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The Relationship Between genetic variations of KCNQ1 with insulin resistance and type 2 diabetes in a sample of Iraqi population

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Abstract

Background and objectives: Type 2 diabetes is a common complex disorder, characterized by chronic hyperglycemia as the result of an incapacity of the pancreatic beta cells to compensate for the degree of insulin resistance .Polymorphisms in the potassium channel, voltage-gated, KQT-like subfamily, member 1 (KCNQ1) have recently been reported to associate with type 2 diabetes. The present study was to investigate the impact of these KCNQ1 polymorphisms (rs2237892, and rsl51290) in Iraqi population.

Methods:

The study was conducted in 600 Iraqi population**.**, This case-control study involved 300 T2DM patients and 300 healthy controls. The KCNQ1 (rs2237892, and rsl51290) polymorphism was genotyped by Restriction Fragment Length Polymorphism (RFLP).

Results: Hardy Weinberg equilibrium for KCNQ1 (rs2237892) control group, patients' group and all subjects as a group possess highly significant deviation ($p < 0.001$), when the dominant, codominant, recessive and additive models were taken into account.. There was highly significant difference in mean BMI, cholesterol, triglyceride, LDL ,insulin and IR among CC, CT and TT genotypes groups ($p <$

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0.001), while There was significant difference in mean FBS,VLDL among CC, CT and TT genotypes groups (p = 0.020)and (p = 0.041) respectively also there was no significant difference in mean HDL among patients with CC, C/T and TT genotypes (p = 0.475). Hardy Weinberg equilibrium for KCNQ1(rsl51290) control group, patients' group and all subjects as a group possess highly significant deviation (p < 0.001) ,when the dominant, codominant, recessive and additive models were taken into account. There was no significant difference in mean of BMI, FBS, cholesterol, HDL, LDL and VLDL among AA, AC and CC genotypes (p= 0.036, p= 0.186, p= 0.731, p= 0.054, p= 0.317, p= 0.521 respectively), while there was a highly significant difference in mean of triglyceride , IR and insulin among AA, AC and CC genotypes groups (p = 0.007), (p = 0.004 *and* p = 0.003). Haplotype analysis of the *KCNQ1* SNPs showed a significant association with T2DM increase to develop the disease under H 4, while there was no association with the H 2. Haplotyping of *KCNQ1* gene SNPs (rs2237892, and rsl51290). However, other models H1 and H3to explore highly significant association.

Conclusion: This study showed that (rs2237892, and rsl51290) polymorphism of the KCNQ1 gene is an important risk factor for type 2 diabetes mellitus in a sample of the Iraqi population.

Keywords: KCNQ1 , rs2237892 , polymorphism , type 2 diabetes mellitus.

Introduction:

Diabetes is a group of metabolic disorders characterized by a chronic hyperglycemic condition resulting from insufficient action of insulin. The main pathophysiological features of type 2 diabetes, are impaired insulin secretion and increased insulin resistance. The impairment of pancreatic _ cell function notably shows progression over time [1]. Ongoing hyperglycemia may related with long haul harm,

brokenness, and disappointment of various organs ,, for example, ; eyes, kidneys, nerves, heart, and veins [2]. The two types (typ1 and typ2)sorts lead to sporadic hyperglycemia, monstrous pee creation, thirst, liquid admission, obscured vision, weight reduction, laziness, and changes in digestion. T2DM were a complex heterogeneous gatherings of metabolic conditions lead to expanded of blood glucose levels because of debilitated in insulin activity as well as insulin emission [3]. The prevalence of type 2 diabetes mellitus (T2DM) is rising rapidly owing to increased economic growth and lifestyle changes in both developed and developing countries. Numerous genetic and environmental factors are analyzed for their involvement in the pathogenesis of the disease [4]. Attempts are continues to realize the genetic background of T2 DM. Genome-wide association studies (GWAS) have led to the identification of diabetes susceptibility genes. To date, at least 40 genetic loci have been suggested to be associated with T2DM, including KCNQ1, CDKAL1, TCF7L2, HMG20A, HNF4A, HNF1B, and DUSP9 [5,6]. However, different findings were obtained, some of them exhibited association in certain populations [7,8]. KCNQ1 gene is situated on chromosome 11p15.5. It codes the pore- forming alpha subunit of the voltage-gated K+ channel one. It is expressed in a few tissues including insulin-secreting cells. It has been accounted for that the hindrance of this channel prompts increment insulin discharge. On the other hand, the over-articulation of KCNQ1 gene brought about impairment of insulin secretion [9].

