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The relationship between adiponectin gene polymorphism and Thyroid Disorders at Zagazig University Hospitals

[1]Shimaa Mohammed Ragab, [2]Mohammed AlmhdyGamalAldeinKamar, [3]Mohammed MohammedAwad, [4]Mayada Mohammed Mousa

Abstract

Background:*Thyroid dysfunction is usually associated with changes in body weight, appetite and thermogenesis. The adiponectin gene has various Single Nucleotide Polymorphisms (SNPs). One of these SNPs is the 45T/G polymorphism encountered, in exon 2 of the adiponectin gene, has been frequently found its association with obesity, and breast cancer, and second rs1501299 (G276T) is in intron 2 of the ADIPOQ gene.The study aimed to identify the role of adiponectingene polymorphism in patients with thyroid disorders either hypothyroidism or hyperthyroidism.****Methods:****The study was carried out in endocrine outpatient clinic, internal medicine department, 150subjects were included in this study; they were divided into the following groups: Group1: Hypothyroid group. Group2: Hyperthyroid group. Participants were subjected to:Full history taking laboratory investigation: included Determination of adiponectin gene****Results:****there is no associations between ADIPO Q 276G>T SNP gene polymorphism and hypothyroidism & hyperthyroidism. Within hypothyroid group, there was statistically significant relation between gene polymorphism and both serum creatinine and albumin. Within hyperthyroid group, there was statistically significant relation between gene polymorphism and serum creatinine, urea, albumin and ALT, the difference was significant between GT and GG groups concerning both urea and albumin level and between GT group with both TT and GT groups concerning creatinine and between TT group and both GG and GT groups concerning ALT with non-significant relation between gene polymorphism and AST. Within hypothyroid group, there was statistically significant relation between gene polymorphism and both serum cholesterol and fasting blood glucose, the difference was significant between TT group and both GT and TT groups concerning cholesterol level. Within hyperthyroid group, there was statistically significant relation between gene polymorphism and both serum cholesterol, fasting and 2 hours postprandial blood glucose, the difference is significant between GT group and both GG and TT groups concerning cholesterol level.****Conclusion:****This study suggests that adiponectin gene polymorphism is not associated with thyroid dysfunctions among both groups of hypothyroidism& hyperthyroidism of Egyptian patients.*

Key words: *Adiponectin- Gene Polymorphism-Thyroid Disorder.*

[1] *Internal Medicine, Faculty of Medicine. ZagazigUniversity, Egypt.*
[2] *Professor of Internal Medicine, Faculty of Medicine – ZagazigUniversity, Egypt.*
[3] *Professor of Internal Medicine, Faculty of Medicine – ZagazigUniversity, Egypt.*
[4] *Assistant Professor of Internal Medicine, Faculty of Medicine – Zagazig University*

I. Introduction:

Thyroid dysfunction is usually associated with changes in body weight, appetite and thermogenesis. However, thyroid dysfunction-related changes in glucose and lipid metabolism are not well-defined. Although it is believed that thyrotoxicosis results in hepatic and peripheral insulin resistance **Dimitriadis et al., [(1)],**increased, decreased or normal insulin sensitivity has been reported in both thyrotoxic and hypothyroid patients in different studies **(2).**

Both hypo &hyperthyroidism are associated with cardiovascular morbidity & mortality. Adiponectin in a fat cell derived hormone that protect against atherosclerotic cardio vascular disease through it is enhancing effect on insulin sensitivity, that protect against atherosclerotic cardio vascular disease through it is enhancing effect on insulin sensitivity. Adiponectin is a peptide produced exclusively in adipose tissue. It plays an important role in the regulation of a variety of processes, ranging from energy homeostasis, lipid metabolism and insulin sensitivity to inflammation and atherosclerosis **(3).**

Adipose tissue, has been recognized to be an active endocrine organ, producing some important molecules involved in fatty acid and glucose metabolism **Nigro et al.,[(4)].**Adiponectin is the most abundant adipocyte-specific protein secreted by adipocytes and accounts for 0.01% or at around 5-10 mg/dl of the total plasma protein**)**. Adiponectin is widely recognized for its antidiabetic,anti-inflammatory, antiatherogenic and cardioprotective effects (**5).**

