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Association of Adiponectin Gene Polymorphisms rs17300539, rs266729 and rs1501299 with Adiponectin Levels, Insulin Resistance and Non-Alcoholic Fatty Liver Disease, in an Iranian Population

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Abstract

Background & Objectives: In this study, we investigated the relationship between polymorphisms in the adiponectin gene and biochemical parameters—specifically adiponectin levels, insulin resistance, and the presence of non-alcoholic fatty liver disease (NAFLD)—in an Iranian population.

Materials & Methods: We conducted a case–control study comprising 80 individuals with NAFLD and 80 healthy controls. Genotyping of the ADIPOQ gene polymorphisms rs17300539, rs266729, and rs1501299 was performed using the polymerase chain reaction-restriction fragment length polymorphism (PCR–RFLP) method, while serum adiponectin and insulin levels were quantified via enzyme linked immunosorbent assay (ELISA).

Results: Our findings demonstrated that patients exhibited significantly higher serum triglyceride levels, fasting blood glucose, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and diastolic blood pressure compared to healthy individuals. In contrast, adiponectin and high density lipoprotein cholesterol (HDL-C) levels were significantly lower in patients, and body mass index (BMI) was significantly elevated ($P<0.05$). None of the analyzed single nucleotide polymorphisms (SNPs) were associated with insulin resistance. However, there was a significant difference in both genotype and allele frequencies of the rs1501299 variant between the patient and control groups. Additionally, within the case group for rs17300539, GA carriers had a higher BMI than GG carriers. Moreover, significant associations were observed between the rs17300539 and rs266729 polymorphisms and AST levels ($P<0.05$).

Conclusion: Our results suggest that the G allele of rs17300539 in the adiponectin gene may play a protective role by reducing the complications associated with NAFLD, while the rs1501299 polymorphism appears to be associated with an increased risk of NAFLD.

Keywords: Non-alcoholic fatty liver, Adiponectin, polymorphism, Fatty tissue, Insulin resistance.

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Introduction

Excessive accumulation of fat in hepatocytes, in the absence of significant alcohol consumption, is the primary cause of non-alcoholic fatty liver

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disease (NAFLD). Histologically, NAFLD can be distinguished from simple non-alcoholic fatty liver steatosis (1). Although the initial stage of NAFLD is typically benign, approximately 25% of patients progress to more severe disease (2, 3). Currently, NAFLD is the second most common cause of chronic liver disease among individuals on the liver transplant waiting list in the United States (4), and liver transplants for NAFLD have increased over the past decade in Britain and Europe (2). NAFLD is a global epidemic, affecting an estimated 20–30% of the population worldwide (5). Metabolic syndromes such as insulin resistance, inflammation, obesity, and type 2 diabetes are closely associated with NAFLD (6, 8), underscoring the importance of treating both NAFLD and its related metabolic disorders (2). Moreover, NAFLD is a risk factor for progression to non-alcoholic steatohepatitis (NASH), fibrosis, cirrhosis, and hepatocellular carcinoma (HCC) (3, 4), and no licensed drug is currently available for its treatment. Adipocytes are the main regulators of energy homeostasis in the body (1). Among the adipokines secreted by adipose tissue, adiponectin plays a crucial role in modulating insulin sensitivity and the pathogenesis of metabolic syndrome (4). Adiponectin is secreted into the bloodstream as three oligomeric complexes: a trimer (67 kDa), a hexamer (a complex of two trimers, 130 kDa), and a high-molecular-weight multimer (300 kDa) comprising at least 18 monomers (8). In its monomeric form, adiponectin is undetectable under physiological conditions; thus, polymerization is essential for its biological function (9). Consequently, adiponectin assembles into trimers (the low-molecular-weight form, LMW) via the establishment of hydrophobic bonds between globular domains and noncovalent interactions within the α-helical regions of its collagenous domains (4). Recent studies have demonstrated that, in addition to environmental factors, genetic factors also play a significant role in the development of NAFLD (6). Genes involved in insulin resistance, including those encoding adiponectin, resistin, and leptin, may influence the prevalence of NAFLD (7). There is evidence that single nucleotide polymorphisms (SNPs) in the ADIPOQ gene are correlated with serum adiponectin levels. Three common SNPs—rs17300539 (11391 G>A), rs266729 (−11377 C>G), and rs1501299 (+276 G>T)—located in the promoter and intronic regions of the ADIPOQ gene have been extensively studied in epidemiological research. The variant allele of rs266729, which is associated with lower adiponectin levels, has been linked to obesity (8). Research by Trilet et al. in the United States demonstrated that the rs17300539 (−11391 G>A) polymorphism impairs adiponectin secretion, resulting in reduced plasma adiponectin levels (9). Conversely, studies in different populations have found that the G allele of rs17300539 is associated with increased adiponectin secretion (10). The rs1501299 polymorphism is associated with diminished adiponectin expression, potentially contributing to weight gain and insulin resistance. Several studies have examined the association between adiponectin gene polymorphisms and NAFLD risk (8). Previous research in NAFLD patients has shown that carriers of the G allele of rs266729 exhibit lower serum levels of triglycerides (TG), total cholesterol (TC), fasting plasma glucose (FPG), and low-density lipoprotein (LDL) compared to non-carriers (11). Insulin resistance is a prerequisite for NAFLD development (12), and NAFLD is also associated with insulin resistance in extrahepatic tissues such as muscle and adipose tissue (12–14). Fernando et al. demonstrated that a hepatic triglyceride accumulation of 2–5% is accompanied by reduced insulin sensitivity in the liver, muscle, and adipose tissue (15). However, there is no linear relationship between intrahepatic triglyceride content and the extent of inflammation, ballooning, or fibrosis (16). Adipose tissue insulin resistance is a critical risk factor for the progression of liver disease

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(11, 12), and NAFLD is closely linked to insulin resistance, with 70–80% of obese and diabetic patients affected by NAFLD (17, 18). Immune cells—including macrophages/Kupffer cells, natural killer cells, and T cells—contribute to the progression of NASH by secreting inflammatory mediators. Hepatic macrophages, particularly those derived from bone marrow, are the principal immune cells that release proinflammatory cytokines such as tumor necrosis factor (TNF)-α and interleukin (IL)-1β, which promote systemic insulin resistance and NASH (19). Macrophages can be classified as M1 (classically activated, proinflammatory) and M2 (alternatively activated, anti-inflammatory) (20–22). Dysregulated polarization of M1 and M2 macrophages is closely associated with metabolic disorders, including obesity, insulin resistance, and NAFLD. Previously, we found that excessive hepatic lipid accumulation activates macrophages/Kupffer cells, exacerbating insulin resistance, hepatic inflammation, and fibrogenesis (23). In this study, we investigated the frequency of the rs266729, rs1501299, and rs17300539 polymorphisms and their associations with biochemical and anthropometric parameters, as well as NAFLD, in an Iranian population.