The aim of this study was to examine KCNQ1 gene, previously shown to be associated with T2DM. what is the impact of haplotype analysis on the risk of T2DM as well as the glycemic indices.

Material and Methods

The collection of specimens was done between January 2019 until January 2020. These study subjects included 300 subjects with T2DM and 300 controls. We selected the gene of KCNQ1 for study and amplified them using the polymerase chain reaction. This was followed by genotyping for single nucleotide polymorphisms Biochemical methods were done in laboratory of the department of Biochemistry in the faculty of medicine, University of Kufa, Iraq.

Inclusion criteria includes patients are diagnosed by physicians as having T2DM. The criteria of diagnosis of diabetes will depend on the WHO guidelines. exclusion

criteria include Patients of < 18 years old and type 1 diabetics or those on insulin injection.

A case-control analysis was study with 300 Iraqi diabetic patients (153 males and 147 females) with T2DM diabetes was chosen for this study. In addition, 300 control group (156 men and 144 women). After fasting for around 10 hours, samples of 5 ml venous blood (2 ml on a dry tube and 3 ml into EDTA tubes) were taken. The DNA was isolated and genetic variation was analyzed using an EDTA tube. Assays involving biochemistry total Cholesterol (TC), Triglyceride (TG), high density lipoprotein (HDL),very low density lipoprotein (VLDL), low density lipoprotein (LDL), insulin resistance (IR), body mass index (BMI), and insulin. were all measured using an enzyme-based approach (Glucose Oxidase Peroxidase) while TC,TG [10], HDL[11], VLDL [12], LDL [12]. on an enzymatic procedures (BIAOLABO kit) ,insulin by ElZA kit [13,14]. The Blood DNA extraction kit was used to remove Molecular Genotyping DNA from whole blood. The purity and concentration of the isolated DNA were determined Store the purified DNA at -20C. For the polymerase chain reaction, the isolated DNA was held (PCR). Restriction fragment length polymorphism was used to genotype the KCNQ1(rs2237892, and rsl51290) polymorphisms (RFLP).

1. Phenotype measurements

The biochemical analyses including FBS, Cholesterol, TG, HDL, LDL, VLDL and serum insulin. The insulin resistance will be calculated according to HOMA-IR=Fasting insulin (μU/mL) x Fasting glucose (mg/dL) /405 Standardized methods will be used to obtain phenotype measurements such as weight and height. The BMI was determined by dividing the weight (in kg) by the square of height (in m). The patient's blood pressure and waist-to-hip circumference will be measured as well[15] .

2. **Statistical Analysis**

The statistical program (SPSS Ver. 21) was used for statistical analysis. The chi-square test was used to determine whether the genotype distributions were in Hardy-Weinberg equilibrium. The frequency of the genotypes and alleles were compared between the two groups using chi-square test. The odds ratios were calculated using a logistic regression model. P-value < 0.05 was considered statistically significant.

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3. Genotyping

DNA will be extracted from blood using DNA extraction kit (TRAN) . Genotyping will be carried out by PCR-restriction fragment length polymorphism (RFLP) for KCNQ1 SNPs (rs2237892 and rsl51290) . PCR products were digested with restriction enzymes and the digestion products were be separated on a 2% agarose gel .Primers were supplied by Alpha-DNA as a lyophilized powder. Lyophilized primers were dissolved by nuclease free water or Tris EDTA buffer (TE- buffer) in order to prepare the master primer`s stock which subsequently utilized in preparation of small aliquots of working solution . In this study the procedure of the primer`s reconstitution according to the instructions of the kit. The primer`s sequence of KCNQ1 gene for rs2237892 and rs151290 SNP were presented by [16]. The primers sequencing applied for PCR amplification of KCNQ1gene SNPs (rs2237892 and rsl51290) are revealed in Table 3.1.

Table 3.1: The primer sequencing employed to amplify KCNQ1 gene polymorphisms (rs2237892 and rsl51290).