Clinical studies investigating the serum adiponectin levels in patients with hypothyroidism and hyperthyroidism have reported conflicting results **Altinovaet al.,[(6)]**,While various studies have demonstrated higher adiponectin levels in hyperthyroid or hypothyroid patients **Yu et al.,[(7)],** other reports have found no differences in the adiponectin levels in individuals with thyroid dysfunction **(8).**

The adiponectin gene has various Single Nucleotide Polymorphisms (SNPs). One of these SNPs is the 45T/G polymorphism encountered, in exon 2 of the adiponectin gene, has been frequently found its association with obesity, and breast cancer, and second rs1501299 (G276T) is in intron 2 of the ADIPOQ gene **(9).**

The study aimed tostudy the role of adiponectin gene polymorphism in patients with thyroid disorders either hypothyroidism or hyperthyroidism.

II. Patients and Methods

The study was carried out in endocrine outpatient clinic, internal medicine department, the laboratory department was done in the medical biochemistry department, Zagazig University Hospital and included 150 patients, 75 patients of hypothyroidism and 75 patients of hyperthyroidism during period from August 2018 to January 2019.

Participants: This is across-sectional study was planned to study the role of adiponectin gene polymorphism in patients with thyroid disorders both hypo&hyperthyroidism. The study design was approved by the Ethical Committee of Faculty of Medicine, Zagazig University.

150subjects were included in this study; they were divided into the following groups:

- **Group 1: Hypothyroid group**

This group included 75 patients diagnosed as hypothyroidism. These patients had been followed up in the Endocrinology Unite, Internal Medicine Department, Zagazig University Hospital.

- **Group2: Hyperthyroid group**

This group included 75 patients diagnosed as hyperthyroidism. These patients had been followed up in the Endocrinology Unite, Internal Medicine Department, Zagazig University Hospital. The age of the included subjects was ranging from 20 to 60 years, 83 were female and the other 67 male, 75 hypothyroidism and 75 hyperthyroidism.

Exclusion criteria :

Patients with liver cell failure, renal failure, elderly patients, pregnancy.

Methods

Participantswere subjected to:

- **Full history taking** (age, sex,).

History of antithyroid medications, thyroxine replacement . Drugs affecting thyroid function, lithium, interferon, corticosteroid.

Past history of drugs, diseases, operations (neck surgery) and irradiations.

laboratory investigation:

They were all done according to the methods applied in the clinical pathology and laboratories of zagazig university hospitals and include:

1. Liver function tests: serum bilirubin (total and direct), serum albumin, serum alanine transferase and aspartate transferase measured by kinetic method**(10).**
2. Renal function tests: serum creatinine**Henry, [11]**, serum urea by colorimetric method **(12)**.
3. lipid profile (Total cholesterol, Serum triglyceride ,LDL and HDL)
4. Fasting,2 hour Postprandial blood glucose level.
5. Fasting serum insulin for caliculation of HOMA-IR.

HOMA-IR = Fasting serum insulin uIU/mL(mU/L) x Fasting blood glucose(mg/dL).

Determinationof adiponectin gene by PCR amplification:

Genomic DNA extraction and analysis for determination of adiponectin genotype by detecting nucleotide variation at position 276 of adiponectin gene was done using polymerase chain reaction restriction fragment length polymorphism (PCR-RFLP).

Blood sampling

Ten ml of whole venous blood sample was taken under complete aseptic condition from every participant and divided into

-2ml was collected on sterile ethylene diamine tetra-acetic acid (EDTA) tubes and was used for DNA extraction. Extracted DNA were stored at (-20ºC) till time of assay.

-2ml left for 30 minutes for spontaneous clotting then centrifuged at 3000 rpm for 5 minutes. Samples were separated and divided into 2 tubes for measurement of serum creatinine, serum albumin, and serum bilirubin, Complete blood count, serum uric acid, blood sugar assessment.

-2ml collected on 3.8% trisodium citrate anticoagulant in a 9:1 ratio, which is centrifuged to produce platelet poor plasma. A complete thromboplastin (typically from rabbit brain) is then added with calcium. The time to fibrin strand formation is then measured automatically by electromechanical device to measure coagulation profile (PT-PTT-INR).

-2ml of peripheral venous blood were taken from each subject after over night fasting and left for 30 minutes for spontaneous clotting then centrifuged at 3000 rpm for 5 minutes then stored at -20°c until the time of assay of lipid **(** Total cholesterol, Serum triglyceride ,LDL and HDL)and fasting blood glucose level and fasting serum insulin.

