	183.8 ± 50.16	190.4 ± 46.29	t=0.639	0.524
Triglycerides (mg/dl)	166.9 ± 85.35	138.9 ± 74.59	U=912.50	0.127
HDL (mg/dl)	39.53 ± 13.80	40.09 ± 10.92	U=1007.0	0.402
LDL (mg/dl)	111.0 ± 47.90	122.4 ± 36.89	t=1.215	0.227
Urea (mg/dl)	38.91 ± 17.18	29.41 ± 16.65	580.0*	<0.001*
Creatinine (mg/dl)	1.05 ± 0.43	0.85 ± 0.24	570.0*	<0.001*
GPT (U/L)	26.17 ± 10.61	22.35 ± 9.96	U=858.50	0.055
GOT (U/L)	29.20 ± 11.40	25.44 ± 8.47	t=1.693	0.094
Hematological profile				
Hb (gm/dl)	12.62 ± 1.58	12.28 ± 1.42	t=1.073	0.286
RBCs 10^6 /µL	4.67 ± 0.44	4.51 ± 0.67	t=1.219	0.229
HCT (%)	37.40 ± 3.97	35.81 ± 4.83	t=1.759	0.082
WBCs 10^3 /µL	8.08 ± 3.33	6.72 ± 1.39	U=857.50	0.054
PLTs 10^3 /µL	263.4 ± 75.49	282. 2 ± 72.99	t=1.199	0.233

t: Student t-test. - **U:** Mann Whitney test- ***:** Statistically significant at $p \leq 0.05$
χ^2: Chi square test - M: Male - F: Female

Table (2): Comparison between the two studied groups according to genotypes

Genotypes	Diabetes (n = 66)		Non diabetes (n = 34)		χ^2	p	OR	CI. 95% (LL – UL)
	No.	%	No.	%				
KCNQ1 (rs2237892)								
CC	16	24.2	10	29.4	0.312	0.577	0.768	0.304 – 1.943
CT	40	60.6	12	35.3	5.760*	0.016*	2.821	1.194 – 6.661
TT	10	15.2	12	35.3	5.306*	0.021*	0.327	0.124 – 0.867
HWE	**0.071**		**0.089**					
Allele								
C	72	54.5	32	47.1	1.008	0.315	1.350	0.751 – 2.427
T	60	45.5	36	52.9			0.741	0.412 – 1.332
KCNQ1 (rs2237895)								
AA	51	77.3	29	85.3	0.902	0.342	0.586	0.193 – 1.779
AC	12	18.2	4	11.8	0.688	0.407	1.667	0.494 – 5.625
CC	3	4.5	1	2.9	0.150	FEp=1.000	1.571	0.157 – 15.706
HWE	**0.064**		**0.117**					
Allele								
A	114	86.4	62	91.2	0.984	0.321	0.613	0.231 – 1.624
C	18	13.6	6	8.8			1.632	0.616 – 4.323
TCF7L2 (rs7903146)								
CC	15	21.2	2	5.9	4.513	0.034*	4.706	1.009 – 21.956
CT	25	37.9	13	38.2	0.001	0.972	0.985	0.420 – 2.309
TT	26	40.9	19	55.9	2.465	0.116	0.513	0.222 – 1.186
HWE	**0.073**		**0.909**					
Allele								
C	55	41.7	17	25.0	5.411*	0.020*	2.143	1.120 – 4.100
T	77	58.3	51	75.0			0.467	0.244 – 0.893

χ^2: Chi square test FE: Fisher Exact p: p value for comparing between the studied groups *: Statistically significant at $p \leq 0.05$ OR_1: Odds ratio
CI: Confidence interval LL: Lower limit UL: Upper Limit
If $P < 0.05$ - not consistent with HWE. Not accurate if <5 individuals in any genotype group

Association between TCF_7L_2 (rs7903146) and $KCNQ_1$ (rs2237895 & rs2237892) genetic variants and risk of developing type 2 diabetes (T_2D) in Egyptian populations

Table (3): Relation between KCNQ1 (rs2237892) and different parameters in diabetes group (n = 66).

