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ORIGINAL ARTICLE

Association of KISS1 Gene SNPs (Rs35431622) with Metabolic Parameters in Iraqi Women Polycystic Ovary Syndrome

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ABSTRACT

Background: Polycystic ovarian syndrome (PCOS) is among the most common types of gynecological hormonal abnormalities and metabolic problems that have an impact females throughout adolescence , with a prevalence of 6-10%.Hyperandrogenism, unreliable menstrual periods, and polycystic ovaries are the hallmarks of PCOS.

Objectives: The goal of this find out about used to be to analyze the affiliation of kiss1 Gene SNPs (rs35431622) with metabolic Parameters in PCOS .

Methodology: a case –control find out about enrolled one hundred sixty members of which eighty female have PCOS and eighty symbolize the manage crew who had-been interestingly healthful. Patients with PCOS had been chosen patients from our health center and the teaching hospital's gynecology and obstetrics department in Tikrit. Assessment of serum (fasting blood glucose , cholesreol .HDL and triglyceride) was performed using smart 150 full automated clinical chemistry machine .and insulin by ELISA KIT ,HOMA-IR By calculation and the maker company's provided methodology was followed to extract genomic DNA from whole blood. KISS1 Gene SNPs rs35431622 T>A gene polymorphisms was once detected by using (T-ARMS-PCR) method .

Results: The findings indicate, the frequency of the kiss1 gene rs35431622 AT and TT genotypes in PCOS-affected women increased 3.524-fold and 9.633- in comparison to the group of healthy women which have odds ratio; 3.524and 9.633, 95% confidence interval [CI], 1.622-7.657 and 2.916-31.816; P-value ≤0.01**and ≤0.01**) respectively. and The levels of FBS ,Insulin ,HOMA-IR, cholesterol, HDL and triglyceride showed significant difference among PCOS against control group (P≤ 0.0001) .

Conclusions: Our find out about suggests a greater awareness of serum (FBS ,Insulin , cholesterol, HDL and triglyceride) seemed in PCOS companies as in contrast with control and also significant difference in the value of HOMA-IR as well, Cases and controls had statistically different frequencies of the identified polymorphisms, and Control 34 had a higher frequency of the homozygous allele (CC) than Cases 12 ., while the frequency of heterozygous allele (AT) were significantly different in cases 51 higher than the controls 41 as well the frequency of mutant allele (tt) were significantly different in cases 17 higher than the controls 5 .The allelic frequency of SNP rs35431622.C/T used.to,be detected extra regularly with significant affiliation infemale with PCOS than in control.

Keywords: PCOS, kiss1,(IR)

INTRODUCTION

PCOS one of the most frequent type of gynecological hormonal abnormalities and metabolic problems that affect females throughout adolescence, with a prevalence of 6-10% [(1-3)] . Hyperandrogenism, unreliable menstrual periods, and polycystic ovaries are the hallmarks of PCOS [(4)] .these aggravate the signs of hyperandrogenemia. researchers have focused particularly on the genetics of this illness in terms of genetic factors associated to the (HPG) axis [(5)] . KISS1, (GPR54) a few of the HPG axis mutations that have been investigated in the past [(6)] . KISS1 has become one of the potential genes playing a controlling function in the female reproductive system, playing a significant good position in the generation of HPG axis gonadotropin [(7)] . Certain SNPs in the KISS1 gene been The KISS1 gene has many SNPs that have been uncovered for restrict HPG axis, impairing the healthy operation of the female reproductive system. These SNPs are expected to play a vital part in the etiopathogenesis of PCOS [(8)]. The KISS1 gene produces peptides called kisspeptins that control the HPG axis [(9)]. KISS1 gene polymorphism in PCOS Finding the complex etiology of PCOS may be helped by the affected ladies[(10)] .

METHODOLOGY

Research Design: The current investigation performed a case-control study for a collection of (160) samples, with 80 PCOS-positive girls and 80 strangely healthy subjects acting as controls.

Sample size: The study was conducted on 160 women participants.

Population: 80 women with PCOS disorders and 80 women in control group.

Research setting: This study was conducted from outpatient patients and the infertility clinic at the Tikrit Gynecology and Obstetrics Teaching Hospital. in Salah Al-Din Governorate, Iraq.

