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Association of Adipokine Gene Polymorphism and Serum Adipokine Levels in Prediabetic Population

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Abstract: Prediabetes is a state of impaired glucose tolerance (IGT) and impaired fasting glycemia (IFG). Studies are showing the link between genetic variations of the adipokine gene and prediabetes, a condition that puts people at greater risk of developing type 2 diabetes (T2DM). The present study aims to evaluate the association of adipokine single nucleotide gene polymorphism (SNP) and the plasma levels of adipokines in prediabetes individuals in the north Kerala population. A case-control study was conducted with 150 prediabetes subjects (40 obese and 110 non-obese) and 150 controls. The single nucleotide polymorphism of adiponectin (ADIPOQ-rs266729), leptin (LEP2548- rs7799039), and resistin (RETN420- rs1862513) were assessed. There was a significant association between adiponectin level, leptin level, and gene polymorphism of ADIPOQ 11377(C>G) and LEP2548 (G>A) in the non-obese prediabetic group. There was a significant association between adiponectin level, leptin level, and gene polymorphism of ADIPOQ 11377(C>G) and LEP2548 (G>A) in the obese prediabetic group. Findings show that plasma adiponectin levels and ADIPOQrs266729C>G polymorphism are associated. Likewise, plasma leptin levels and LEP2548- rs7799039 G>A polymorphism are associated. These associations may contribute to the genetic risk of prediabetes. The current data would be useful in the genetic screening for the prediabetes population.

Keywords: prediabetes; adipokine; adiponectin; resistin; leptin; polymorphism; ELISA; PCR.
Abbreviations: IGT, impaired glucose tolerance; IFG, impaired fasting glycemia; T2DM, type 2 diabetes; MetS, metabolic syndrome; GWAS, Genome-wide association studies; RETN, resistin gene; SNP, Single nucleotide polymorphism; IR, insulin resistance; OGTT, oral glucose tolerance test; HbA1C, glycated hemoglobin, HOMA-IR, Homeostasis Model Assessment; EDTA, Ethylenediaminetetraacetic acid; DNA, Deoxyribonucleic acid; PCR, polymerase chain reaction;

1. Introduction

Diabetes and prediabetes are rapidly growing in India. Comprehensive global prevalence data on prediabetes are lacking. In 2021, around 9.1% of the global population, equivalent to 464 million people, had impaired glucose tolerance (IGT), and it is estimated that this number will rise to 10.0% (638 million) by 2045. Similarly, 5.8% of the global population, or 298 million individuals, had impaired fasting glucose (IFG) in 2021, and it is projected to increase to 6.5% (414 million) by 2045. High-income countries had the highest prevalence of

IGT and IFG in 2021, but by 2045, low-income countries are expected to experience the greatest relative increase in cases of IGT and IFG [1-2]. Though obesity and T2D are ubiquitous, a pattern of prevalence exists based on ethnicity [3]. Obesity (BMI > 30kg/m^2) is an increasingly common, multi-factor health problem. Its prevalence is increasing at an alarming rate globally, posing a serious public health problem [4].

Prediabetes frequently coexists with metabolic syndrome (MetS), thus showing an imbalance of glucose and lipid metabolism. Prediabetes and T2DM are inseparably connected with excessive visceral adiposity. Prediabetes is a stage that precedes T2DM. In prediabetes, resistance to insulin action is compensated by the higher level of insulin in the serum. The American diabetes association estimates that 70% of all individuals with prediabetes will eventually transition to T2DM [5]. Genome-wide association studies (GWAS) showed that T2DM has a strong genetic link, and many genes are responsible for developing T2DM and its complications [6]. Adipose tissue is an important endocrine organ that secretes several factors called adipokines. Several proteins produced by adipose tissue have been discovered that may provide the link between insulin resistance, obesity, and the development of diabetes [7-9].

Adiponectin molecule, a 30-kDa protein, is homologous to collagen and complements 1q family consisting of 244 amino acids [10]. It is encoded by the Adipo Q gene on chromosome locus 3q27 [11]. This chromosomal region is a locus susceptible to T2DM and metabolic syndrome [12]. A functional single nucleotide polymorphism, rs266729, in a promotor region of the adipoq gene, causes an amino acid change leading to the replacement of cytosine with guanine at nucleotide position -11377(-11377C>G) and is associated with T2DM [13]. However, the Gallele of ADIPOQ rs266729 may appear important in association with T2DM risk in various populations [14-15]. ADIPOQ rs266729 C>G polymorphism may contribute to the genetic risk of prediabetes and provide preliminary data useful in the genetic screening among this [16]. A decrease in plasma adiponectin level is strongly correlated with the pathogenesis of T2DM and obesity. Serum adiponectin level and SNP, the adipoq gene, are associated with prediabetes in Jordan [17].