	KCNQ1 (rs2237892)						Test of Sig.	p
	CC (n = 16)		CT (n = 40)		TT (n = 10)			
	No.	%	No.	%	No.	%		
Age (years)								
30 – 40	1	6.3	2	5.0	1	10.0		
41 – 50	4	25.0	8	20.0	4	40.0		
51 – 60	4	25.0	13	32.5	3	30.0	χ^2=4.717	0.809
61 – 70	5	31.3	15	37.5	2	20.0		
71 – 80	2	12.5	2	5.0	0	0.0		
Min. – Max.	40.0 – 74.0		40.0 – 77.0		37.0 – 66.0			
Mean ± SD.	56.81 ± 11.0		57.38 ± 9.55		52.10 ± 9.31		F=1.154	0.322
Median	58.0		59.0		50.50			
Gender								
Male	7	43.8	18	45.0	5	50.0	χ^2=0.105	0.949
Female	9	56.3	22	55.0	5	50.0		
FBS (mg/dl)								
Min. – Max.	104.0 – 422.0		82.0 – 455.0		100.0 – 471.0			
Mean ± SD.	229.9 ± 102.3		183.3 ± 101.0		183.2 ± 129.4		H=4.203	0.122
Median	214.0		151.0		130.5			
HbA1c (%)								
Min. – Max.	5.50 – 15.60		4.80 – 14.80		5.70 – 15.60			
Mean ± SD.	11.36 ± 3.67		8.77 ± 2.45		9.13 ± 3.58		F=4.448*	0.016*
Median	11.05		7.95		7.85			
Total cholesterol (mg/dl)								
Min. – Max.	108.0 – 298.0		98.0 – 311.0		122.0 – 341.0			
Mean ± SD.	184.4 ± 50.11		183.5 ± 47.3		183.9 ± 65.52		F=0.002	0.998
Median	181.0		174.0		160.5			
Triglycerides (mg/dl)								
Min. – Max.	65.0 – 362.0		60.0 – 449.0		72.0 – 270.0			
Mean ± SD.	165.7 ± 79.96		166.9 ± 89.97		169.1 ± 82.86		H=0.057	0.972
Median	165.0		150.0		178.0			
HDL (mg/dl)								
Min. – Max.	21.0 – 51.0		21.0 – 73.0		20.0 – 90.0			
Mean ± SD.	37.81 ± 9.34		41.20 ± 12.84		35.60 ± 21.90		H=3.973	0.137
Median	38.50		39.0		28.0			
LDL (mg/dl)								
Min. – Max.	48.0 – 242.0		21.0 – 217.0		55.0 – 232.0			
Mean ± SD.	113.4 ± 49.76		109.2 ± 46.87		114.4 ± 53.74		F=0.071	0.932
Median	102.0		100.0		102.0			
Urea (mg/dl)								
Min. – Max.	22.0 – 75.0		20.0 – 126.0		23.0 – 55.0			
Mean ± SD.	39.25 ± 15.52		39.68 ± 19.38		35.30 ± 9.26		H=0.152	0.927
Median	33.0		34.0		32.50			
Creatinine (mg/dl)								
Min. – Max.	0.80 – 1.88		0.62 – 3.98		0.88 – 1.20			
Mean ± SD.	1.06 ± 0.30		1.05 ± 0.52		1.01 ± 0.11		H=0.803	0.669
Median	0.97		0.96		1.0			

GPT (U/L)					
Min. – Max.	17.0 – 41.0	11.0 – 59.0	10.0 – 52.0		
Mean ± SD.	25.38 ± 6.53	26.13 ± 11.84	27.60 ± 11.43	H=0.511	0.774
Median	24.0	23.50	26.0		
GOT (U/L)					
Min. – Max.	18.0 – 53.0	14.0 – 66.0	10.0 – 53.0		
Mean ± SD.	28.19 ± 8.26	29.82 ± 12.52	28.30 ± 11.89	F=0.150	0.861
Median	26.0	29.0	28.0		
Hb					
Min. – Max.	10.60 – 16.70	8.80 – 15.60	10.80 – 14.50		
Mean ± SD.	13.19 ± 1.54	12.34 ± 1.61	12.85 ± 1.36	F=1.847	0.166
Median	13.50	12.35	13.35		
RBCs					
Min. – Max.	4.03 – 5.57	3.45 – 5.64	4.05 – 5.17		
Mean ± SD.	4.71 ± 0.45	4.63 ± 0.45	4.73 ± 0.42	F=0.342	0.711
Median	4.76	4.65	4.82		
HCT					
Min. – Max.	31.90 – 46.20	28.20 – 42.90	31.80 – 43.40		
Mean ± SD.	39.10 ± 4.07	36.61 ± 3.75	37.83 ± 4.13	F=2.416	0.098
Median	38.60	36.80	39.10		
WBCs					
Min. – Max.	4.50 – 14.50	2.70 – 14.20	1.90 – 21.40		
Mean ± SD.	8.30 ± 2.92	7.87 ± 2.93	8.55 ± 5.29	H=0.188	0.910
Median	7.85	7.30	7.20		

χ^2: Chi square test MC: Monte Carlo H: H for Kruskal Wallis test

F: F for ANOVA test

p: p value for comparison between different categories *: Statistically significant at $p \leq 0.05$

Association between TCF_7L_2 (rs7903146) and $KCNQ_1$ (rs2237895 & rs2237892) genetic variants and risk of developing type 2 diabetes (T_2D) in Egyptian populations

Table (4): Relation between KCNQ1 (rs2237895) and different parameters in diabetes group (n = 66).