- 2ml of peripheral venous blood were taken from each subject and left for 30 minutes for spontaneous clotting then centrifuged at 3000 rpm for 5 minutes then stored at -20°c until the time of assay of thyroid function.

Determination of adiponectin 276G>T polymorphism by PCR-based restriction fragment length polymorphism

Genomic DNA analysis for identification of adiponectin gene polymorphism at position (G276 T) was done using polymerase chain reaction PCR followed by restriction fragment length polymorphism RFLP technique.

The test was done in 5 main steps:

1. Extraction of genomic DNA from peripheral blood leucocytes of EDTA sample.
2. Amplification of the extracted DNA.
3. Detection of PCR amplification products using agarose gel electrophoresis and ultraviolet (UV) light transillumination.
4. The amplified products were digested with the (Bsml) restriction enzyme for single nucleotide polymorphism for G/T transition at position 276 in intron 2 of human adiponectin gene.
5. After digestion the amplified products were then detected by electrophoresis on agrose gel containing ethdium bromide, and visualized by ultraviolet transilluminator for identification of polymorphism.

DNA Extraction:

DNA was isolated using the PUREGENE DNA Isolation Kit purchased from Gentra. DNA was extracted using TIAN genomic DNA kit from TIANGEN (Beijing, China). Expected yield: 5-15 µg DNA.

Cell Lysis:

1. 300 µL whole EDTA blood was added to a 1.5 mL centrifuge tube containing 900 µL red blood corpusclelysis solution, invert to mix and incubated 10 minutes at room temperature; and it was inverted again at least once during the incubation.

2. Then it was centrifuged for 20 seconds at 13,000 rpm. The supernatant was removed with a pipette leaving behind the visible white cell pellet and about 10-20 µL of the residual liquid.

3. The tube was shaken vigorously using vortex to resuspend the cells in the residual liquid.

4. 300 µLcell lysis solution was added to the resuspended cells and pipeted up and down to lyse the cells.

RNase Treatment:

1. 1.5 µLRNase A solution was added to the cell lysate.

2. The sample was mixed by inverting the tube 25 times and incubated at 37°C for 15 minutes.

Protein Precipitation:

1. 100 µLprotein precipitation solution was added to the cell lysate.

2. Then it was shaken vigorously using vortex for 20 seconds to mix theprotein precipitation solution uniformly with the cell lysate.

3. Then it was centrifuged at 13,000 rpm for 3 minutes. The precipitated proteins formed a tight, dark brown pellet.

DNA Precipitation:

1. The supernatant containing the DNA (leaving behind precipitated protein pellet) was poured into a clean 1.5 mL centrifuge containing 300 µL100% isopropanol.

2. The sample was mixed by inverting gently 50 times.

3. Then it was centrifuged at 13,000 rpm for 1 minute; the DNA was visible as a small white pellet.

4. The supernatant was poured off and the tube was drained briefly on clean absorbent paper. 300µL 70%ethanol was added and the tube was inverted several times to wash the DNA pellet.

5. Then it was centrifuged at 13,000 rpm for 1 minute. The ethanol was carefully poured.

6. The tube was inverted and drained on a clean absorbent paper and allowed to air dry for 10 minutes.

DNA Hydration:

1. 100 µLDNA hydration solution was added to DNA precipitated.

2. DNA was rehydrated by incubating sample for 1 hour at 65°C for 5 minutes.

3. The tubes were shaken using vortex for 5 seconds at medium speed to collect sample at the bottom of the tube.

4. DNA was stored at 4°C.

Amplification of Arg130Gln Polymorphism:

Primers (FromBiosynthesis)**:**

5' – GGC CTC TTT CAT CAC AGA CC – 3' (sense)

5'– AGA TGC AGC AAA GCC AAA GT -3'(antisense)

PCR was performed in a final volume of 20 µl containing 5 µl of genomic DNA, 1 µl(0.2 µmol/l) of each primer and 10 µl of Taq PCR Master Mix (BIORON), 3 µl of H_2o.

PCR CONDITIONS:

The amplification was carried out using thermal cycler PTC-100 machine (MJ Research, Inc., Watertown, Mass. USA) according to the following protocol; 1 cycle of 95 ^{o}cfor 5 minutes ,then 35 cycles of 95^{o}c for 60 sec, 58 ^{o}c for 45 sec , 72 ^{o}c for 60 sec ,and then 1 cycle 72 ^{o}c for 10 minutes. Then it was stored at 4°C till use.