Leptin is an adipokine hormone secreted primarily by adipocytes [18]. It is a protein with a molecular weight of 16 KD. It contains 167 amino acids. It is one of the most important hormones derived from adipose tissue [19]. The human leptin gene (LEP) is located on 7q31.3 and comprises 3 exons and two introns, which span approximately 18kb [20-21]. Among these, the common G-2548A leptin promotor variant, which results from a G to A substitution at nucleotide-2548 upsteam of the ATG start site [22], was associated with increased plasma leptin levels, obesity, metabolic syndrome, and hypertension [23]. There is a significant positive association between plasma leptin levels and diabetes [24]. The genotype distribution G-2548 Varient of the lep gene is associated with increased plasma leptin and glucose level in a set of soudi individuals.lep gene polymorphism as a genetic factor in diabetes mellitus risk [25].

Resistin is a 12.5Kd cysteine-rich peptide secreted from adipocytes in rodents and macrophages in humans [26]. The human resistin gene (RETN) is located on chromosome 19p13.3, with several identified SNP associated with T2DM [27]. Several human studies report serum resistin levels in patients with obesity, insulin resistance, and T2DM. The RETN -420C>G SNPs G alleles are significantly associated with T2DM in the Taiwan population. The present study hypothesizes that adiposity or their related complications in prediabetes cause significant changes in adipokines levels.

The study aims to evaluate the association of adipokine single nucleotide gene polymorphism (SNP) of adiponectin (ADIPOQ-rs266729), leptin (LEP2548- rs7799039), and resistin (RETN420- rs1862513) and the plasma levels of adipokines (Adiponectin, Leptin and Resistin) in prediabetes individuals in the north Kerala population.

2. Materials and Methods

This case-control study was carried out in rural and urban areas in Kerala, India. Informed consent was obtained from the subjects, and ethical clearance was obtained prior to the study. The study was conducted at the Aster Mims Hospital, Calicut-Kerala, India, in which we took 300 individuals (150 control and 150 experimental-prediabetic subjects, both obese (40) and non-obese (110)) within the age group 30-50 years of both sexes will be recruited.

- **Selection criteria**:

The age and sex-matched healthy control subjects without prediabetes and any family history of diabetes were recruited. A detailed assessment has been conducted, which includes Demographic Data (age, sex, height, weight, etc.), family history, and medical history. Insulin level were measured by CLIA, and insulin resistance (IR) was estimated by Homeostasis Model Assessment (HOMA-IR). The calculation was done as glucose (mg/dl) x insulin (μU/ml)/405. HbA1C level was used to screen prediabetes by HPLC method. A 2-hour oral glucose tolerance test (OGTT) was performed to rule out prediabetes. OGTT using 75 g of glucose was performed according to WHO criteria [2]: the first criterion for impaired fasting glucose (IFG) is fasting plasma of 110-126mg/dl and 2hrs post glucose load less than 140mg/dl or impaired glucose tolerance (IGT) is fasting plasma glucose ≤110mg/dl) and 2hrs post glucose load of 140- 200mg/dl. The elderly subjects with diabetes and other serious physical or mental illnesses are excluded.

Blood samples for glucose analysis include collecting and storing the blood in the evacuated tube containing sodium fluoride (glycolytic inhibitor) and potassium oxalate (anticoagulant). Plasma glucose is determined by the glucose oxidase-peroxidase method. A total of 5ml blood was collected from each subject and separated into 2 containers: 2ml in an EDTA-coated tube for DNA analysis and 3ml for serum isolation and further biochemical analysis. All samples are stored at -20°C before use. The blood samples were collected for DNA isolation, and the plasma samples were collected for adipokine estimation. The estimation of adipokines (adiponectin, leptin, and resistin) was performed through ELISA. The gene polymorphism was assessed by real-time PCR. The genotyping result for each SNP marker will be verified using DNA sequencing. Genomic DNA was extracted from EDTA whole blood using a nucleospin blood mini kit (Broad Institute) according to the manufacturing protocol; SNPs were genotyped using the KASP genotyping assay kit (USA). SNP information was obtained from the NCBI dbSNP database (Table 1). The allelic discrimination analysis was conducted by step 1ABC, which applied a bio real-time PCR system. The primers were designed to amplify the DNA region for each SNP marker. 40 samples were randomly selected for forward and reverse sequencing (Europhins Banglore). Statistical analysis was performed using IBM SPSS version 21.0 software (Chicago USA). Numerical variables were represented using mean and standard deviation. To test the statistical significance of the comparison of demo and biochemical parameters, Adiponectin, Leptin, and Resistin levels between obese, non-obese, and control groups and also the comparison of Adiponectin, Leptin, and Resistin levels between their respective polymorphisms, One-way ANOVA followed by multiple comparison Bonferroni test was applied.