SNP	primer	sequences
rs2237892	F	**5'-CTTGTGCCCTTGTCACCCAC-3'**
	R	**5'-GGCTTCCAGCCTCCAAGCTG-3'**
rsl51290	F	**5′-AGCCGTTCCTGCTTGCTACT -3′**
	R	**5′-TGGGAGTGGTTCCAAGGACA-3′**

4.Results:

4.1. KCNQ1 gene locus rs2237892 PCR-RFLP electrophoresis results.

DNA was extracted from the blood and the amplification of the KCNQ1 gene was performed using template DNA and specific primers. The product of PCR was electrophoresed on 2% agarose (120min and 75V) and immediately envisaged under the UV light. The amplification product of KCNQ1gene SNP (rs2237892*CT*) was found to be 354bp (Fig 4.1).

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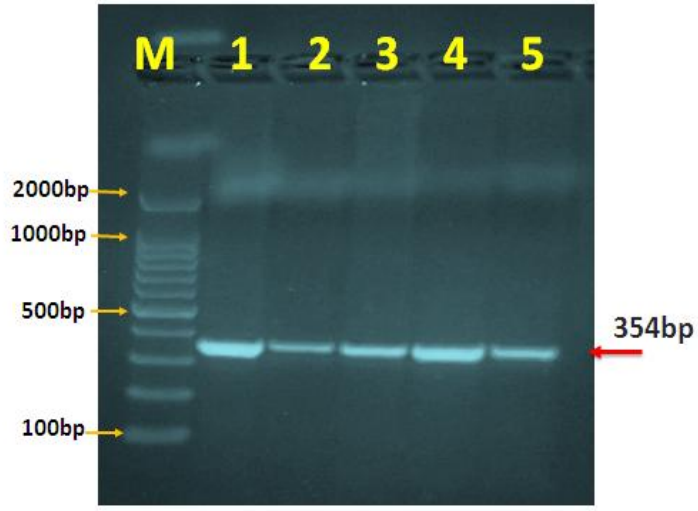

Fig 4.1. KCNQ1 gene locus rs2237892 PCR-RFLP electrophoresis results.

4.2. KCNQ1 gene locus rsl51290 PCR-RFLP electrophoresis results.

DNA was extracted from the blood and the amplification of the KCNQ1 gene was performed using template DNA and specific primers. The product of PCR was electrophoresis on 2% agarose (120min and 75V) and immediately envisaged under the UV light. The amplification product of KCNQ1gene SNP (rs151290AC) was found to be 105bp (Fig 4.2).

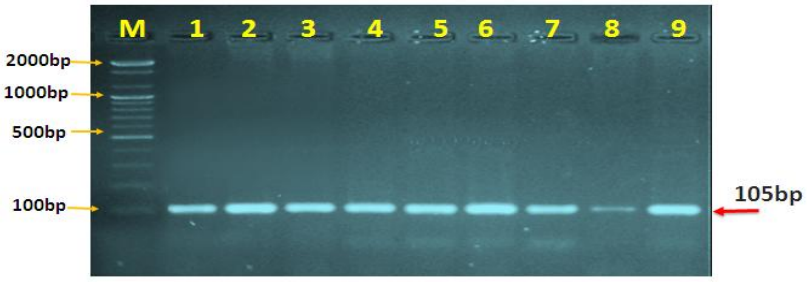

Fig 4.2 . KCNQ1 gene locus rsl51290 PCR-RFLP electrophoresis results.

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4.3.RFLP analysis

The digestion of PCR product of rs2237892 SNP of KCNQ1 gene has been carried out by *MspI* restriction enzyme. The agarose gel electrophoresis has been used to examine the digestion products. The outcomes demonstrated two bands of wild type (CC) (296, 85 bp) bands, one bands of homozygous (TT) (354 bp) band and three bands of heterozygous (CT) (354, 269, 85 bp) bands genotypes as illustrated in figure 4.3 and table 4.1