Materials and Methods

Study Design and Anthropometric Parameters

This research was conducted using a case–control design. Participants were recruited from Bo Ali and Amirul Mominin Hospitals in Tehran between 15 April 2016 and 20 October 2016, with 80 patients—whose diagnosis of NAFLD was confirmed by ultrasound—selected as cases and 80 healthy individuals as controls. The sample size was calculated using MedCalc (version 14.8.1) software, based on an alpha of 0.05, 80% power, a mean difference of 0.8 mg/L in adiponectin levels (the primary outcome), and a standard deviation of 1.8 mg/L, with an equal ratio between groups. Current diagnostic methods for NAFLD include ultrasound, computed tomography (CT), magnetic resonance imaging (MRI), liver biopsy, and laboratory tests; in this study, sonography and MRI were used to definitively diagnose NAFLD under the supervision of a gastroenterology and liver specialist (24). The study protocol adhered to the Helsinki Declaration and was approved by the Research Ethics Committee of Islamic Azad University, Tehran Medical Branch (Ethics Code: IR.IAU.TMU.REC.1396.293). All participants provided written informed consent after the study objectives were thoroughly explained. Body height, weight, were evaluated using standard methods. BMI was calculated as [weight (kg) /height (m2)].

Biochemical Assessment

Biochemical measurements and genotyping for polymorphisms were performed at the Endocrine and Metabolism Research Institute of Shahid Beheshti University, Iran. Only Iranian subjects were included in the study, and eligibility required non-consumption of alcohol and metabolic drugs, as medications such as metformin—which modulates several signaling pathways, including AMP-activated protein kinase—can alter adiponectin levels (25, 26). Participants received detailed information about the study, and those who consented completed a comprehensive questionnaire covering medical history, medication use, and other relevant factors (15). Subsequently, a 10 mL blood sample was collected from each participant, with 5 mL transferred into a tube containing ethylenediaminetetraacetic acid (EDTA) and the remaining 5 mL into a tube without anticoagulant. After clot formation in the non-anticoagulated tube, serum was separated by centrifugation (10 minutes at 3000 RPM) and stored at -80°C. Genomic DNA was extracted from whole blood in EDTA tubes using the salting-out method and stored at -20°C. Serum adiponectin and insulin levels were determined using a Mercodia enzyme linked immunosorbent assay (ELISA) kit, while fasting blood glucose, total cholesterol,

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triglycerides, LDL-C, HDL-C, ALT, and AST were measured using the Pars Azmoon test kit on a Biotechnica BT3500 analyzer.

PCR Amplification

The polymerase chain reaction-restriction fragment length polymorphism (PCR–RFLP) technique was employed to genotype the rs17300539, rs266729, and rs1501299 polymorphisms in the adiponectin gene. Further validation was achieved by sequencing a subset of DNA samples (n=16), confirming the results obtained via PCR–RFLP. Two primers were designed for each polymorphism using Gene Runner and Oligo software; their sequences are provided in Table 1.

The specific performance of the primers was confirmed by querying the basic local alignment search tool (BLAST) database. Two SNPs (rs17300539 and rs266729), both located in the promoter region and positioned adjacent to each other, were amplified using a single primer pair. The DNA fragment containing the rs1501299 polymorphism in the adiponectin gene, measuring 196 bp, was amplified by PCR (Table 1). For the PCR reaction, a 25 µl reaction mixture was prepared, comprising Master Mix (including dNTPs, Taq polymerase, and $MgCl_2$), 1 µl of genomic DNA, 1 µl of each primer (at a concentration of 10 picomol/µl), and distilled water. All PCR reagents were obtained from Sinagen Company. The thermocycler program was optimized for primer performance in two stages for rs17300539 and rs266729: an initial denaturation at 94°C for 10 minutes, followed by 10 cycles consisting of 45 seconds of denaturation at 94°C, 45 seconds of primer annealing at 65°C, and 1 minute of extension at 72°C; this was succeeded by 20 cycles with denaturation at 94°C for 45 seconds, annealing at 60°C for 45 seconds, extension at 72°C for 1 minute, and a final extension at 72°C for 5 minutes. The accuracy of amplification of the target fragment was verified by electrophoresis on an 8% acrylamide gel, which was subsequently stained with silver nitrate. For rs1501299 in the ADIPOQ gene, the PCR conditions were set at 93°C for 10 minutes, followed by 35 cycles of 45 seconds at 93°C, 30 seconds at 58°C, 45 seconds at 72°C, and a final extension at 72°C for 5 minutes. Thereafter, the PCR products were digested with MspI, HhaI, and BsmI restriction enzymes to detect rs17300539, rs266729, and rs1501299, respectively.

Statistical Analysis

Statistical analysis was performed using SPSS (statistical package for social science) version 21.0 (SPSS, Chicago, IL, USA). Descriptive and inferential tests were applied, including the Kolmogorov–Smirnov test (to assess the distribution of study variables), the independent t-test and Mann–Whitney test (to compare case and control groups), the Chi-square or Fisher's exact test (for qualitative variables), and logistic regression (to investigate the relationship between disease risk and genotypes). A P-value of<0.05 was considered statistically significant. Normally distributed quantitative variables were expressed as mean±standard deviation, whereas skewed quantitative variables were reported as median with interquartile range, and qualitative variables as percentages.

Table 1. Primers used for PCR

Polymorphisms	Amplicon size (bp)	Forward primer (5'→3') Reverse Primer (5'→3')
rs17300539 (-11391 G/A) rs266729 (-11377 G/C) rs1501299 (+276G/T)	(GG 167bp,296bp) (GA198bp,167bp,296bp) (AA296bp) (GG 183bp,113b) (CG 113bp, 183bp,296bp) (CC 296bp) (GT 196bp,148b) (GG 148bp, 48bp) (TT 196bp)	AGGCTCTGTGTGGACT GTGGA CCTGGAGAACTGGAA GCTGC AGGCTCTGTGTGGACT GTGGA CCTGGAGAACTGGAA GCTGC GGCCTCTTTCATCACAGACC AGATGCAGCAAAGCCAAAGT

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Table 2. Distribution of demographic variables and biochemical profiles in the study groups.

Characteristics	Control (N=80)	Case (N=80)	P value
Age(years)	35.42±8.5	6	NS.9±33.44
Kg/M²) BMI	9.2±23.61	28.74±4.6	P<0.0001
Mg/Dl) FPG)	8.03±92.08	91.98±13.8	P<0.0001
Cholesterol (Mg/DL)	105.68±25.01	152.01±69.9	NS
Triglyceride (Mg/DL)	97.5±42.9	170.30±43.2	P<0.0001
LDL (Mg/DL)	89.06±22.5	94.16±30.6	NS
HDL (Mg/DL)	48.42±12.1	35.15±12.6	P<0.0001
AST (IU/L)	16.55±4.4	26.44±8.3	P<0.0001
ALT (IU/L)	17.91±7.8	35.33±17.2	P<0.0001
Insulin (Mm/L)	11.57±11.4	22.45±33	NS
Adiponectin (Mm/L)	71.43±30.4	53.89±25.6	P<0.0001
Dystolic Pressure(mmHg)	7.95±0.35	8.09±0.67	P<0.0001
Systolic Pressure(mmHg)	11.48±1.3	12.2±1.8	NS

BMI Body mass index, lipoprotein, LDL low-density lipoprotein, HDL higher -density lipoprotein, FPG fasting plasma glucose AST aspartate aminotransferase ALT alanine aminotransferase.