Table 1. SNP information of adipokine gene.

Adipokine SNP Information

SNP ID	Gene Position	Location	Forward Primer Reverse Primer
rs266729	ADIPOQ11377 (C>G)	Promoter	ACTTGCCCTGCCTCTGTCTG GCCTGGAGAACTGGAAGCTG
rs7799039	LEP2548(G>A)	Promoter	5^1 - TTTCTGTAATTTTCCCGTGAG-3^1 3^1-AAAGCAAAGACAGGCATAAAAA-5^1
rs1862513	RETN420(C>G)	Promoter	5^1-TGTCATTCTCACCCAGAGACA-3^1 3^1-GGGCTCAGCTAACCAAATC-5^1

SNP information was obtained from the NCBI dbSNP database.

3. Results

Based on the HbA1c and OGTT report, the study subjects were grouped into a normal control group (N=150) and a prediabetes group (N=150). Based on their BMI, the prediabetes group was further divided into obese (N=40) and non-obese (N=110). Initially, the socio-demographic data of study subjects were compared with biochemical parameters, which are shown in Table 1. This analysis found that the mean age of participants in the current study showed various significant results. Of a total of 300 patients enrolled in the present study, the control group was 39.03±5.72, but it was 38.39±6.31 in the case of prediabetic non-obese group and 39±5.20 in prediabetic obese group. However, the age was insignificant, with a p-value of 0.78. The mean comparison of other demographic details such as BMI (Kg/m2), Systolic BP (mmHg), Diastolic BP (mmHg), HbA1c (%), Fasting blood sugar (mg/dl), Postprandial blood sugar (mg/dl), fasting insulin (µIU/ml) and fasting insulin resistance results among three groups found to be significant with a p-value of <0.001.

The mean comparison of adiponectin, leptin, resistin levels, and adiponectin-leptin (A/L) ratio between all three groups analyzed showed a statistically significant difference p-valuee <0.001). It was found that the serum adiponectin levels decreased significantly in obese prediabetes (7.21±2.15µg/ml) when compared to non-obese prediabetes (7.28±2.41µg/ml) and healthy control subjects (13.64 ±2.88µg/ml, p<0.001). The results indicated that serum leptin levels increased significantly In obese prediabetes (13.59±2.59ng/ml) when compared to non-obese prediabetes (9.84±2.66ng/ml) and healthy control subjects (12.28±2.65ng/ml, p<0.001). Serum resistin levels increased significantly in obese prediabetes (17.67±3.60ng/ml) when compared to non-obese prediabetes (17.2±3.93ng/ml) and healthy control subjects (14.46±4.16ng/ml, p<0.001). The A/L ratio decreased significantly in obese prediabetes (0.56±0.22) when compared to non-obese prediabetes (0.79±0.4) and healthy control subjects (1.15 ±0.37, p<0.001) (Table 2).

Table 2. Comparison of adipokines level and A/L ratio of study subjects.

Parameters	Control (N=150) Mean ± SD	Non-obese Pre-diabetic (N=110) Mean ± SD	Obese Pre Diabetic (N=40) Mean ± SD	p-Value
Adiponectin (µg/ml)	13.64±2.88	7.28±2.41	7.21±2.15	<0.001
Leptin (ng/ml)	12.28±2.65	9.84±2.66	13.59±2.59	<0.001
Resistin (ng/ml)	14.46±4.16	17.2±3.93	17.67±3.60	<0.001
A/L ratio	1.15±0.37	0.79±0.40	0.56±0.22	<0.001

Mean comparison (Mean ± SD); p-value of <0.05 considered to be significant.

Data presented in Table 3 showed no statistically significant association between serum adiponectin level and the Single Nucleotide Polymorphisms present in the adiponectin gene of the control group (χ^2 = 1.549, p>0.05). Data presented in Table 3 showed a significant association between Adiponectin level and Adiponectin Single Nucleotide Polymorphisms in

the non-obese prediabetic group ($\chi 2 = 16.684$, $p<0.001$). Data presented in Table 3 showed a significant association between Adiponectin level and Adiponectin Single Nucleotide Polymorphisms in the obese prediabetic group($\chi^2 = 12.462$, $p>0.05$).