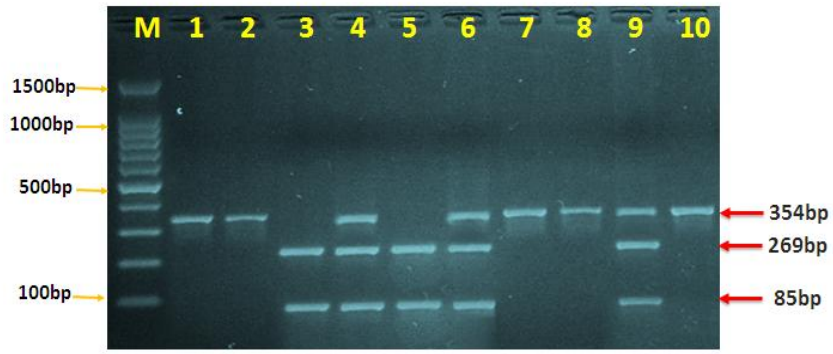

Figure 4.3. PCR product of rs2237892 (C / T) SNP of KCNQ1gene digested by restriction enzyme and electrophoresed on 2% agarose gel electrophoresis. Lane 1: 3, 5: Marker of DNA100bp was CC. Lanes 2: 4,6,9: CT genotype. Lanes3: 1,2,7,8,10 was TT genotypes using gel stain.

Table 4.1. Digestion results of rs2237892C/T SNP of KCNQ1gene product.

Geno type		No of bands	Size of (bp)
Wild type	C	2	269,85
Heterozygous	C	3	354,269,85
Homozygous	T	1	354

The digestion of PCR product of rs151290 SNP of KCNQ1gene has been carried out by *BgII* restriction enzyme. The agarose gel electrophoresis has been used to assess the digestion products. Results indicated a wild type (*AA*) with one (105 bp) band, homozygous (*CC*) genotype with one (81 bp) bands and heterozygous (*AC*) genotypes with two (105, 81 bp) bands, as shown in Figures (4.4) and Table (4.2).

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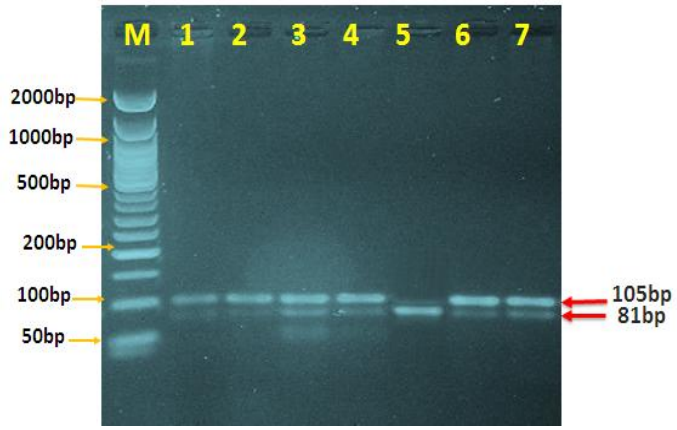

Figure 4.4. PCR product of rs151290*AC* SNP of KCNQ1gene digested by restriction enzyme and electrophoresed on 2% agarose gel electrophoresis. Lane 1:1,2: Marker of DNA50bp was AA. Lanes 2: 3,4,6,7: AC genotype. Lanes3: 5 :CC genotypes using gel stain.

Table 4.2. Digestion results of rs151290*AC* SNP of KCNQ1gene product

Genotype		No of	Size of (bp)
Wild type	A	1	105
Heterozygous	A	2	105,81
Homozygous	C	1	81

4.4. The frequency distribution of KCNQ1 rs2237892 (*CT*) SNP genotypes and alleles among patients and control subjects

Hardy Weinberg equation statistics of KCNQ1 rs2237892 (*CT*) SNP genotypes among patients, control subjects and all participants are shown in table 4.3. It has been shown that control group, patients' group and all subjects as a group possess highly significant deviation from natural Hardy Weinberg equilibrium ($p < 0.001$).

Table 4.3. Hardy Weinberg equation statistics of KCNQ1 rs2237892 (*CT*) SNP genotypes among patients, control subjects and all participants**.**

Group	*n*	χ^2	*p*
Control	300	115.77	<0.001 C HS
Patient	300	90.89	<0.001 C

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			HS
All	600	221.27	<0.001 C HS

n: number of cases; **C**: Chi-square test; **HS**: highly significant at $p \leq 0.01$

Comparison of KCNQ1 rs2237892 (CT) SNP genotypes and alleles frequencies between control and patients' groups is shown in table 4.5. The codominance model shown highly significant variation between control and patient groups ($p < 0.001$), in such a way that genotype CC is more frequent in patients group than in control group, whereas, both genotypes CT and CC were less frequent in patients group than in control group. Hence, genotype CT was protective factor against the disease with and odds ratio (OR) of 0.45 (providing protection by a fraction of 55 %) and genotype TT is also protective against disease with an OR of 0.30 (providing protection by a fraction of 70 %).