Results

The study included 80 patients and 80 control subjects. The mean age of patients was 44.32 years, compared to 35.42 years for healthy subjects. The control group comprised 46 women (57.5%) and 34 men (42.5%), whereas the patient group included 37 women (46.3%) and 43 men (53.7%); the difference in gender distribution between the groups was not statistically significant. Serum triglyceride levels, fasting blood glucose, HDL, AST, ALT, and diastolic blood pressure were significantly higher in patients than in healthy individuals, while adiponectin levels were lower and body mass index (BMI) was higher in patients (P<0.05) (Table 2).

Result of electrophoresis of PCR products of rs17300539, rs266729 and rs1501299 polymorphism was performed using RFLP technique which is shown in Figures 1, 2, 3. In rs17300539 polymorphism, GA genotype consists of three bands with lengths of 296, 167 and 129 bp, GG genotype consists of two bands with lengths of 129 and 167 bp and AA genotype contains one fragment with a length of 296 bp which was not observed in the present study (Figure 1).

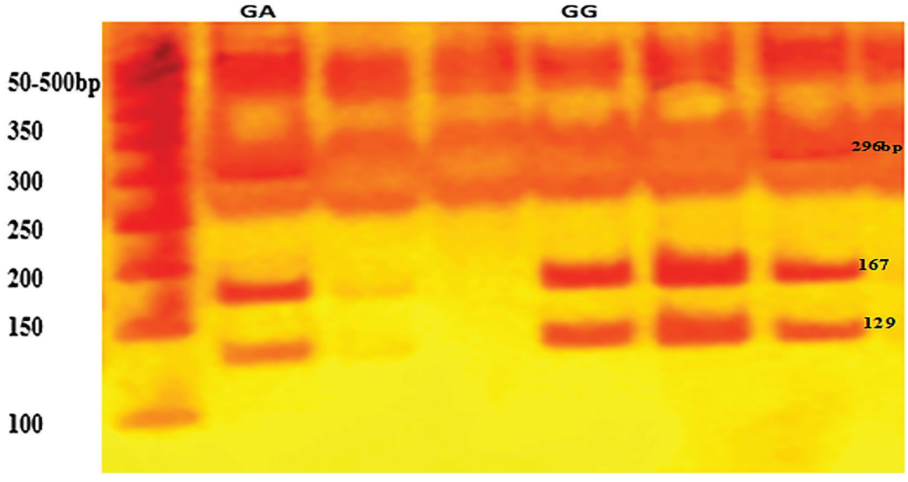


Figure 1. Enzymatic digestion of the rs17300539 polymorphism by MspI enzyme is depicted here. In this figure, the GA genotype is characterized by three bands (296, 167, and 129 bp), while the GG genotype displays two bands (129 and 167 bp). The AA genotype would also display a 296 bp band; however, it was absent in our analysis.

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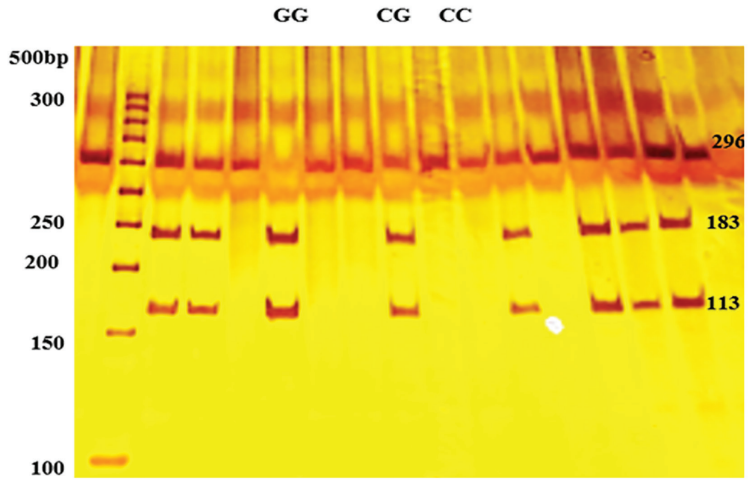


Figure 2. Following amplification of the target fragments of the rs266729 polymorphism and subsequent digestion with the HhaI enzyme, electrophoresis on an acrylamide gel revealed that the CG genotype is characterized by three bands (296, 183, and 113 bp), the GG genotype by two bands (183 and 113 bp), and the CC genotype by a single band (296 bp).

The frequency of the GG genotype for the rs17300539 polymorphism was 96.3% in healthy individuals and 90% in patients, whereas the GA genotype was observed in 3.8% of healthy subjects compared to 10% of patients. Regression analysis revealed no significant association between the GG and GA genotypes and non-alcoholic fatty liver disease. Similarly, the frequency of the G allele was 98% in healthy subjects and 95% in patients, and regression analysis indicated no statistically significant difference in G allele frequency between the two groups (P>0.05) (Table 3).

Furthermore, the relationship between the GG and GA genotypes of the rs17300539 adiponectin gene polymorphism and various biochemical and anthropometric parameters was assessed in both healthy and patient groups. Results indicated that, among patients, individuals with the GA genotype exhibited higher body mass index and diastolic blood pressure compared to those with the GG genotype, while no significant associations between these variables and genotype were observed in the healthy group (Table 4).

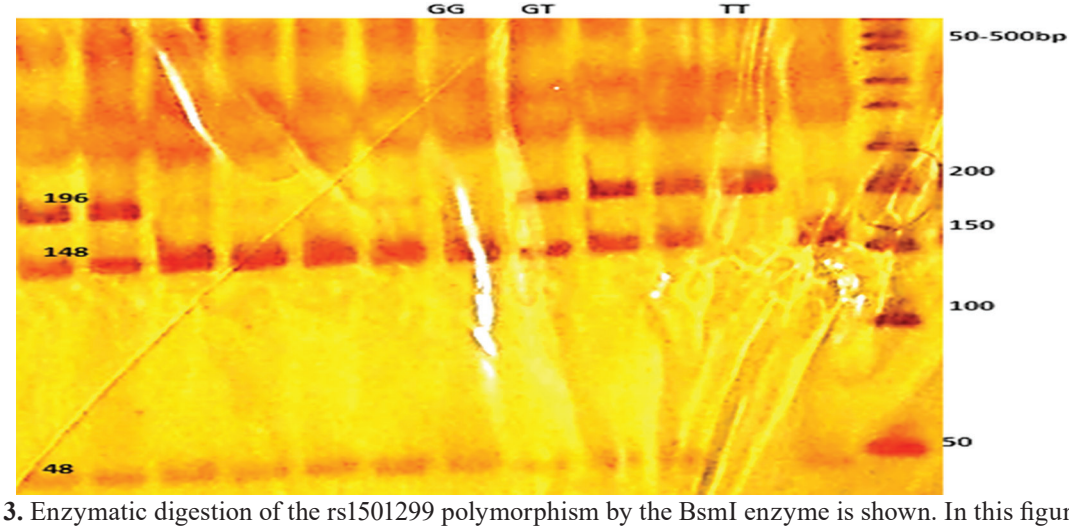


Figure 3. Enzymatic digestion of the rs1501299 polymorphism by the BsmI enzyme is shown. In this figure, the GT genotype is represented by three bands (196 bp, 148 bp, and 48 bp), the GG genotype by two bands (148 bp and 48 bp), and the TT genotype by a single band (196 bp).