	KCNQ1 (rs2237895)						Test of Sig.	p
	AA (n = 51)		AC (n = 12)		CC (n = 3)			
	No.	%	No.	%	No.	%		
Age (years)								
30 – 40	2	3.9	2	16.7	0	0.0		
41 – 50	11	21.6	3	25.0	2	66.7		
51 – 60	16	31.4	3	25.0	1	33.3	χ^2=7.166	^{MC}p=0.417
61 – 70	19	37.3	3	25.0	0	0.0		
71 – 80	3	5.9	1	8.3	0	0.0		
Min. – Max.	40.0 – 77.0		37.0 – 74.0		46.0 – 60.0		F=1.109	0.336
Mean ± SD.	57.41 ± 9.55		53.42 ± 11.69		52.0 ± 7.21			
Gender								
Male	22	43.1	7	58.3	1	33.3	χ^2=1.187	^{MC}p=0.641
Female	29	56.9	5	41.7	2	66.7		
FBS (mg/dl)								
Min. – Max.	82.0 – 455.0		84.0 – 413.0		123.0 – 471.0		H=0.828	0.661
Mean ± SD.	190.3 ± 104.1		196.6 ± 98.82		258.7 ± 186.2			
HbA1c (%)								
Min. – Max.	4.80 – 15.60		5.90 – 15.10		5.70 – 14.30		F=0.930	0.400
Mean ± SD.	9.20 ± 2.97		10.56 ± 3.45		9.20 ± 4.52			
Total cholesterol (mg/dl)								
Min. – Max.	98.0 – 341.0		108.0 – 232.0		155.0 – 239.0		F=0.027	0.973
Mean ± SD.	184.5 ± 52.53		180.7 ± 43.53		183.7 ± 47.93			
Triglycerides (mg/dl)								
Min. – Max.	60.0 – 362.0		65.0 – 449.0		78.0 – 241.0			
Mean ± SD.	165.6 ± 83.20		170.8 ± 101.0		175.0 ± 85.81		H=0.105	0.494
Median	152.0		152.5		206.0			
HDL (mg/dl)								
Min. – Max.	20.0 – 90.0		21.0 – 54.0		20.0 – 37.0		H=5.123	0.077
Mean ± SD.	41.39 ± 13.80		34.92 ± 12.52		26.33 ± 9.29			
LDL (mg/dl)								
Min. – Max.	21.0 – 242.0		57.0 – 186.0		72.0 – 178.0		F=0.111	0.895
Mean ± SD.	109.8 ± 49.85		113.3 ± 41.22		122.3 ± 53.20			
Urea (mg/dl)								
Min. – Max.	20.0 – 126.0		22.0 – 60.0		30.0 – 41.0		H=0.024	0.988
Mean ± SD.	39.55 ± 18.44		37.25 ± 13.50		34.67 ± 5.69			
Creatinine(mg/dl)								
Min. – Max.	0.62 – 3.98		0.72 – 1.88		0.98 – 1.20		H=0.969	0.616
Mean ± SD.	1.05 ± 0.47		1.0 ± 0.30		1.06 ± 0.12			
GPT (U/L)								
Min. – Max.	10.0 – 56.0		19.0 – 59.0		18.0 – 26.0		H=1.284	0.526
Mean ± SD.	25.69 ± 10.08		29.50 ± 13.37		21.0 ± 4.36			
GOT (U/L)								
Min. – Max.	14.0 – 53.0		15.0 – 66.0		10.0 – 27.0		F=1.380	0.259
Mean ± SD.	29.06 ± 10.75		32.08 ± 14.02		20.0 ± 8.89			