In the dominant model, it has been shown that genotype CC was a risk factor for the disease in a highly significant manner ($p < 0.001$), with an OR of 2.67 indication that individuals with genotype CC had approximately 33 times risk of having the disease in comparison with individuals having either genotype C/T or TT.

The recessive model has shown that genotype TT is protective in a highly significant manner ($p = 0.004$), with an OR of 0.32 (providing protection by a fraction of 68 %). The additive model confirmed the risk implied by CC genotypes in a highly significant manner ($p < 0.001$). Analysis of alleles has shown that allele C is a risk factor for the disease and allele T is a protective factor against the disease in a highly significant manner ($p < 0.001$). The risk in association with allele C was 2.79 in terms of OR indicating that individuals having allele C are approximately 3 times more liable to have the disease in comparison with individuals having allele T.

Table 4. 5: Comparison of KCNQ1 rs2237892 (CT) SNP genotypes and alleles frequencies between control and patients' groups.

Mode	**KCNQ1 rs2237892 (CT)**	**Control *n* = 300**	**Patient *n* = 300**	***p***	**OR**	**95% CI**

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		***n* (%)**	***n* (%)**			
Codominance	CC	252 (84.0 %)	280 (93.3 %)	0.001 C HS	Reference	
	CT	24 (8.0 %)	12 (4.0 %)		0.45	0.22 -0.92
	TT	24 (8.0 %)	8 (2.7 %)		0.30	0.13 -0.68
Dominant	CC	252 (84.0 %)	280 (93.3 %)	<0.001 C HS	2.67	1.54 -4.62
	CT+TT	48 (16.0 %)	20 (6.7 %)		0.38	0.22 -0.65
Recessive	CC+CT	276 (92.0 %)	292 (97.3 %)	0.004 C HS	Reference	
	TT	24 (8.0 %)	8 (2.7 %)		0.32	0.14 -0.71
Additive	2TT+CT	72	28	<0.001 C HS	0.35	0.22 -0.56
	CC	252	280		Reference	
Allele	C	528 (88.0 %)	572 (95.3 %)	<0.001 C HS	2.79	1.77 -4.38
	T	72 (12.0 %)	28 (4.7 %)		0.36	0.23 -0.56

n: number of cases (or alleles); **OR**: Odds ratio; **CI**: confidence interval; **C**: Chi-square test; **HS**: highly significant at $p \leq 0.01$

Comparison of BMI and biochemical characteristics according to KCNQ1 rs2237892 (CT) SNP genotypes based on codominance model is shown in table 4.6. There was highly significant difference in mean BMI, cholesterol , triglyceride, LDL ,insulin and IR among CC, CT and TT genotypes groups ($p < 0.001$) . There was significant difference in mean FBS,VLDL among CC, CT and TT genotypes groups ($p = 0.020$)and ($p = 0.041$) respectively .There was no significant difference in mean HDL among patients with CC, CT and TT genotypes ($p = 0.475$).

Table 4.6: Comparison of BMI and biochemical characteristics according to KCNQ1 rs2237892 (CT) SNP genotypes based on codominance model .

Characteristic	**CC** ***n* = 280**	**C/T** ***n* = 12**	**TT** ***n* = 8**	***p***
BMI (kg/m^2)	28.90 ±4.49 A	24.47 ±1.33 B	21.95 ±1.12 C	< 0.001 A HS
FBS (mg/dl)	200.38 ±58.33 C	224.00 ±72.60 B	253.00 ±50.25 A	0.020 A S
Cholesterol (mg/dl)	211.20 ±57.19 B	149.33 ±21.60 C	275.50 ±47.57 A	< 0.001 A HS

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TG (mg/dl)	203.04 ±76.20 B	123.00 ±38.87 C	245.00 ±5.35 A	< 0.001 A HS
HDL (mg/dl)	43.90 ±3.39 A	45.00 ±2.26 A	44.50 ±0.53 A	0.475 A NS
VLDL (mg/dl)	41.43 ±20.76 B	28.93 ±9.78 C	49.00 ±1.07 A	0.041 A S
LDL (mg/dl)	137.86 ±47.32 B	94.40 ±12.73 C	187.50 ±42.23 A	< 0.001 A HS
Insulin mIU/L	19.79 ±6.17 B	22.33 ±3.45 B	29.00 ±5.35 A	< 0.001 A HS
IR	8.45 ±4.41 B	13.87 ±0.88 A	14.60 ±2.57 A	< 0.001 HS