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Table 3. Regression analysis of polymorphism genotypes rs1501299, rs266729, rs17300539

Polymorphism	Genotype	Control (N=80)	Case (N=80)	OR (CI=%95)	P value	Insulin-sensitive	Insulin resistant	OR (95%CI)	P value
rs17300539	GG	72(%90)	77(%96.3)	2.85(0.2-23.4)	NS				
	GA	8(%10)	3(%3.8)	0.35(0.09-1.37)	NS	87(96.7)	62(88.6)	0.27(0.07-1.05)	0.058
	G	152(%95)	157(%98)	2.75(0.72-10.58)	NS	3(3.3)	8(11.4)	0.27(0.07-1.05)	0.058
	A	8(%0.5)	3(%2)	0.36(0.09-1.39)	NS				
rs266729	CC	50(%62.5)	48(%60.0)	0.90(0.48-1.70)	NS				
	CG	30(37.5)	30(37.5)	1.0(0.53-1.90)	NS	52(57.8)	46 (65.7)	1.40 (0.73-2.67)	0.307
	GG	0(0)	2(2.5)	_	NS	36(40)	24(34.3)	0.78(0.41-1.50)	0.459
	G	30(%3.15)	34(%4.65)	1.73(0.4-1.3)	NS	2(2.2)	0 (0)		
	C	130(%96.95)	126(%95.35)	2.86(0.64-19.58)	NS				
rs1501299	TT	3(%3.8)	1(%1.3)	0.33(0.03-3.28)	NS 2(2.2)				
	GT	40(%50)	54(%69.2)	2.25(1.17-4.31)	P<0.0002	54(60)	2(2.9)	1.33(0.18-9.71)	0.459
	GG	37(%46.2)	23(%29.5)	0.49(0.25-0.94)	P<0.0002	34(37.8)	40(58.8)	0.95(0.50-1.81)	0.881
	T	38(%47.5)	34(%30)	0.47(0.25-0.91)	P<0.0002		26 (38.2)	1.02(0.53-1.95)	0.953
	G	20(%36)	29 (%52)	0.47(0.25-0.88)	P<0.0002				

The level of triglycerides and AST in women with the GA genotype was significantly higher than in those with the GG genotype (P<0.05). Likewise, male patients carrying the GA genotype exhibited higher diastolic blood pressure compared to those with the GG genotype (Table 5).

Table 5 does not include data on the rs1501299 polymorphism, as no significant differences in parameter values were observed between its genotypes.

For the rs266729 polymorphism, the CG genotype produced three bands measuring 296, 183, and 113 bp; the GG genotype yielded two bands (183 and 113 bp); and the CC genotype resulted in a single fragment of 296 bp (Figure 2).

The frequency of the GG genotype for the rs266729 polymorphism was 96.95% in healthy individuals and 95.35% in patients. Regression analysis indicated no significant association between the CC and CG genotypes and non-alcoholic fatty liver disease. Similarly, the frequency of the C allele was 96.95% in the healthy group and 95.35% in the patient group, and C-allele regression analysis revealed no significant difference between the two groups (P<0.05) (Table 3). Table 5 does not include data for the rs1501299 polymorphism, as no significant differences were detected between its genotypes.

For the rs1501299 polymorphism, the GT genotype produced three bands measuring 196 bp, 148 bp, and 48 bp; the GG genotype yielded two bands (148 bp and 48 bp); and the TT genotype displayed a single band of 196 bp (Figure 3).

The frequency of the GG genotype for the rs1501299 polymorphism was 50% in healthy individuals and 69.5% in patients, whereas the GT genotype was observed in 49.2% of healthy individuals and 29.5% of patients. Regression analysis for rs1501299 indicated a significant association between the TG and GG genotypes and non-alcoholic fatty liver disease. Furthermore, the frequency of the G allele was 74.1% in healthy subjects compared to 84% in patients, and regression analysis of the G allele revealed a significant difference between the two groups (P<0.05) (Table 3). In comparing the two groups, the number of GT genotype carriers was higher among patients, whereas the GG genotype was more prevalent in healthy individuals (Tables 3 and 4). Additionally, a significant difference in BMI was observed between patients carrying the GG and GT genotypes, with those carrying the GT genotype exhibiting a higher BMI (P<0.05) (Table 4).

We also examined the distribution of ADIPOQ gene polymorphisms among insulin-resistant (HOMA-IR≥2.6) and non-insulin-resistant

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Table 4. Relationship between rs1501299, rs266729 and rs17300539 polymorphisms with Biochemical and Anthropometric variables