Sampling Criteria

Each patient had their medical and biochemical histories, as well as their heights and weights, recorded. The self-reported questionnaire collected the sociodemographic information of the patients, including their age, BMI, , and the presence of illnesses.

Methodology: Assessment of serum The levels of insulin were measured by using ELISA kit. and the level of FBS , cholesterol , HDL and triglyceride was performed using smart 150 full automated clinical chemistry machine .and ,HOMA-IR by calculation and The genetic evaluation used to be carried out at Tikrit University Department of Biology, College of Science. Each PCOS and manage woman has contributed five milliliters of peripheral blood. Blood samples were stored at 4 degrees Celsius in anticoagulant tubes. Historically, peripheral leukocyte genomic DNA was isolated using (Thermo Fisher Scientific, USA) According to the producer protocol, the isolation used to be made. NanoDropTM evaluated the DNA's quality and integrity (Thermo Scientific, USA). (TETRA-ARMS-PCR) method was used for genotyping of the SNP rs35431622 T>A KISS1 gene since it is a quick and inexpensive method for SNP detection. Two external primers were used out of the four that were used[(11-16)] .

RESULTS AND DISCUSSION

Metabolic parameter: According to the research, Women with PCOS are very different from women in the control group in regards of FBS ,Insulin , cholesterol, HDL and triglyceride) and also significant difference in the value of HOMA-IR. The Mean ± SD with p-value depicted in the table (-1-)

Table 1: metabolic changes between PCOS patients and the control group:

Parameters	Patients(No. 80) Mean ± Std	Control (No. 80) Mean ± Std	P - value
Fasting blood sugar (mg /dl)	99.4±8.22	85.16±7.06	≤ 0.0001

Cholesterol (mg/dl)	188.82±16.95	166.53±12.53	≤ 0.0001
Triglyceride (mg/dl)	163±22.72	103.05±12.98	≤ 0.0001
Insulin	13.50±0.93	11.04±0.56	≤ 0.0001
HOMA-IR	3.31±0.34	2.32±0.23	≤ 0.0001
HDL (mg/dl)	31.37±1.10	35.962±3.53	≤ 0.0001

Given that the (FBS) in the PCOS group was higher than in the control group, there was a significant difference between the two groups. indicating that the cystic ovarian syndrome patients were more likely to have high blood sugar. Such studies are invaluable. (Metzger , Lowe , Dyer et al.) [17], Mild glucose abnormalities found in the PCOS population and in women with PCOS trying to conceive may require more intensive lifestyle intervention and follow-up. Many studies by (Barcellos , Rocha , Hayashida et al.) [18], Evaluation of fasting blood glucose alone is not sufficient to screen for prediabetes in women with PCOS because it is difficult to identify women with poor postprandial glucose tolerance with just one fasting blood level. (Kim et al).[19]Insulin levels and FBS were significantly increased in case groups Studies have shown hat people with PCOS should not be diagnosed with diabetes using plasma fasting blood glucose measurement as a screening tool, according to. An important reason why our results differ from other studies is that, in contrast to other research, this one is population-based. Based on the presented results it is recommended that all PCOS patients be sensitive to the risk of developing glucose metabolism disorders and that All PCOS sufferers, regardless of age or BMI results, must make lifestyle modifications. For instance, diabetes and hyperlipidemia. , See also Dunaif et al. [20] Roya et al. [21] Oreo et al. 2009 in Venezuela. [22] Legro et al. In Italy [23] Erel et al . In Turkey [24] Overall, this is consistent with our study. Results showed that PCOS patients had higher total serum levels (cholesterol and total triglycerides) and lower HDL levels than healthy controls. However In our investigation, the difference was statistically significant.

Genotype and allelic frequency: The distribution of alleles and genotypes for rs35431622 between the groups with PCOS and controls (Table:2) lists the genotype frequencies and counts for PCOS and control groups Cases and controls had significantly differing frequencies of the detected polymorphisms. The quantity of the heterozygous allele (AT) There were 41 in the controls compared to 51 in the PCOS group . , and the p-value (≤ 0.01**) indicate significant difference. , while the homozygous (TT) allele was 17 in PCOS group while 5 in controls and the p- value (≤ 0.01 **) and there was a big difference In this study the frequency of allele for SNP rs35431622 T/A proven to be substantially related to PCOS compared to control, and with OR of **2.422** and CI (1.536 - 3.817) (P value = ≤ 0.01 **).