Data were expressed as mean ±standard deviation; ***n***: number of cases; **BMI**: body mass index; **FBS**: fasting blood sugar; **TG**: triglyceride; **HDL**: high density lipoprotein; **VLDL**: very low density lipoprotein; **LDL**: low density lipoprotein; **A**: one way **ANOVA**; capital letters were used to indicate the level of significance following performing **post hoc Dunnet's 3 test** (unequal size and unequal variance) so that similar letters indicate no significant difference whereas different letters indicate significant difference in such a way that letter **A** takes the highest value followed by letter **B** and then by letter **C; NS:** not significant at $p > 0.05$**; S:** significant at $p \leq 0.05$**; HS: highly** significant at $p \leq 0.01$**.**

4.5 The frequency distribution of KCNQ1 rsl51290 (A/C) SNP genotypes and alleles among patients and control subjects

Hardy Weinberg equation statistics of KCNQ1 rsl51290 (A/C) SNP genotypes among patients, control subjects and all participants are shown in table 4. It h.7as been shown that control group, patients' group and all subjects as a group possess highly significant deviation from natural Hardy Weinberg equilibrium ($p < 0.001$).

Table 4.7: Hardy Weinberg equation statistics of KCNQ1 rsl51290 (AC) SNP genotypes among patients, control subjects and all participants

Group	***n***	χ^2	***p***
Control	300	58.690	<0.001 C HS
Patient	300	64.02	<0.001 C HS
All	600	121.050	<0.001 C HS

n: number of cases; **C**: Chi-square test; **HS**: highly significant at $p \leq 0.01$

Comparison of KCNQ1 rsl51290 (AC) SNP genotypes and alleles frequencies between control and patients' groups is shown in table 4.8. The codominance model, the dominant model, the recessive model, the additive model and the allele analysis

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have failed to show any significant variation between control and patient groups ($p > 0.05$); therefore, it can be inferred that KCNQ1 rsl51290 (AC) SNP is not significantly associated with disease.

Table 4.8: Comparison of KCNQ1 rsl51290 (AC) SNP genotypes and alleles frequencies between control and patients' groups

Model	KCNQ1 rsl51290 (AC)	Control *n* = 300 *n* (%)	Patient *n* = 300 *n* (%)	*p*	OR	95% CI
Codominance	AA	36 (12.0 %)	46 (15.3 %)	0.194 C NS	Reference	
	AC	216 (72.0 %)	219 (73.0 %)		0.79	0.49 - 1.28
	CC	48 (16.0 %)	35 (11.7 %)		0.57	0.31 - 1.06
Dominant	AA	36 (12.0 %)	46 (15.3 %)	0.235 C NS	1.33	0.83 - 2.12
	AC+CC	264 (88.0 %)	254 (84.7 %)		0.75	0.47 - 1.20
Recessive	AA+AC	252 (84.0 %)	265 (88.3 %)	0.124 C NS	Reference	
	CC	48 (16.0 %)	35 (11.7 %)		0.69	0.43 - 1.11
Additive	2CC+AC	312	289	0.173 C NS	0.72	0.46 - 1.15
	AA	36	46		Reference	
Allele	A	288 (48.0 %)	311 (51.8 %)	0.184 C NS	1.17	0.93 - 1.46
	CC	312 (52.0 %)	289 (48.2 %)		0.86	0.68 - 1.08

n: number of cases (or alleles); **OR**: Odds ratio; **CI**: confidence interval; **C**: Chi-square test; **NS**: not significant at $p > 0.05$

Comparison of BMI and biochemical characteristics according to KCNQ1 rsl51290 (AC) SNP genotypes based on codominance model is shown in table 4.9. There was no significant difference in mean of BMI, FBS, cholesterol, HDL, LDL and VLDL among AA, AC and CC genotypes (p= 0.036, p= 0.186, p= 0.731, p= 0.054, p= 0.317, p= 0.521 respectively) ,while there was a highly significant difference in mean of

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triglyceride , IR and insulin among AA, AC and CC genotypes groups (p = 0.007), (p = 0.004 *and* p = 0.003).