Chaiac-teristics	rs17300539		Control(n=80)		P value	P value	rs266729		Control (78)		P value	P value	rs1501299		Control (n=77)		P value	P value
	Case (n=80)						Case (n=80)						Case (n=76)					
	GG	GA	GG	GA	p-case	p-control	CC	CG	CC	CG	p-case	p-control	GG	GT	GG	GT	p-case	p-control
Number	72	8	77	3			50	30	48	30			53	23	40	37		
BMI (kg/ m^2)	26.2± 5.7	29.8± 4.6	22.66± 2.8	23.7± 4.8	P< 0.0001	NS	29.4± 5.2	27.8± 4.8	23.9± 6.8	22.4± 8.4	NS	NS	29.6± 4.7	27.2± 4.3	23.42± 2.44	23.81± 3.48	P< 0.05	NS
FPG (Mg/Dl)	91.67± 14.09	94.75± 11.2	90.87± 8.02	87.75± 10.01	NS	NS	93.44± 11.59	79.50± 2.71	90.80± 8.1	94.20± 7.58	NS	NS	90.16± 24.23	92.32± 27.54	92.63± 8.24	92.16± 7.47	NS	NS
Cho-lesterol (Mg / DL)	170.81± 42.06	165.75± 51.02	141.75± 25.39	168.18± 3	NS	NS	169.65± 44.26	171.03± 43.49	166.34± 26.66	164.57± 22.39	NS	NS	168.82± 37.22	166.89± 23.15	160.57± 25.76	171.52± 23.56	NS	NS
Triglyc-eride (Mg / DL)	151.19± 68.4	156.35± 87.6	96.18± 42.97	95.25± 52.02	NS	NS	150.6± 71.24	156.27± 69.12	98.44± 44.88	95.93± 40.39	NS	NS	110.44± 81.68	103.01± 76.29	82.52± 62.21	91± 62.95	NS	NS
LDL (Mg / DL)	92.71± 31.2	107.18± 24.8	89.88± 22.44	88.86± 25.86	NS	NS	93.34± 23.73	93± 16.97	89.16± 22.86	88.90± 22.52	NS	NS	92.13± 27.53	90.17± 26.61	92.11± 22.78	86.8± 21.79	NS	NS
HDL (Mg/ DL)	34.81± 13.7	38.25± 6.3	51.45± 11.8	48.99± 20	NS	NS	36.27± 14.63	33.25± 8.75	47.92± 13.41	50.37± 9.77	NS	NS	41.53± 14.11	43.42± 13.94	49.25± 10.43	48.79± 13.26	NS	NS
AST (IU/ L)	26.23± 8.4	28.38± 7.7	18.05± 4.41	17.65± 3	NS	NS	25± 6.71	28.11± 9.85	17.86± 7.67	17.27± 7.76	NS	NS	22.46± 16.84	19.83± 22.7	16.14± 8.77	17.14± 9.18	NS	NS
ALT (IU/ L)	35.20± 16.9	35.63± 20.6	18.35± 7.89	16.64± 3.21	NS	NS	34.24± 16.93	36.36± 18.26	17.68± 7.76	18.30± 8.07	NS	NS	23.84± 15.98	20.42± 27.78	15.29± 12.22	18.24± 14.28	NS	NS
Insulim (Mn/L)	21. 96± 11.4	26.88± 30.2	12.54± 11.26	8.65± 14.9	NS	NS	26.18± 40.02	17.3± 17.61	13.56± 13.69	8.26± 4.46	NS	P< 0.0001	9.81± 15.82	10.24± 5.74	9.36± 5.18	6.58± 8.84	NS	NS
Adipo-nectin (Mm/L)	5.41± 2.6	5.16± 5.4	7.72± 2.88	7.55± 4.17	NS	NS	5.49± 2.87	5.19± 1.99	7.39± 2.93	6.72± 2.88	NS	NS	5.51± 7.75	5.65± 4.28	6.54± 5.44	6.31± 8.62	NS	NS
Dystolic Pressure (mmHg)	8.04± 0.63	8.5± 0.82	7.92± 1.42	8± 0.57	P< 0.0001	NS	8.19± 0.68	7.93± 0.67	7.92± 0.34	8± 0.37	NS	NS	8.17± 0.9	8.21± 0./08	8.27± 0.87	8.29± 0.99	NS	NS
Systolic (mmHg) Pressure	12.19± 1.8	13.06± 1.9	11.59± 0.35	13.06± 0.03	NS	NS	12.5± 0.70	12.23± 1.81	11.52± 0.76	11.34± 2.07	NS	NS	12.21± 0.44	12.4± 0.16	11.06± 0.97	12± 0.34	NS	NS

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Table 5. Investigation of biochemical parameters and body mass index in rs17300539 and rs266729 polymorphisms according to gender

Chaiac-teristics	rs17300539		Male(n=43)		P value	P value	rs266729				P value	P value
	Female(n=37)						Female(n=48)		Male(n=32)			
	GG	GA	GG	GA	p-female	p-male	CC	CG	CC	CG	p-female	P-male
Number	33	4	39	4			35	13	35	13		
BMI(kg/ m^2)	27.62± 4.5	29.89± 4.6	29.29± 5.6	34.16± 6.4	NS	NS	26.82± 3.18	28.92± 4.67	25.21± 4.73	23.18± 4.21	NS	NS
FPG(Mg/ Dl)	92.62± 7.21	101.75± 14.8	90.87± 8.18	87.74± 7.59	NS	NS	96.91± 12.83	89.29± 22.62	90.5± 9.72	91.50± 10.2	NS	NS
Choles-terol (Mg / DL)	173.91± 49.43	189.75± 35.6	168/19± 39/34	141.37± 23.64	NS	NS	173.14± 53.42	180.46± 49.98	166.69± 35.59	162.63± 67.76	NS	NS
Triglycer-ide (Mg / DL)	139.33± 28.56	223.5± 52.3	159.56± 38.94	151.37± 43.54	P<0.0001	NS	151.32± 71.82	140.43± 70.52	149± 14.12	168.38± 67.79	NS	NS
LDL(Mg / DL)	83.79± 22.97	103.6± 21.54	100.26± 26.11	110.75± 28.74	NS	NS	83.75± 39.64	90.07± 33.94	101.46± 23.32	90.07± 23.72	NS	NS
HDL(Mg/ DL)	34.85± 9.41	37.51± 14.9	34.77± 10.49	39± 13.94	NS	NS	335.48± 15.22	35.31± 7.34	39.96± 14.37	31.44± 9.23	NS	NS
AST(IU/ L)	24.91± 9.67	31.25± 7.16	27.34± 7.43	25.5± 8.3	P<0.0001	NS	23.79± 7.3	28.41± 9.75	26.03± 6.12	84.27± 10.65	NS	P<0.0001
ALT(IU/ L)	33.64± 7.26	38.75± 15.18	36.52± 8.68	23.81± 12.82	NS	NS	33.65± 19.35	33.92± 19.63	34.74± 14.97	38.5± 17.23	NS	NS
Insulim (Mn/L)	17.26± 12.41	38.92± 14.9	25.94± 13.12	14.852± 11.24	NS	NS	17.4± 20.35	33.88± 23.47	33.61± 50.38	11.53± 6.82	NS	NS
Adipo-nectin (Mm/L)	7.04± 2.99	5.35± 3.6	4.87± 1.98	4.98± 3.94	NS	NS	6.68± 2.91	4.46± 1.37	4.49± 0.48	5.64± 0.58	P<0.0001	NS
Dystolic Pressure (mmHg)	8.03± 0.64	8.5± 0.82	8.05± 0.48	8.94± 0.76	NS	P<0.0001	8.12± 0.9	8.92± 0.91	8.21± 0.08	8.93± 0.83	NS	NS
Systolic Pressure (mmHg)	12.18± 1.09	13± 0.8	12.2± 0.72	13.12± 0.6	NS	NS	12.4± 1.62	12± 1.56	12.22± 0.44	12.43± 0.5	NS	NS

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subjects (HOMA-IR<2.6). The results indicated no significant differences in allele or genotype frequencies between these groups (Table 3). Moreover, as no differences were observed in haplotype frequencies among the ADIPOQ SNPs (rs17300539, rs266729, rs1501299), the corresponding table has been omitted.