Table 3. Association of adiponectin level with adiponectin single nucleotide polymorphisms in control, non-obese prediabetic and obese prediabetic group.

Control (n=150)	**Adiponectin SNP**	**Adiponectin level µg/dl**		**Total**	**χ^2 value**	**p-value**
		≤Median (≤13.50)	**>Median (>13.50)**			
	CC	44	40	84	1.549	0.461 (NS)
	CG	15	19	34		
	GG	19	13	32		
Non-obese Prediabetic group (N=150)	**Adiponectin SNP**	**Adiponectin level**		**Total**	**χ^2 value**	**p-value**
		≤Median (≤7.20)	**> Median (>7.20)**			
	CC	3	20	23	16.68	<0.001**
	CG	25	16	41		
	GG	28	18	46		
Obese prediabetic group (N=40)	**Adiponectin SNP**	**Adiponectin level**		**Total**	**χ^2 value**	**p-value**
		≤Median (≤7.20)	**>Median (>7.20)**			
	CC	2	11	13	12.462	0.002*
	CG	7	7	14		
	GG	11	2	13		

NS- Not significant; *Significant at 0.01 level;** Significant at 0.001 level.

Data presented in Table 4 showed no significant association between Adiponectin level and Adiponectin SNP in the control group ($\chi^2 = 0.797$, $p>0.05$). Data presented in Table 4 showed a significant association between leptin level and leptin Single Nucleotide Polymorphisms in the non-obese prediabetic group ($\chi^2 = 7.725$, $p>0.05$). Data presented in Table 4 showed that there was a significant association between leptin level and leptin. Single Nucleotide Polymorphisms in obese prediabetic group ($\chi^2 = 6.973$, $p>0.05$).

Table 4. Association of leptin level with leptin single nucleotide polymorphisms in control, non-obese prediabetic and obese prediabetic group.

Control (n=150)	**Leptin SNP**	**Leptin level ng/dl**		**Total**	**χ^2 value**	**p-value**
		≤ Median (≤12.15)	**> Median (>12.15)**			
	AA	15	12	27	0.797	0.671 (NS)
	GA	31	29	60		
	GG	29	34	63		
Non-obese prediabetic group (N=150)	**Leptin SNP**	**Leptin level**		**Total**	**χ^2 value**	**p-value**
		≤ Median (≤10.40)	**> Median (>10.40)**			
	AA	7	13	20	7.725	0.021*
	GA	32	34	66		
	GG	18	6	24		
Obese prediabetic group (N=40)	**Leptin SNP**	**Leptin level**		**Total**	**χ^2 value**	**p-value**
		≤ Median (≤10.40)	**> Median (>10.40)**			
	AA	3	9	12	6.973	0.031*
	GA	14	8	22		
	GG	5	1	6		

NS- Not significant; *Significant at 0.05 level.

Data presented in Table 5 represent the association of resistin level with resistin Single Nucleotide Polymorphisms in the control, non-obese prediabetic, and obese prediabetic groups. The data showed no significant association between resistin level and resistin Single Nucleotide Polymorphisms in the control group ($\chi^2 = 5.004$, $p>0.05$). Similarly, in the case of the non-obese diabetic category, the data presented in the table shows that there was no significant association between resistin level and resistin Single Nucleotide Polymorphisms in the non-obese prediabetic group ($\chi^2 = 0.813$, $p>0.05$). Similarly, in the case of the obese

diabetes category, no association was found between the serum resistin level and resistin Single Nucleotide Polymorphisms in the best prediabetic group (χ^2 = 1.,000 p>0.05).

Table 6 demonstrates the genotype and allele of adiponectin polymorphism distribution and association between the prediabetic and control groups. The co-dominant, dominant, recessive, and alleles were found to have a statistically significant association for cases compared to controls.

Table 5. Association of resistin level with resistin single nucleotide polymorphisms in control, non-obese prediabetic, and obese prediabetic group.