Table 4.9.: Comparison of BMI and biochemical characteristics according to KCNQ1 rsl51290 (AC) SNP genotypes based on codominance model.

Characteristic	AA *n* = 46	AC *n* = 219	CC *n* = 35	*p*
BMI (kg/m^2)	27.34 ±3.44 A	28.60 ±4.66 A	29.71 ±5.00 A	0.063 A NS
FBS (mg/dl)	190.67 ±56.07 A	206.49 ±57.56 A	195.03 ±72.06 A	0.186 A NS
Cholesterol (mg/dl)	209.30 ±56.84 A	209.51 ±58.95 A	217.77 ±56.18 A	0.731 A NS
TG (mg/dl)	232.83 ±75.93 A	194.41 ±73.76 B	200.06 ±81.34 B	0.007 A HS
HDL (mg/dl)	44.65 ±4.47 A	43.66 ±3.14 A	44.91 ±2.16 A	0.054 A NS
VLDL (mg/dl)	45.15 ±15.22 A	40.62 ±21.68 A	39.05 ±16.94 A	0.317 A NS
LDL (mg/dl)	143.85 ±43.73 A	136.98 ±49.62 A	131.97 ±40.42 A	0.521 A NS
Insulin (mIU/L)	21.12 ±6.94 B	19.46 ±6.32 B	23.14 ±3.14 A	0.003 A HS
IR	9.55 ±4.99 B	8.35 ±4.52 B	10.87 ±3.03 A	0.004 A HS

Data were expressed as mean ±standard deviation; ***n***: number of cases; **BMI**: body mass index; **FBS**: fasting blood sugar; **TG**: triglyceride; **HDL**: high density lipoprotein; **VLDL**: very low density lipoprotein; **LDL**: low density lipoprotein; **A**: one way **ANOVA**; capital letters were used to indicate the level of significance following performing **post hoc Dunnet's 3 test** (unequal size and unequal variance) so that similar letters indicate no significant difference whereas different letters indicate significant difference in such a way that letter **A** takes the highest value followed by letter **B** and then by letter **C; NS:** not significant at $p > 0.05$**; S:** significant at $p \leq 0.05$**; HS: highly** significant at $p \leq 0.01$

4.6.The association between haplotypes and risk of disease

The association between risk of disease and haplotypes resulting from KCNQ1 rs2237892 (CT) versus rsl50190 (AC) interaction is shown in table 4.10. The presence of H 1 haplotypes (the existence of both major alleles) was associated with highly significant risk of disease (p = 0.005) with and OR of 2.08. The H2 haplotype (Major allele/Minor allele) was not significantly associated with disease risk (p = 0.561). The presence of H 3 haplotypes (Minor allele/Major allele) was associated with highly significant protection against the disease (p = 0.005) with an approximate OR of 0.04.

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The presence of H 4 haplotypes (the existence of both minor alleles) was associated with significant protection against the disease (p = 0.025) with an OR of 052.

Table 4.10.: The association between risk of disease and haplotypes resulting from KCNQ1 **rs2237892** (CT) versus rsl50190 (AC) interaction

KCNQ1rs rs2237892 (CT) vs rsl50190 (AC)	**Control *n* = 300**	**Patient *n* = 300**	***p***	**OR**	**95 % CI**
	***n* (%)**	***n* (%)**			
H1	24 (8.0 %)	46 (15.3 %)	0.005 C HS	2.08	1.24 -3.51
H2	228 (76.0 %)	234 (78.0 %)	0.561 C NS	1.12	0.77 -1.64
H3	12 (4.0 %)	0 (0.0 %)	<0.001 C HS	0.04*	---
H4	36 (12.0 %)	20 (6.7 %)	0.025 C S	0.52	0.30 -0.93

n: number of cases; **OR**: odds ratio; **CI**: confidence interval; **C**: Chi-square test; **HS**: highly significant at $p \leq 0.01$; **S**: significant at $p \leq 0.05$; **NS**: not significant at $p > 0.05$; *: approximate odds ratio**.**