Discussion

In the present study, we investigated the frequency of the rs17300539, rs266729, and rs1501299 polymorphisms in the adiponectin gene and examined their relationships with various biochemical parameters, insulin resistance, BMI, and NAFLD. Numerous studies have demonstrated that NAFLD increases the risk of developing metabolic disorders (25, 26). Specifically, analysis of the rs17300539 polymorphism revealed significant differences in the mean levels of triglycerides and AST between women carrying the GG genotype and those with the GA genotype; notably, triglyceride levels were significantly higher in women with the GA genotype than in those with the GG genotype. Similarly, among men, carriers of the GA genotype exhibited significantly higher diastolic blood pressure compared to GG carriers. However, no statistically significant differences were observed in insulin levels between GA and GG carriers. Furthermore, our data did not reveal any significant differences in the frequency of rs17300539 genotypes between healthy individuals and patients, indicating no association between this polymorphism and NAFLD.

In contrast to our findings, Hivert et al. reported that the G allele of the rs17300539 polymorphism is associated with an increased risk of metabolic syndrome and type 2 diabetes (27). Similarly, a study by Henneman et al., involving 1,285 women and 967 men in the United States, demonstrated that the rs17300539 polymorphism impairs adiponectin secretion, thereby reducing plasma adiponectin levels and its function (28). Conversely, Wassel et al. reported an association between the rs17300539 polymorphism and elevated serum adiponectin levels in a population with cardiovascular disease (29), while Vasseur et al. observed a significant relationship between alleles and increased serum adiponectin levels among French Caucasians (30). Moreover, research in an Italian population indicated that carriers of the GG genotype of rs17300539 exhibited lower levels of adiponectin and insulin, with significant correlations noted between this polymorphism and serum levels of adiponectin, fasting blood glucose, fasting insulin, HDL, cholesterol, and triglycerides (31).

Contrary to these studies, our investigation found no correlation between rs17300539 genotype and insulin or adiponectin levels; instead, a significant association was observed between this polymorphism and both BMI and diastolic blood pressure among patients. In women with NAFLD, serum AST levels were significantly higher in GA genotype carriers compared to those with the GG genotype, and similarly, diastolic blood pressure was higher in male NAFLD patients carrying the GA genotype. In line with a study by Menzaghi et al. on a Caucasian population in central Italy, carriers of the A allele of the rs17300539 polymorphism exhibited lower weight and BMI compared to GG carriers (32). Likewise, research by Morandi et al. in a European cohort demonstrated that A allele carriers had a lower BMI than GG carriers (31). However, Jun Wang and colleagues found that the G allele of rs17300539 increases the risk of NAFLD, which contradicts our findings (33). Additionally, Henneman et al. reported that NAFLD patients with the GA genotype had higher BMI compared to those with the GG genotype (28), a result that aligns with our observations. Finally, Morandi et al. indicated that, among obese individuals, carriers of the AA and GA genotypes were more insulin resistant, although this association did not reach statistical significance (31).

In our study population, we also examined

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the rs266729 polymorphism. Statistical analysis revealed no significant difference in genotype frequencies between healthy subjects and patients, indicating that these genotypes are not associated with an increased risk of NAFLD. Specifically, in the context of the rs266729 polymorphism, men with the CG genotype exhibited significantly higher AST levels than those with the CC genotype, while women with the CC genotype had higher adiponectin levels. Hashemi et al. demonstrated that carriers of the CG genotype in the rs266729 polymorphism show decreased adiponectin levels and an increased likelihood of developing NAFLD due to the presence of the G allele (34). Similarly, in a study of 150 NAFLD patients in Egypt, Moshira Zaki found that carriers of the G allele were at higher risk of developing NAFLD compared to carriers of the C allele, with CC genotype carriers exhibiting elevated serum adiponectin levels—a finding consistent with our results (35). Moreover, Divella et al. reported that individuals with NAFLD who carry the G allele of rs266729 are more likely to be obese and insulin resistant (36). Research conducted in Pakistan yielded similar findings, and a study by Nadeem et al. on diabetic patients found no association between the rs266729 polymorphism and diabetes (37). Furthermore, Moushira Zaki's study in fatty liver patients revealed that insulin resistance was higher in individuals with GG and GC genotypes compared to those with the CC genotype (35). In our study, the increase in insulin levels among CC genotype carriers was not statistically significant, and although Rosa Divella et al. observed increased insulin resistance in carriers of the rs266729 polymorphism with liver metastasis, these changes were not significant in our cohort (36).

We also examined the rs1501299 polymorphism in the present study. Our analysis revealed significant differences in allele frequencies between healthy subjects and patients; specifically, the frequency of the T allele in healthy individuals differed significantly from that of the G allele in patients. Furthermore, there was a significant difference in the frequency of the GG genotype between the healthy and patient groups, as well as in the frequency of the GT genotype. According to our findings, carriers of the GT genotype are more likely to develop NAFLD, leading us to conclude that the presence of the G allele is associated with a reduced risk of developing NAFLD. In contrast to our results, Hashemi et al. did not find a relationship between the presence or absence of different alleles of the rs1501299 polymorphism and NAFLD susceptibility (34). Conversely, Jiaxing Liu et al. reported that the risk of NAFLD increases in carriers of various rs1501299 genotypes (38), and Mengwei Liu et al. concluded that carriers of rs1501299 polymorphism genotypes are more susceptible to NAFLD (39). Additionally, among NAFLD patients in our study, those with the GT genotype had a significantly higher BMI than those with the GG genotype, a finding that aligns with Hashemi et al., who reported that BMI, waist circumference, and systolic blood pressure were elevated in NAFLD patients with the rs1501299 polymorphism (34). However, while Hong-Jue Li et al. observed higher insulin resistance in NAFLD patients carrying the rs1501299 polymorphism, this difference was not statistically significant in our study (40). Similarly, Mohammadzadeh et al. reported no significant relationship between rs1501299 and HOMA-IR, which is consistent with our findings (41).

Prakash et al. demonstrated a significant association between carriers of the rs1501299 polymorphism in the adiponectin gene and HOMA-IR, a finding that contrasts with our results (42). Similarly, Jung Kim et al. reported increased insulin resistance in HCC—particularly among individuals with metabolic disorders—which also contradicts our findings (43). In contrast, Reyhane Ebrahimi, Mavilia, and Nezhadali observed that adiponectin levels

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were significantly lower in obese individuals with NAFLD compared to controls, a result that is consistent with our study (44–46).

Several adipokines exert critical functions, including the modulation of tissue injury and fibrosis (47). NAFLD is recognized as the most prevalent liver disease (48), and inflammation, followed by subsequent fibrosis and cirrhosis, constitutes a pivotal step in its pathogenesis (49). Discrepancies between our findings and those of other studies in this field may be attributable to variations in sample size, environmental influences, participant age and race, as well as the effects of other polymorphisms and genes.

The limitations of this study include the influence of advanced age on fatty liver incidence and the exclusion of alcohol consumption and metabolic drug use among patients. Notably, both healthy individuals and NAFLD patients included in this project had no history of using metabolic drugs, which is a critical aspect of our study design. In summary, the G allele of rs17300539 appears to mitigate complications associated with NAFLD, whereas the presence of the G allele in the rs1501299 polymorphism increases NAFLD risk. Conversely, for the rs266729 polymorphism, the G allele does not appear to influence the risk of developing NAFLD.