Hb					
Min. – Max.	8.80 – 16.70	9.80 – 15.20	10.70 – 13.50	F=1.355	0.265
Median	12.40	13.50	11.20		
RBCs					
Min. – Max.	3.45 – 5.64	4.11 – 5.57	4.07 – 4.66	F=2.936	0.060
Mean ± SD.	4.62 ± 0.44	4.91 ± 0.42	4.38 ± 0.30		
HCT					
Min. – Max.	28.20 – 45.0	32.60 – 46.20	31.80 – 39.70	F=1.430	0.247
Mean ± SD.	37.20 ± 3.99	38.86 ± 3.69	35.03 ± 4.14		
WBCs					
Min. – Max.	1.90 – 14.50	5.0 – 11.70	7.0 – 21.40	H=2.757	0.252
Mean ± SD.	7.70 ± 3.05	8.63 ± 2.42	12.30 ± 7.92		
PLTs					
Min. – Max.	120.0 – 404.0	184.0 – 407.0	179.0 – 450.0	F=1.183	0.313
Mean ± SD.	260.0 ± 71.91	261.7 ± 74.19	328.7 ± 137.7		

χ^2: Chi square test MC: Monte Carlo H: H for Kruskal Wallis test
F: F for ANOVA test p: p value for comparison between different categories

Association between TCF_7L_2 (rs7903146) and $KCNQ_1$ (rs2237895 & rs2237892) genetic variants and risk of developing type 2 diabetes (T_2D) in Egyptian populations

Table (5): Relation between TCF7L2 (rs7903146) and laboratory investigation in diabetes group (n = 66).

	TCF7L2 (rs7903146)						Test of Sig.	p
	CC (n = 15)		CT (n = 25)		TT (n = 26)			
	No.	%	No.	%	No.	%		
Age (years)								
30 – 40	1	6.7	2	8.0	1	3.8		
41 – 50	2	13.3	6	24.0	8	30.8		
51 – 60	4	26.7	10	40.0	6	23.1	χ^2=6.098	^{MC}p=0.657
61 – 70	7	46.7	5	20.0	10	38.5		
71 – 80	1	6.7	2	8.0	1	3.8		
Min. – Max.	40.0 – 73.0		37.0 – 74.0		40.0 – 77.0		F=0.331	0.719
Mean ± SD.	5787 ± 9.87		55.28 ± 10.34		56.73 ± 9.77			
Gender								
Male	9	60.0	10	40.0	11	42.3	χ^2=1.684	0.431
Female	6	40.0	15	60.0	15	57.7		
FBS (mg/dl)								
Min. – Max.	86.0 – 471.0		83.0 – 422.0		82.0 – 455.0		H=2.021	0.364
Mean ± SD.	162.9 ± 98.52		198.5 ± 101.3		209.1 ± 117.8			
HbA1c (%)								
Min. – Max.	5.30 – 15.10		4.80 – 15.60		5.70 – 15.60		F=1.236	0.297
Mean ± SD.	8.74 ± 3.08		10.19 ± 3.56		9.14 ± 2.61			
Toal cholesterol (mg/dl)								
Min. – Max.	131.0 – 341.0		108.0 – 298.0		98.0 – 311.0		F=0.963	0.387
Mean ± SD.	198.1 ± 52.3		175.3 ± 48.5		183.6 ± 50.59			
Triglycerides (mg/dl)								
Min. – Max.	73.0 – 302.0		60.0 – 362.0		66.0 – 449.0		H=0.363	0.834
Mean ± SD.	162.4 ± 71.87		161.0 ± 90.36		175.3 ± 89.93			
HDL (mg/dl)								
Min. – Max.	20.0 – 90.0		20.0 – 73.0		21.0 – 70.0		H=0.601	0.740
Mean ± SD.	38.40 ± 16.71		39.36 ± 12.93		40.35 ± 13.29			
LDL (mg/dl)								
Min. – Max.	78.0 – 232.0		22.0 – 242.0		21.0 – 217.0		F=1.187	0.312
Mean ± SD.	127.2 ± 46.15		103.7 ± 48.52		108.7 ± 47.93			
Urea (mg/dl)								
Min. – Max.	20.0 – 67.0		23.0 – 126.0		21.0 – 75.0		H=0.220	0.896
Mean ± SD.	37.87 ± 15.33		40.76 ± 21.42		37.73 ± 13.78			
Creatinine(mg/dl)								
Min. – Max.	0.76 – 1.50		0.70 – 3.98		0.62 – 1.40		H=0.009	0.996
Mean ± SD.	1.01 ± 0.22		1.13 ± 0.65		0.98 ± 0.20			
GPT (U/L)								
Min. – Max.	12.0 – 59.0		10.0 – 52.0		13.0 – 56.0		H=1.161	0.560
Mean ± SD.	28.07 ± 13.66		26.60 ± 9.58		24.65 ± 9.75			
GOT (U/L)								
Min. – Max.	10.0 – 66.0		14.0 – 53.0		14.0 – 48.0		F=0.305	0.738
Mean ± SD.	29.73 ± 15.16		30.28 ± 11.24		27.85 ± 9.21			
Hb								
Min. – Max.	8.80 – 15.60		9.50 – 16.70		9.80 – 15.20		F=0.201	0.818
Mean ± SD.	12.81 ± 1.94		12.66 ± 1.56		12.48 ± 1.42			