RESTRICTION DIGEST REACTION:

The digestion was performed in a total volume 35µl that contained:

-10X NEBuffer 4 3.5 µl

-100X BSA 0.35 µl

-1 U/µl Mva 1269I 5 µl

-DdH2O 11.15 µl

-PCR Product 15 µl

Incubate at 37 °C for 15 minutes.

Gel electrophoresis for PCR-digested products :

Preparation of 1.5% agarose:

1.5 % agarose gel was prepared by adding 1.5 gmagarose to 100 ml of 1X TAE buffer with boiling to dissolve the agarose. After the agarose reached about 50ºC , 10µl of stock ethidium bromide (5 mg/ml) was

added to the agarose before pouring into the tray. A part of the gel was kept in the flask to determine the appropriate time of gel hardening and comb removal.

Sample preparation and loading:

The electric current was set at 100 mA & 70 volts for about 1hour, and then the gel was visualized under UV transilluminator with 100 base pair ladder and photographed.

Fragment size: 148 and 48 for homozygous wild type (GG); 196,148 and 48 for heterozygous (GT) and 196 for homozygous variant type (TT).

Statistical analysis: Data collected throughout history, basic clinical examination, laboratory investigations and outcome measures coded, entered and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) **(**Statistical Package for the Social Sciences) software for analysis. According to the type of data qualitative represent as number and percentage , quantitative continues group represent by mean ± S D and were analyzed using ANOVA test , the following tests were used to test differences for significance;. difference and association of qualitative variable by Chi square test (X^2) . Differences between quantitative independent groups by t test or Mann Whitney, , correlation by Pearson's correlation or Spearman's . P value was set at <0.05 for significant results &<0.001 for high significant result.

III. Results:

There is statistically non-significant difference between the studied groups regarding age or gender **Table (1)**

There is statistically non-significant difference between the studied groups regarding genotype. GG genotype increase in hyper thyroid group (49.3%) than in hypothyroid group (41.3%).Where GT genotype increase in hypothyroid group (49.3%) than in hyperthyroid group (34.7%).Where TT genotype increase in hyper thyroid group (16%) than in hypothyroid group (9.3%). In allele distribution, the frequency of G allele was (66%) in hypothyroid group and was (66.7%) in hyperthyroid group, whereas the T allele increase in hypothyroid group (34%) than in hyperthyroid group(33.3%). **Table (2)**

There is statistically non-significant relation between patient gender and either gene or allele polymorphism among patients within hypothyroid group. **Table (3)**

There is statistically non-significant relation between patient gender and either gene or allele polymorphism among patients within hyperthyroid group. **Table (4)**

Within hypothyroid group, there is statistically significant relation between gene polymorphism and both serum creatinine and albumin. On LSD comparison, the difference is significant between GT group and both GG and TT group concerning creatinine level. However, regarding serum albumin, the difference is significant between TT group and both GG and GT groups. There is statistically non-significant relation between gene polymorphism and either urea, ALT or AST. **Table (5)**

Within hypothyroid group, there is statistically significant relation between gene polymorphism and both serum cholesterol and fasting blood glucose. On LSD comparison, the difference is significant between TT group and both GT and TT groups concerning cholesterol level. However, regarding fasting blood glucose, the difference is significant only between GT group and GG groups. There is statistically non-significant relation between gene polymorphism and either triglycerides level, fasting insulin, HOMA-IR or 2 hour postprandial blood glucose. **Table (6)**

Within hypothyroid group, there is statistically significant relation between gene polymorphism and both serum creatinine, urea, albumin and ALT. On LSD comparison, the difference is significant between GT and GG groups concerning both urea and albumin level. However, regarding serum creatinine, the difference is significant between GT group and both TT and GT groups. Regarding ALT, the difference is significant between TT group and both GG and GT groups There is statistically non-significant relation between gene polymorphism and AST. **Table (7)**

Within hyperthyroid group, there is statistically significant relation between gene polymorphism and both serum cholesterol, fasting and 2 hours postprandial blood glucose. On pairwise comparison, the difference is significant between GT group and both GG and TT groups concerning cholesterol level. However, regarding fasting blood glucose, the difference is significant only between GT group and GG groups. There is statistically non-significant relation between gene polymorphism and either triglycerides level, fasting insulin, or HOMA-IR. **Table (8)**