	Resistin SNP	**Resistin level µg/dl**		**Total**	**χ^2 value**	**p-value**
		≤ Median (≤13.00)	**> Median (>13.00)**			
Control (n=150)	CC	42	18	60	5.004	0.082 (NS)
	CG	32	27	59		
	GG	15	16	31		
	Resistin SNP	**Resistin level**		**Total**	**χ^2 value**	**p-value**
		≤ Median (≤17.00)	**> Median (>17.00)**			
Non-obese prediabetic group (N=150)	CC	24	19	43	0.813	0.666 (NS)
	CG	20	23	43		
	GG	13	11	24		
	Resistin SNP	**Resistin level**		**Total**	**χ^2 value**	**p-value**
		≤Median (≤17.00)	**>Median (>17.00)**			
Obese prediabetic group (N=40)	CC	7	5	12	1.000	0.607 (NS)
	CG	11	11	22		
	GG	2	1	6		

NS- Not significant

Table 6. Genotype and allele association of leptin polymorphism between prediabetics and controls.

	Polymorphism	**Polymorphism**	**Prediabetics (%)**	**Control n(%)**	**OR(95% CI)**	**P value**
Adiponectin	**Co Dominant**	**CC**	36 (24)	84 (56)	1	-
		CG	55 (36.7)	34 (22.7)	0.265 (0.148, 0.473)	<0.001
		GG	59 (39.3)	32 (21.3)	0.232 (0.130, 0.416)	<0.001
	Dominant	**CC**	36 (24)	84 (56)	1	-
		CG+GG	114 (76)	66 (44)	0.248 (0.15, 0.407)	<0.001
	Recessive	**CG+CC**	91 (6.7)	118 (78.7)	1	-
		GG	59 (39.3)	32 (21.3)	0.418 (0.251, 0.696)	0.001
	Alleles	**C**	127 (42.3)	202 (67.3)	1	-
		G	173 (57.7)	98 (32.7)	0.356 (0.255- 0.497)	<0.001
Leptin	**Co Dominant**	**GG**	31 (20.7)	63 (42)	1	-
		GA	88 (58.7)	60 (40)	0.335 (0.195, 0.576)	<0.001
		AA	31 (20.7)	27 (18)	0.429 (0.219, 0.839)	0.013
	Dominant	**GG**	31.7 (20.7)	63 (42)	1	-
		GA+AA	119 (79.3)	87 (58)	0.36 (0.216, 0.6)	<0.001
	Recessive	**GA+GG**	119 (79.3)	123 (80)	1	-
		AA	31 (20.7)	27 (18)	0.843 (0.475, 1.496)	0.004
	Alleles	**G**	150 (50)	186 (62)	1	-
		A	150 (50)	114 (38)	0.613 (0.443, 0.848)	0.003
Resistin	**Co Dominant**	**CC**	55 (36.7)	60 (40)	1	-
		CG	65 (43.3)	59 (39.3)	0.832 (0.501 – 1.383)	0.478
		GG	30 (20)	31 (20.7)	0.947 (0.501 – 1.763)	0.864
	Dominant	**CC**	55 (36.7)	60 (40)	1	-
		CG+GG	95 (63.3)	90 (60)	0.868 (0.545 – 1.384)	0.533
	Recessive	**CG+CC**	120 (80)	119 (79.3)	1	-
		GG	32 (20)	31 (20.7)	1.042 (0.596 – 1.829)	0.886
	Alleles	**C**	175 (58.3)	(179 (59.7)	1	-
		G	125 (41.7)	121 (40.3)	0.946 (0683 -1.31)	0.74

In the case of leptin, the association of co-dominant, dominant, recessive genotype, and allele between cases and controls was found to be statistically significant. Compared to the control category of all genotypes and alleles, the prominent polymorphisms were less likely to occur in cases than in controls. It was also observed that none of the polymorphisms showed significant association with cases compared to controls in the case of resistance.

All the SNP markers at the ADIPOQ (rs266729), LEP (rs7799039), and RETN(rs1862513) loci were in Hardy-Weinberg Equilibrium. Statistical analysis showed no significant association between adiponectin level and adiponectin SNP in the control group, and there was a significant association between adiponectin level and adiponectin SNP in obese and non-obese prediabetes. The genotype and allele frequencies of rs 266729 promoter region ADIPOQ gene polymorphism in prediabetes and healthy control are shown in Table 6. The frequency of the CC, CG, and GG genotypes of rs266729 were 36%, 55%, and 59% in prediabetes cases and 56%, 22.7%, and 21.3% in healthy control, respectively. C and G allele frequencies were 42.3% and 57.5% in prediabetes and 67.3% and 32.5% in healthy control, respectively. There was a significant association of homozygous CC and heterozygous CG genotype with prediabetes (OR:0.276, Cl:0.148-0.473: P<0.001), and C, G allele frequency of rs266729 had a significant association with prediabetes as compared to healthy controls (OR:0.356, Cl:0.255-0.497: P<0.001). It also analyzed the dominant genotype (CC vs CG+GG) and found significant differences between prediabetes cases and healthy control (OR:0.248, Cl:0.151-0.407:P<0.001). Similarly, the recessive genotype CG+CC vs. GG did show a significant difference between prediabetes cases and healthy control (OR:0.418, Cl:0.251-0.696 :P<0.001).