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Conflict of Interests

The authors declare that they have no conflicts of interest.

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Code of Ethics

The study was approved by the Research Ethics Committee of Islamic Azad University, Tehran Medical Branch (Ethics Code: IR.IAU.TMU.REC.1396.293).

Authors' Contribution

F.R. drafted the manuscript; J.R.M. and M.N. revised the manuscript and improved its language; L.A.M. analyzed the data; and M.H. and M.N. designed the study. All authors approved the final version of the article.

Data Availability Statement

All data generated or analyzed during this study are available from the corresponding author upon reasonable request.

List of Abbreviations

SNPs: Single nucleotide polymorphisms; NAFLD: Non-alcoholic fatty liver disease; PCR-RFLP: Polymerase chain reaction–restriction fragment length polymorphism; ELISA: Enzyme-linked immunosorbent assay; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; HDL-C: High-density lipoprotein cholesterol; BMI: Body mass index; TG: Triglyceride; TC: Total cholesterol; FPG: Fasting plasma glucose; LDL: Low-density lipoprotein; TNF: Tumor necrosis factor; IL: Interleukin.

References

1 Yki-Järvinen H, Luukkonen PK, Hodson L, Moore JB. Dietary carbohydrates and fats in nonalcoholic fatty liver disease. Nature reviews Gastroenterology & hepatology. 2021; 18:770-86.
2 MazzoliniG, SowaJ P, Atorrasagasti C, Kücükoglu Ö, SynW K, Canbay A. Significance of simple steatosis: an update on the clinical and molecular evidence. Cells. 2020; 9:2458.
3 Farrell G, Wong VW, Chitturi S. NAFLD in Asiaas common and important as in the West. Nat Rev Gastroenterol Hepatol. 2013; 10:307-18.
4 Barbe A, Bongrani A, Mellouk N, Estienne A, Kurowska P, Grandhaye J, et al. Mechanisms of adiponectin action in fertility: an overview from gametogenesis to gestation in humans and animal models in normal and pathological conditions. Int J

[Downloaded from jabs.fums.ac.ir on 2026-11-11]
[DOI: 10.18502/jabs.v15i1.17554]

Mol Sci. 2019; 20:1526.
5 Møhlenberg M, Terczynska-Dyla E, Thomsen K.L, George J, Eslam M, Grønbæk H, et al. The role of IFN in the development of NAFLD and NASH. Cytokine. 2019; 124:154519.
6 Rezaei F, Nezhadali M, Hedayati M. Association of adiponectin rs17300539 gene polymorphism with a non-alcoholic fatty liver disease in an Iranian population. KAUMS Journal (FEYZ). 2018; 22: 379-386. [In Persian]
7 Kitade, H, Chen G, Ni Y, Ota T. Nonalcoholic fatty liver disease and insulin resistance: new insights and potential new treatments. Nutrients. 2017; 9:387.
8 Abenavoli L, Milic N, DiRenzo L, Preveden T, Medić-Stojanoska M, De Lorenzo A. Metabolic aspects of adult patients with nonalcoholic fatty liver disease. World J. Gastroenterol. 2016; 22:7006.
9 Almeda-Valdes P, Aguilar-Olivos N, Uribe M,Méndez-Sánchez N. Common features of the metabolic syndrome and nonalcoholic fatty liver disease. Rev Recent Clin Trials. 2014; 9:148-58.
10 Machado M.V, Cortez-Pinto H. Diet microbiota, obesity, and NAFLD: a dangerous quartet. Int. J Mol Sci. 2016; 17:481.
11 Matsuzawa N, Takamura T, Kurita S, Misu H, Ota T, Ando H, et al. Lipid-induced oxidative stress causes steatohepatitis in mice fed an atherogenic diet. J Hepatol. 2007; 46, 1392-1403.
12 Marchesini G, Brizi M, Morselli-Labate AM, Bianchi G, Bugianesi E, McCullough AJ, et al. Association of nonalcoholic fatty liver disease with insulin resistance. Am J Med. 1999; 107:450-5.
13 Ide T, Shimano H, Yahagi N, Matsuzaka T, Nakakuki M, Yamamoto T, et al. SREBPs suppress IRS-2-mediated insulin signalling in the liver. Nat cell boil. 2004; 6:351-7.
14 Gastaldelli A, Sabatini S, Carli F, Gaggini M, Bril F, Belfort-DeAguiar R, et al. PPAR-γ-induced changes in visceral fat and adiponectin levels are associated with improvement of steatohepatitis in patients with NASH. Liver Int. 2021; 41:2659-70.
15 Sanyal AJ, Brunt EM, Kleiner DE, Kowdley KV, Chalasani N, Lavine JE, et al. Endpoints and clinical trial design for nonalcoholic steatohepatitis. J Hepatol. 2011; 54:344-353.
16 BrilF, Barb D, Portillo-Sanchez P, Biernacki D, Lomonaco R, Suman A, et al. Metabolic and histological implications of intrahepatic triglyceride content in nonalcoholic fatty liver disease. J Hepatol. 2017; 65; 1132-44.
17 Loomba R, Abraham M, Unalp A, Wilson L, Lavine J, Doo E, et al. Nonalcoholic Steatohepatitis Clinical Research Network. Association between diabetes, family history of diabetes, and risk of nonalcoholic steatohepatitis and fibrosis. J Hepatol. 2012; 56:943-51.
18 Williams CD, Stengel J, Asike MI, Torres DM, Shaw J, Contreras M,et al. Prevalence of nonalcoholic fatty liver disease and nonalcoholic steatohepatitis among a largely middle-aged population utilizing ultrasound and liver biopsy: a prospective study. J Gastroenterol. 2011; 140: 124-31.
19 Odegaard JI, Ricardo-Gonzalez RR, Eagle AR, Vats D, Morel CR, Goforth MH, et al. Alternative M2 activation of Kupffer cells by PPARδ ameliorates obesity-induced insulin resistance. Cell metab.2008; 7:496-507.
20 Martinez FO, Gordon S. The M1 and M2 paradigm of macrophage activation: time for reassessment. F1000prime rep. 2014; 6:13.
21 Sica A, Mantovani A. Macrophage plasticity and polarization: in vivo veritas. J Clin Invest. 2012; 122:787-95.
22 Haas JT, Francque S, Staels B. Pathophysiology and mechanisms of nonalcoholic fatty liver disease. Annu Rev Physiol. 2016; 78,181-205.
23 Chen J, Deng X, Liu Y, Tan Q, Huang G, Che Q, et al. Kupffer cells in non-alcoholic fatty liver disease: friend or foe? Int J Biol Sci. 2020; 16: 2367.
24 Fu Y, Zhou Y, Shen L, Li X, Zhang H, Cui Y, et al. Diagnostic and therapeutic strategies for non-alcoholic fatty liver disease. Frontiers in Pharmacology. 2022; 13, 973366.
25 Li B, Po SS, Zhang B, Bai F, Li J, Qin F, et al. Metformin regulates adiponectin signaling in epicardial adipose tissue and reduces atrial fibrillation vulnerability. J Cell Mol Med. 2020; 24:7751-66.
26 Wei Z. Li-Qun Z, Xiao-Ling H, Jian Q, Guo-Yue Y. Association of adiponectin gene polymorphisms and additional gene-gene interaction with nonalcoholic fatty liver disease in the Chinese Han population. Hepatol Int. 2016; 10:511-7.
27 Hivert MF, Manning AK, McAteer JB, Florez JC, Dupuis J, Fox CS, et al. Common variants in the adiponectin gene (ADIPOQ) associated with plasma adiponectin levels, type 2 diabetes, and diabetes-related quantitative traits: the Framingham Offspring Study. Diabetes. 2008; 57:3353-9.
28 Henneman P, Aulchenko YS, Frants RR, Zorkoltseva IV, Zillikens MC, Frolich M,et al. Genetic Architecture of Plasma Adiponectin Overlaps with the Genetics of Metabolic Syndrome–Related Traits. Diabetes care. 2010; 33:908-13.
29 Wassel CL, Pankow JS, Jacobs Jr DR, Steffes MW,