Table (1) Comparison of the studied groups according to demographic characteristics:

Demographic characteristics	**Groups**		Test	
	Hypothyroid group	**Hyperthyroid group**	χ^2/t	p
	N=75 (%)	**N=75 (%)**		
Gender:				
Female	27 (36)	23 (30.7)	0.48	0.488
Male	48 (64)	52 (69.3)		
Age (years)				
Mean ± SD	41.23 ± 7.15	41.56 ± 7.85	-0.272	0.7786
Range	26 – 55	26 – 54		

t independent sample t test

Table (2) Comparison of the studied groups according to adiponectin genotype:

	Groups		Test		COR (95% CI)
	Hypothyroid group	**Hyperthyroid group**	**χ^2/t**	**p**	
	N=75 (%)	**N=75 (%)**			
Genotype					
GG	31 (41.3)	37 (49.3)			
GT	37 (49.3)	26 (34.7)	0.014	0.906	1.7(0.85 – 3.39)
TT	7 (9.3)	12 (16)			0.7(0.24 – 1.98)
Alleles:					
G	99 (66)	100 (66.7)	0.015	0.903	1.03(0.64 – 1.66)
T	51 (34)	50 (33.3)			

COR crude odds ratio CI confidence interval

Table (3) Relation between genotype and gender of the studied patients with hypothyroidism:

	Gender		Test	
	Female	**Male**	**χ^2**	**p**
	N=27 (%)	**N=48 (%)**		
Genotype				
GG	12 (44.4)	19 (39.6)	1.594	0.207
GT	15 (55.6)	22 (45.8)		
TT	0 (0)	7 (14.6)		
Alleles:	N=54	N=96		
G	39 (72.2)	60 (62.5)	1.456	0.228
T	15 (27.8)	36 (37.5)		

Table (4) Relation between genotype and gender of the studied patients with hyperthyroidism:

	Gender		**Test**	
	Female	**Male**	χ^2	**p**
	N=23 (%)	**N=52* (%)**		
Genotype				
GG	12 (52.2)	25 (48.1)	1.534	0.215
GT	3 (13)	23 (44.2)		
TT	8 (34.8)	4 (7.7)		
Alleles:	N=46	N=104		
G	27 (58.7)	73 (70.2)	1.456	0.228
T	19 (41.3)	31 (29.8)		

Table (5) relation between genotype polymorphism and both liver and kidney function test among the studied patients among hypothyroid group:

Parameters	**Genotype**			**Test**	
	GG	**GT**	**TT**	**F**	**p**
	Mean ± SD	**Mean ± SD**	**Mean ± SD**		
Creatinine	1.1 ± 0.22	0.92 ± 0.2[¥]	1.13 ± 0.43	5.542	0.006*
Urea	32.42±10.08	32.65±13.53	30.57±6.11	0.093	0.911
Albumin	3.9 ± 0.36	3.89 ±0.42	4.37 ±0.67[¥]	4.082	0.021*
ALT	24.74 ± 11.02	28.11 ± 11.52	31.14 ± 18.83	1.976	0.372
AST	23.74 ± 10.23	23.15 ± 12.41	28.14 ± 14.85	1.282	0.572

F One way ANOVA [¥] the group responsible for significant difference *p<0.05 is statistically significant

Table (6) relation between genotype polymorphism and both lipid and glycemic profile among the studied patients among hypothyroid group:

Parameters	Genotype			Test	
	GG	GT	TT	F	p
	Mean ± SD	Mean ± SD	Mean ± SD		
Cholesterol	185.26±54.8	192.22±40.92	247.86±45.1[¥]	5.041	0.009*
Triglycerides	139.84±39.98 [1,2]	159.51±31.14[1,2]	137.71±30.17	3.088	0.052
Fasting blood glucose	188.26±84.75[1,2]	138.76±46.67[1,2]	143.71±49.08	7.445[#]	0.024*
Fasting insulin	32.65 ±20.03	29.14 ± 14.72	31.86 ± 13.55	0.202[#]	0.904
HOMA-IR	16.19 ± 15.53	10.43 ± 8.51	11.8 ± 8.04	1.325[#]	0.516
2 hour postprandial	209.03 ± 105.5	156.59 ± 64.34	170.14±86.51	2.575[#]	0.276