RBCs					
Min. – Max.	3.45 – 5.64	3.49 – 5.35	4.07 – 5.57	F=0.823	0.444
Mean ± SD.	4.79 ± 0.56	4.62 ± 0.44	4.63 ± 0.36		
HCT					
Min. – Max.	28.20 – 43.90	28.20 – 46.20	31.80 – 44.80	F=0.189	0.828
Mean ± SD.	37.96 ± 4.45	37.25 ± 4.20	37.22 ± 3.56		
WBCs					
Min. – Max.	1.90 – 21.40	2.70 – 13.30	3.90 – 14.20	H=5.420	0.067
Mean ± SD.	9.91 ± 4.67	7.89 ± 2.71	7.20 ± 2.59		
PLTs					
Min. – Max.	137.0 – 450.0	143.0 – 407.0	120.0 – 392.0	F=0.350	0.706
Mean ± SD.	252.9 ± 74.08	272.8 ± 74.97	260.5 ± 78.66		

χ^2: Chi square test MC: Monte Carlo H: H for Kruskal Wallis test
F: F for ANOVA test p: p value for comparison between different categories

العلاقة بين المتغيرات الجينية $KCNQ_1$(rs2237895&rs2237892) , TCF_7L_2 (rs7903146) وخطر الإصابة بمرض السكرمن النوع الثاني في السكان المصريين

محمود عبد الحميد الشناوي[1] * ، مصطفى عبد الصمد صقر[2] ، محمد فاروق الشال[1]، شهيرة مرسى الشافعي[3] ، محمد يونس نصر[1]
1- قسم البيولوجيا ، معهد بحوث الهندسة الوراثية والتكنولوجيا الحيوية (GEBRI) ، جامعة مدينة السادات ، مدينة السادات ، مصر.
"2- قسم المشخصات الجزيئية والعلاجيات، معهد بحوث الهندسة الوراثية والتكنولوجيا الحيوية (GEBRI) ، جامعة مدينة السادات ، مصر"
3- - قسم الباثولوجيا الاكلينيكية ، كلية الطب، جامعة الفيوم ، مصر.
*البريد الالكترونى للباحث الرئيسى: mahmoud.abdelhamid.stu@gebri.usc.edu.eg
البريد اللكترونى للباحثين المشاركين:
Mostafa.sakr@gebri.usc.edu.eg
mohamed.younis@gebri.usc.edu.eg

المستخلص

يعد مرض السكر حالة خطيرة يرتفع فيها مستوى الجلوكوز في الدم وذلك بسبب عدم افراز كمية كافية من الأنسولين أو عدم قدرة الجسم على إستخدام الأنسولين وهو النوع الأكثر انتشارا من السكر، ويؤثر على ما يقرب من 90٪ من مرضى السكر على مستوى العالم. في مرضى السكر من النوع الثاني لا تستجيب العضلات والدهون وخلايا الكبد بشكل مناسب للأنسولين، وبالتالي لا تستطيع امتصاص الجلوكوز من الدم أو تخزينه بشكل فعال. ويعرف هذا بمقاومة الإنسولين. ولتعويض ذلك يقوم البنكرياس بإنتاج كميات إضافية من الأنسولين ، وبمرور الوقت لا يتمكن البنكرياس من الإستمرار في إنتاج الأنسولين الكافي للمحافظة على مستويات الجلوكوز الطبيعية في الدم. كان الهدف من هذه الدراسة هو استنتاج وجود علاقة بين الجينات (TCF_7L_2) and $KCNQ_1$) ومرض السكر في السكان المصريين . تم إجراء تحليل PCR-RFLP على $KCNQ_1$ (rs2237892 and rs2237895)، TCF_7L_2 (rs7903146)بواقع 66 مريضا من T_2D و 34 من الأصحاء. وقد تبين وجود علاقة بين مرض السكر وبين الجينات $KCNQ_1$ (rs2237892) and TCF_7L_2 (rs7903146) وعدم وجود علاقة بين مرض السكر و الجين KCNQ1 (rs2237895). في الختام ، يعتبر كل من TCF_7L_2 (rs7903146) و $KCNQ_1$ (rs2237892) من أكثر العوامل الوراثية التي تؤثر على مرض السكري من النوع الثاني في مصر.