Table 2: the distribution of alleles and genotypes for rs35431622 in control groups and the PCOS.

	Patients No. (80)		Control No. (80)				
Genotypes	No.	%	No.	%	OR	(95% CI)	P value
AA	12	15	34	42.5	1 Ref.	-	-
AT	51	63.75	41	51.25	3.524	1.622 - 7.657	≤ 0.01 **
TT	17	21.25	5	6.25	9.633	2.916 - 31.816	≤ 0.01 **
AT=TT	68	85	46	57.5	4.188	1.964 – 8.929	0.0002
Alleles	No.	%	No.	%	OR	(95% CI)	P value
A	75	46.9	109	68.1	1 Ref.	-	
T	85	53.1	51	31.9	2.422	1.536 - 3.817	≤ 0.01 **

The outcomes of the current inquiry showed a favorable correlation between PCOS and the kiss1 **rs35431622** T>A gene polymorphism. In PCOS women compared to control women, the TT-genotype frequency and CT-genotype frequency was statistically different. Positive (association) from various populations were reported .Our results Disagree with previous reports (10). They discovered no measurable difference between PCOS and control in rs35431622 .

Table 3: The metabolic markers and patients' alleles Among rs35431622 in patient and control.

Biochemical parameters	Genotyping frequency		p-value	Genotyping frequency		p-value	Genotyping frequency		p-value
	PCOS Mean ± Std	Control Mean ± std		PCOS Mean ± SD	Control Mean ± std		PCOS Mean ± std	Control Mean ± std	
FBS (mg/dl)	99.1667±7.3957	85.3235±6.7452	≤ 0.0001	99.6471±8.4091	84.4634±7.376	≤ 0.0001	98.0588±8.7569	85.2±8.7864	0.0092
Ch (mg/dl)	187.4167±11.5007	165.7353±13.0089	≤ 0.0001	187.6471±17.9998	166.7805	≤ 0.0001	192.9412±17.0934	170.2±13.1415	0.0129
Tg (mg/dl)	166±16.9008	104.0588±13.4659	≤ 0.0001	160.2549±22.6996	101.7073±12.9465	≤ 0.0001	167.7059±25.685	104.4±13.069	≤ 0.0001
Insulin	13.4975±1.0991	11.0406±0.5934	≤ 0.0001	13.5124±0.9114	11.0559±0.5769	≤ 0.0001	13.5012±0.918	10.75±0.4205	≤ 0.0001
HOMA-IR	3.29±0.4388	2.3418±0.2156	≤ 0.0001	3.3218±0. 0.3241	2.2922±0.2482	≤ 0.0001	3.2547±0.3439	2.262±0.2672	≤ 0.0001
HDL (mg/dl)	31.1667±1.2673	36.2647±3.3422	≤ 0.0001	31.4314±1.2673	84.4634±7.376	≤ 0.0001	31.3529±0.9963	37.6±4.7223	≤ 0.0001

It can be seen from the Table(3) revealed that there is a statistically significant difference in the allele frequency AA between the PCOS groups and the control in FBS ,Insulin , cholesterol, HDL and triglyceride also among the AT allele showed significant difference in FBS ,Insulin , cholesterol, HDL and triglyceride between the PCOS groups and control . and observed that the allele frequency TT is statistically significant between the PCOS groups and control in FBS ,Insulin , cholesterol, HDL and triglyceride and HOMA-IR.

CONCLUSION

This study there high significant differences in serum FBS , insulin , HDL , cholesterol and triglyceride and HOMA-IR values among the control group & PCOS group. Between cases and controls, there were significant differences in the frequencies of the detected polymorphisms, with case 12 having a lower frequency of the homozygous allele (AA) compared to control 34, and case 51 having a higher frequency of the heterozygous allele (AT). 41. Significantly diverse from the control group. As opposed to the c the SNP rs35431622 T/A allele was detected more frequently in women with PCOS which was significantly correlated with the control group. KISS1 genotype frequencies were significantly associated with HDL cholesterol FBS triglycerides insulin and HOMA-IR. in polycystic ovary syndrome.

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