F One way ANOVA [¥] the group responsible for significant difference *p<0.05 is statistically significant [#]Kruskal Wallis test

Table (7) relation between genotype polymorphism and both liver and kidney function test among the studied patients among hypothyroid group:

Parameters	Genotype			Test	
	GG	GT	TT	F	p
	Mean ± SD	Mean ± SD	Mean ± SD		
Creatinine	1.04 ± 0.31	0.87 ± 0.2[¥]	1.09 ± 0.39	3.511	0.035*
Urea	36.3 ± 5.88[2,1]	42.96 ±9.34[2,1]	37.92±12.82	4.754	0.012*
Albumin	4.14 ± 0.43[2,1]	3.87 ±0.4[2,1]	4.07 ±0.42	3.212	0.046*
ALT	33.3 ± 9.73	35.19 ± 10.25	26 ± 7.21[¥]	3.884	0.025*
AST	31.84 ± 7.18	33.5 ± 8.54	27.5 ± 5.84	2.632	0.079

F One way ANOVA [¥] the group responsible for significant difference *p<0.05 is statistically significant

Table (8) relation between genotype polymorphism and both lipid and glycemic profile among the studied patients among hyperthyroid group:

Parameters	Genotype			Test	
	GG	GT	TT	F	p
	Mean ± SD	Mean ± SD	Mean ± SD		
Cholesterol	179.92 ± 46.79	208.65 ± 31.1[¥]	156.17 ± 57.23	6.575	0.002*
Triglycerides	125.57 ± 26.74	129.77 ± 27.84 [2,3]	112.17 ± 8.96[2,3]	2.109	0.14
Fasting blood glucose	173.62±89.73 [1,2]	130.12±80.57[1,2]	166.25±91.72	7.361	0.025*
Fasting insulin	37.24 ± 22.92	30.23 ± 13.35	25.5 ± 20.23	5.497	0.064
HOMA-IR	11.62 ± 12.45	11.82 ± 10.87	8.97 ± 15.63	5.184	0.075
2 hour postprandial	141.73 ± 75.5	170.88 ± 84.04	121.83 ± 21.78	6.106	0.047*

F One way ANOVA [¥] the group responsible for significant difference *p<0.05 is statistically significant [#]Kruskal Wallis test

IV. Discussion

To the best of our knowledge there are no previous studies concerning the role of AdipoQ gene polymorphism in Egyptian thyroid diseases either hypo and hyper thyroid patients have been reported.

In the current study, suggests there is no associations between ADIPO Q 276G>T SNP gene polymorphism and hypothyroidism & hyperthyroidism.

In current study, although male gender was associated with higher risk of T allele polymorphism, there was non-significant relation between patient **gender** and either gene or allele polymorphism among patients within hypothyroid group and hyperthyroid group.

Our study in harmony with study by **Tabatabaei-Malazy et al.,**[(13)]found that, no significant difference was found in male, or female, carriers of different genotypes of adiponectin gene polymorphisms **(13)**

Moreover, among 363 subjects with newly diagnosed type 2 diabetes in **Chung et al.,** [(14)]study, Adiponectin gene single nucleotide polymorphisms (SNPs) were examined and reported no significant differences in terms of sex distribution associated with SNP genotypes. **(14)**

In current study, within **hypothyroid** group, there was statistically significant relation between gene polymorphism and both serum creatinine and albumin, the difference was significant between GT groups and both GG and TT group concerning creatinine level and between TT group and both GG and GT groups

concerning albumin with non-significant relation between gene polymorphism and either urea, ALT or AST. Within **hyperthyroid** group, there was statistically significant relation between gene polymorphism and serum creatinine, urea, albumin and ALT, the difference was significant between GT and GG groups concerning both urea and albumin level and between GT group with both TT and GT groups concerning creatinine and between TT group and both GG and GT groups concerning ALT with non-significant relation between gene polymorphism and AST.