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[DOI: 10.18502/jabs.v15i1.17554]

Li NA, Schreiner PJ. Variants in the adiponectin gene and serum adiponectin: the Coronary Artery Development in Young Adults (CARDIA) Study. Obesity. 2010; 18:2333-8.
30 Vasseur F, Helbecque N, Lobbens S, Vasseur-Delannoy V, Dina C, Clement K, et al. Hypoadiponectinaemia and high risk of type 2 diabetes are associated with adiponectin-encoding (ACDC) gene promoter variants in morbid obesity: evidence for a role of ACDC in diabesity. Diabetologia. 2005; 48:892-9.
31 Morandi A, Maffeis C, Lobbens S, Bouatia-Naji N, Heude B, Pinelli L,et al. Early detrimental metabolic outcomes of rs17300539-A allele of ADIPOQ gene despite higher adiponectinemia. Obesity. 2010; 18:1469-73.
32 Menzaghi C, Ercolino T,Salvemini L, Coco A, Kim SH, Fini G, et al. Multigenic control of serum adiponectin levels: evidence for a role of the APM1 gene and a locuson14q13. Physiol genomics. 2004; 19: 170-4.
33 Wang J, Guo XF, Yu SJ, Song J, Zhang JX, Cao Z, et al. Adiponectin polymorphisms and non-alcoholic fatty liver disease risk: a meta-analysis. J Gastroenterol Hepatol. 2014; 29:1396-405.
34 Hashemi M, Bojd HH, Nasab EE, Bahari A, Hashemzehi NA, Shafieipour S, et al. Association of adiponectin rs1501299 and rs266729 gene polymorphisms with nonalcoholic fatty liver disease. Hepatmont. 2013; 13(5):1-7.
35 Zaki M. Association of Adiponectin− 11377 C/G (rs266729) Gene Polymorphism with Nonalcoholic Fatty Liver Disease and Metabolic Features in Egyptian Women. Al-Azhar University Journal of Virus Researches and Studies. 2020, 2:1-10.
36 Divella R, Daniele A, De Luca R, Mazzocca A, Ruggieri E, Savino E,et al. Synergism of adipocytokine profile and ADIPOQ/TNF-α polymorphisms in NAFLD-associated MetS predict colorectal liver metastases outgrowth. Cancer Genom. Proteom. 2019; 16:519-30.
37 Nadeem A, Mumtaz S, Naveed AK, Mansoor Q, Aslam M, Ismail M. Association of ADIPOQ C-11377G (rs266729), TNF-[alpha] G-308A (rs1800629) and TNF-[alpha] G-238A (rs361525) Single Nucleotide Polymorphisms with Type 2 Diabetes Mellitus in Pakistani Population. Journal of the College of Physicians and Surgeons Pakistan. 2017; 27:625-631.
38 Liu J, Xing J, Wang B, Wei C, Yang R, Zhu Y,et al. Correlation between adiponectin gene rs1501299 polymorphism and nonalcoholic fatty liver disease susceptibility: a systematic review and meta-analysis. Med sci monit. 2019; 25:1078.
39 Liu M, Liu S, Shang M, Liu X, Wang Y, Li Q, et al. Association between ADIPOQ G276T and C11377G polymorphisms and the risk of non-alcoholic fatty liver disease: An updated meta-analysis. Mol Genet Genomic Med. 2019;7: 624.
40 Li HJ, Li CP, Zhang C, Zhong XL, Shi L. Association of Adiponectin gene polymorphisms and nonalcoholic fatty liver disease. Int J Clin Exp Med. 2015; 8:16676.
41 Mohammadzadeh G, Ghaffari MA, Heibar H, Bazyar M. Association of two common single nucleotide polymorphisms (+ 45T/G and+ 276G/T) of ADIPOQ gene with coronary artery disease in type 2 diabetic patients. Iran Biomed J. 2016; 20:152.
42 Prakash J, Mittal B, Awasthi S, Srivastava N. Association of adiponectin gene polymorphism with adiponectin levels and risk for insulin resistance syndrome. Int J Prev Med. 2015; 6: 31.
43 Kim JH, Sinn DH, Gwak GY, Kang W, Paik YH, Choi MS, et al. Insulin resistance and the risk of hepatocellular carcinoma in chronic hepatitis B patients. J gastroenterol Hepatol. 2017; 32:1100-6.
44 Ebrahimi R, Shanaki M, Mohassel Azadi S, Bahiraee A, Radmard AR, Poustchi H, et al. Low level of adiponectin predicts the development of Nonalcoholic fatty liver disease: is it irrespective to visceral adiposity index, visceral adipose tissue thickness and other obesity indices? Arch Physiol Biochem. 2022, 128, 24-31.
45 Mavilia MG, Wu GY. Liver and serum adiponectin levels in non-alcoholic fatty liver disease. J Dig Dis. 2021; 22:214-21.
46 Nezhadali M, Mesbah-Namin SA, Hedayati M, Akbarzadeh M, Najd Hassan Bonab L, Daneshpour MS. Serum adiponectin and cortisol levels are not affected by studied ADIPOQ gene variants: Tehran lipid and glucose study. BMC Endocrine Disorders. 2022; 22:1-10.
47 Wang J, Brymora George J. Roles of adipokines in liver injury and fibrosis. Expert Rev Gastroenterol Hepatol. 2008; 2:47-57.
48 Vakili O, Borji M, Saffari-Chaleshtori J, Shafiee SM. Ameliorative effects of bilirubin on cell culture model of non-alcoholic fatty liver disease. Molecular Biology Reports.2023; 50: 4411-4422.
49 Montefusco DJ, Allegood JC, SpiegelS,Cowart LA. Non-alcoholic fatty liver disease: insights from sphingolipidomics. Biochem. Biophys. Res. Commun. 2018; 504: 608-16.

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