Statistical analysis showed no significant association between leptin level and leptin SNP in the control group, and there was a significant association between leptin level and leptin SNP in obese and non-obese prediabetes. The genotype and allele frequencies of rs7799039 promoter region LEP gene polymorphism in prediabetes and healthy control are shown in Table 6. The frequency of the GG, GA, and AA genotypes of rs7799039 were 20.7%, 58.7%, and 20.7% in prediabetes cases and 42%, 40%, and 18% in healthy control, respectively. The allele frequencies of G and A were 50%, 50% in prediabetes, and 62%, 38% in healthy control, respectively. There was a significant association of homozygous GG and heterozygous GA genotype with prediabetes (OR:0.335, Cl:0.195-0.576:P<0.001), and GA allele frequency of rs7799039 had a significant association with prediabetes as compared to healthy controls (OR:0.613, Cl:0.443-0.848: P=0.003). It also analyzed the dominant genotype (GG vs. GA+AA) and found a significant difference between the prediabetes case and healthy control (OR:0.36, Cl:0.216-0.6:P<0.001). Similarly, the recessive genotype GA+GG vs. AA did show a significant difference between prediabetes cases and healthy controls (OR:0.843, Cl:0.475-0.496 :P=0.004).

Statistical analysis showed a non-significant association between resistin level and resistin SNP in the control group, and there was no significant association between resistin level and resistin SNP in obese and non-obese prediabetes. The genotype and allele frequencies of rs1862513 promoter region RETN gene polymorphism in prediabetes and healthy control are shown in Table 6. The frequency of the CC, CG, and GG. Genotypes of rs1862513 were 36.7%, 43.3%, and 20% in prediabetes cases and 40%, 39.3%, and 20.7% in healthy control, respectively. The allele frequencies of C and G were 58.3% and 41.7% in prediabetes and 59.7% and 49.3% in healthy control, respectively. There was no significant association of homozygous CC and heterozygous CG genotype with prediabetes (OR:0.8, Cl:0.501-1.383:

P=0.478) and CG allele frequency of rs1862513 had no significant association with prediabetes as compared to healthy controls (OR:0.946, Cl:0.683-1.31: P=0.74).it also analyzed the dominant genotype (CCvs CG+GG) and found no significant difference between prediabetes case and healthy control (OR:0.868, CI:0.545-1.384:P<0.55). Similarly, the recessive genotype CG+CC vs. GG did not show a significant difference between prediabetes cases and healthy control (OR:1.042, Cl:0.596-1.829 :P=0.89).

4. Discussion

Adipokine serum patterns in individuals with IFG and IGT suggest a specific role of adipose tissue in the pathogenesis of these prediabetic states [11]. A known association of adiponectin with diabetes risk is evident at a much earlier stage in pathogenesis, during the transition from normoglycemia to prediabetes [23]. Serum adiponectin is statistically higher in patients with normoglycemia compared to those with prediabetes. It has a predictive value for distinguishing between patients with and without insulin resistance in the studied population. Serum leptin has a good predictive value for distinguishing between patients with and without MetS in the studied population [3]. Adiponectin gene polymorphisms are associated with serum adiponectin concentrations and the presence of MetS [25]. The present study is the first in Jordan to have reported an association between serum leptin levels and the GA genotype of rs2167270 with an increased risk of prediabetes, identified both in the univariate and multivariate models [26]. These findings suggest resistin levels are linked with MS and the RETN −420C>G and +299G>A polymorphisms have impacted the circulating resistin concentrations [27].

5. Conclusions

The present study revealed that plasma adiponectin levels and ADIPOQrs266729C>G polymorphism have an association among study subjects with prediabetes. Similarly, the plasma leptin levels and LEP2548- rs7799039 G>A polymorphism also showed an association between study subjects with prediabetes compared to the rest. From these associations, the role of genetic risk of prediabetes was understood. The current observations in this study would be useful in the genetic screening for prediabetes among the Kerala population.

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Conflicts of Interest

The authors declare no conflict of interest.

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