According to**Hashemi et al., [(15)]**case-control study was performed on 138 patients with nephrotic syndrome (NS) and 150 healthy children. In NS patients the genotype was not associated with total protein and albumin levels **(15)**

On the other hands, in study by **Fadel et al., [(16)]**on total of 150 subjects were enrolled by on 80 diagnosed leukemia patients and 70 healthy controls) to investigate the association between ADIPOQ SNP with Egyptian leukemia patients. There were no significant genotype-related differences associated with kidney function, liver function **(16)**

In current study, within **hypothyroid** group, there was statistically significant relation between gene polymorphism and both serum cholesteroland fasting blood glucose, the difference was significant between TT group and both GT and TT groups concerning cholesterol level. However, regarding fasting blood glucose, the difference is significant only between GT group and GG groups with non-significant relation between gene polymorphism and eithertriglycerides level,fasting insulin,HOMA-IR or2 hour postprandial blood glucose. Within **hyperthyroid** group, there was statistically significant relation between gene polymorphism and both serum cholesterol, fasting and 2 hours postprandial blood glucose, the difference is significant between GT group and both GG and TT groups concerning cholesterol level. However, regarding fasting blood glucose, the difference is significant only between GT group and GG groups with non-significant relation between gene polymorphism and either triglycerides level, fasting insulin, or HOMA-IR.

While in study by **Rajendran et al., [(17)]**TG (Heterozygous) phenotype had a strong association was perceived with Insulin resistance (p = 0.006)**(17)**

Also, in study by **Tsuzaki et al.,[(18)]**the extent of decrease in triglyceride levels was greater in the subjects with the T/T genotype than in those with the T/G genotype **(18)**

An earlier study by **Li et al., [(19)]**on TG/GG genotype in obese and non-obese non-diabetics also revealed that SNP + 45 T > G genotype was associated with enhanced fasting blood glucose, Insulin levels **(19)**

Melistas et al., [(20)]explored potential associations of polymorphisms (SNPs) in the adiponectin gene (ADIPOQ) with insulin resistance (IR), and markers of obesity in a healthy Greek female population, they found SNP +276G>T was associated with higher fasting insulin levels (P = 0.01) and higher homeostasis model assessment index for IR (HOMA-IR; P = 0.009), and SNP +45T>G was associated with lower insulin levels and HOMA-IR (P = 0.05 and P = 0.07 respectively) **(20)**

In accordance with the findings of the present study, **Vionnet et al.,[(21)]**first reported lower insulin sensitivity for +45T allele in a Chinese and Japanese population, **(21)** while in a Mediterranean population of Italy +276T allele was associated with higher insulin levels and HOMA-IR **(22)**

However, in nondiabetic Germans, the +45G allele was associated with higher IR indexes as reported by **Stumvoll et al., [23]**whereas in nondiabetic Korean, as well as in Japanese men, +276T allele was found to be protective for IR (association with lower HOMA-IR) **(24)**

Also, among 150 subjects were enrolled for **Fadel et al., [16]**study (80 newly diagnosed leukemia patients and 70 healthy controls). There were no significant genotype-related differences associated with TC, TrG and LDL-C levels. However, a significant elevation of FBS level, LDL/HDL, TC/HDL ratios, and a significant decrease in HDL levels were observed in G carriers.

However, **Chung et al.,[14]**found baseline serum glucose levels were significantly higher in GG subjects than in TG and TT subjects, TG/TG subjects showed higher insulin levels and HOMA-IR indexes than did non-TG subjects (X/X).

Moreover, **Sun et al., [25]**reported the levels of FPG, PPG, FINs, HOMA-IR and LDL-c in T2D patients with CG/TT were significantly higher than those in patients with other diplo types (CCTT, CCTG, CGTG, CCGG, CGGG, GGTT, GGTG)

This result is not in accordance with **Jang et al.,[26]** who found an association between the TG haplotype and increased HOMA-IR index.

Similarly, **Ooda et al., [27]**study included 40 patients with T2DM and 40 normal individuals revealed that, there were no significant differences in lipid profile (TCH, LDL, TG, and HDL) for both groups between the genotypes.

Our findings are in agreement with a **Zhao and Zhao,[28]**meta-analysis of available studies, which concluded that the SNP 45 is not significantly associated with lipid profile

However, other studies found an association between this SNP and two components of plasma lipids. In Egypt, the study by **Khodeer et al.**, **[29]** revealed that, compared with SNP 45 T carriers, G carriers showed higher levels of LDL-C and TCH. However, no significant differences were found in TG and HDL between these two genotypes.

V. Conclusion:

This study suggests that adiponectin gene polymorphism is not associated with thyroid dysfunctions among both groups of hypothyroidism& hyperthyroidism of Egyptian patients.

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