Discussion

The study of the relationship between the KCNQ1 gene seven SNPS polymorphisms and the T2DM hazard. Our outcomes give proof that two KCNQ1 polymorphisms (rs2237892 and rs151290) may be essentially connected with expanded T2DM hazard. These critical affiliations are more articulated among Iraqi populaces .altogether expanded T2DM chances were found for C allele of rs2237892 (OR = 2.79; P < 0:001), and An allele of rs151290 (OR = 1:17; P 0:184). A past populace based examination has demonstrated that the polymorphisms of KCNQ1 (rs2237892) were altogether connected with the OGTT-inferred insulin discharge file. Moreover, the rs151290 gene KCNQ1 polymorphism was essentially related with the 30-minute C-peptide level during OGTT, the main stage insulin discharge, and the proinsulin file[17]. It was additionally proposed that the methylation distinction of KCNQ1 was related with insulin affect ability and that CpG site-explicit hereditary variety anticipated the methylation contrast [18] . The molecular mechanism by which KCNQ1 is related with the risk of T2DM might be clarified by the reasons referenced previously. We additionally tracked down that under various genotypes of rs2237892the articulation level of KCNQ1 gene was altogether unique. In any case,

more examination studies ought to be directed to test the relationship between different SNPs with KCNQ1 gene articulation levels. After defined by race, the assessed chances were more obvious among Asians than among Caucasians for rs2237892 and rs151290. Meta regression investigations additionally affirmed these marvels. As per our information, the altogether lower extent in the recurrence of minor alleles in controls for KCNQ1 polymorphisms was seen among Asians and Caucasians (e.g., in rs2237892, and in rs151290), which may have prompted a distinction in the outcomes between the two SNPS[19]. KCNQ1 rs2237892 C/T gene polymorphism was uniquely connected with expanded T2DM danger in the Asian populace, aside from Indian populace. Individuals with the C allele may be defenseless toT2DM risks [20]. KCNQ1 gene is the principal T2DM helpless gene recognized in Asian populace. Researchers of Japan and Korea have checked solid relationship be tween's the polymorphism at rs2237892 locus and T2DM [21]. .Compared with other gene loci, there is less investigation on the relationship between the polymorphism at rs2237892 and T2DM. Researchers of Japan have checked the relationship between the polymorphism of rsl51290 and T2DM , however this has not been demonstrated in the German populace[22]. The conflicting examination results might be brought about by clear hereditary heterogeneity of T2DM, and diverse hereditary foundations and conditions of contrast districts and countries. This examination has shown that critical contrasts exist in genotype dispersions and allelic frequencies at KCNQ rs2237892 locus between Han T2DM patients and solid individuals in Huaihai locale of China, which additionally proposes that KCNQ1 rs2237892 polymorphism might be related to the rate of T2DM in the Chinese Han populace in Huaihai district of China. It has likewise shown that no huge contrasts exist in genotype conveyances and allelic frequencies at KCNQ1 rsl51290 locus between Han T2DM patients and sound individuals in the Huaihai district of China, which may imply that KCNQ1 rsl51290 polymorphism is immaterial to the occurrence of T2DM in the Chinese Han populace in the Huaihai area of China.

The reasons for such outcomes may include: (1) The example size of this investigation was little, which straightforwardly influenced the measurable outcomes; (2) the gene test strategies were limited, which may have caused the deviation of test outcomes; or (3) the role of the locus KCNQ1 rsl51290 was feeble in causing T2DM, and it is difficult for the distinction to accomplish factual importance. The

investigation result was negative, yet the chance of relationship between' rsl51290 polymorphism and T2DM in the number of inhabitants in the Huaihai district of China can't be wiped out. All in all, early mediation to the populace with the danger of conveying related alleles has extraordinary importance for deferring and forestalling T2DM, and furthermore gives a premise to the last, clinical acknowledgment of quality situated, customized medicine. In future examinations, we should additionally build the quantity of T2DM patients and control cases, and improve the genotype test strategy, to make the outcomes more logical, exact and objective; what's more, the instrument of KCNQ1 gene polymorphism bringing about T2DM stays hazy, which requires further inside and out examination [16].

Conclusion:

early intercession to the populace with the danger of conveying related alleles has incredible importance for delaying and forestalling T2DM.also gives a premise to the last, clinical acknowledgment of quality arranged, customized medicine. In future examinations, we should additionally build the quantity of T2DM patients and control cases and improve the genotype test method, to make the outcomes more logical, precise and objective; also, the system of KCNQ1 quality polymorphism bringing about T2DM stays muddled, which requires further top to bottom examination.

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