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RESEARCH ARTICLE

Biochemical Markers and Omentin-1 Rs2274908 Variant Genotype Analysis in Coronary Artery Disease among South Indian Population – A Case Control Study

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Abstract: ***Background:*** Omentin-1 is an anti-inflammatory adipokine primarily secreted by visceral adipose tissue and altered circulating levels implicated in the pathogenesis of coronary artery disease (CAD). Despite this, the role of genetic variants within the omentin-1 gene in modulating CAD risk remains insufficiently explored. The current study aims to assess the association between the rs2274908 (G/A) polymorphism in the omentin-1 gene and CAD susceptibility in a South Indian population. **Methods:** Venous blood samples were collected from 100 CAD patients and 100 age- and sex-matched healthy controls recruited from Tamil Nadu, India. Genomic DNA was extracted and genotyped for the rs2274908 variant using the ARMS-PCR, and serum omentin-1 levels were quantified via ELISA. Genotype-phenotype correlations were evaluated using fasting blood glucose (FBG), body mass index (BMI), lipid profile parameters, and derived lipid indices. ***Results:*** No statistically significant association was observed between rs2274908 genotypes and CAD risk under various genetic models: GA [OR: 0.877 (0.431–1.783)], AA [OR: 0.900 (0.114–7.067)], A allele [OR: 0.959 (0.644–1.428)], dominant model [OR: 0.878 (0.432–1.781)], co-dominant model [OR: 1.128 (0.570–2.229)], and recessive model [OR: 1.000 (0.138–7.242)]. The rs2274908 polymorphism also showed no significant correlation with BMI or other clinical parameters. However, serum omentin-1 levels were significantly reduced in CAD patients ($p < 0.0001$), although no association was found between omentin-1 levels and rs2274908 genotypes or clinical variables. ***Conclusion:*** Our findings suggest that decreased circulatory Omentin-1 levels could pose a risk towards CAD susceptibility.

Keywords: Omentin-1, adipokines, rs2274908, CAD, genetic variations.

INTRODUCTION

Coronary artery disease (CAD) remains one of the foremost causes of mortality and long-term disability across the globe. According to the Global Burden of Disease (GBD) study, an estimated 315 million individuals are currently living with CAD worldwide, underscoring its vast public health impact.1 In India, the situation is particularly concerning, with the country contributing to approximately 20% of all cardiovascular disease (CVD)-related deaths globally. Epidemiological data reveal a stark contrast in prevalence between urban and rural populations—urban regions report a CAD prevalence of around 12%, while rural areas show a lower rate of 6%. This disparity reflects differences in lifestyle, healthcare access, and exposure to risk factors.2 The incidence of CAD continues to rise both globally and within India, driven by a complex interplay of genetic predispositions and environmental influences. The pathophysiological foundation of CAD lies in atherosclerosis, a progressive condition characterized by the accumulation of lipid-rich plaques within the coronary arteries. These plaques often begin as fatty streaks that gradually obstruct blood flow, compromising myocardial perfusion and leading to ischemic damage.

CAD is widely acknowledged as a multifactorial disorder, where genetic susceptibility converges with modifiable risk factors. Key contributors to its development include elevated blood lipids (hyperlipidemia), excessive body weight (obesity), high blood pressure (hypertension), impaired glucose metabolism (diabetes mellitus), and tobacco use. These factors collectively accelerate vascular inflammation and plaque formation.3 Among the molecular players implicated in CAD, omentin has garnered attention for its role in regulating metabolism and promoting cardiovascular health. Initially identified in omental adipose tissue, omentin exists in two isoforms—omentin-1 and omentin-2. Of these, omentin-1 is the predominant variant, comprising 313 amino acids and expressed in multiple tissues, including the heart, intestines, and visceral fat. It plays a pivotal role in enhancing insulin sensitivity, modulating inflammatory pathways, regulating lipid metabolism, and supporting vascular function.4,5

Clinical studies have observed that diminished levels of omentin-1 are frequently associated with metabolic syndromes and cardiovascular disorders, including coronary atherosclerosis.6,7 The gene encoding omentin-1 is located on chromosome 1q22-q23 and consists of eight exons and seven introns. A notable single-nucleotide polymorphism (SNP) within this gene is rs2274908, situated in exon 4. This SNP involves a silent substitution of guanine (G) with adenine (A), which does not alter the amino acid sequence but may influence gene expression or mRNA stability.

Despite its potential relevance, the genetic variation in

omentin-1—particularly rs2274908—has received limited investigative focus in the context of CAD. Preliminary studies suggest that this polymorphism may be linked to altered lipid profiles and increased susceptibility to CAD in specific ethnic groups.7,8 In light of this, the present research aims to explore the association between the rs2274908 SNP of the omentin-1 gene and serum lipid parameters, as well as its potential contribution to CAD risk among individuals from Tamil Nadu.

MATERIAL AND METHOD

STUDY SELECTION

The study adhered to the ethical standards outlined in the Helsinki Declaration and was approved by the Institutional Human Ethics Committee (IHEC) of Chettinad Academy of Research and Education, Chettinad Hospital and Research Institute, Tamil Nadu, India (Approval No.: II/0336/23, dated 11.04.2023). Prior to participation, all individuals were thoroughly briefed about the study and provided written informed consent. A total of 200 participants were enrolled, comprising 100 CAD patients (41 females, 59 males) and 100 healthy controls (45 females, 55 males), matched for sex and ethnicity. CAD diagnosis in the patient group (Group I) was established by certified clinicians through clinical history and physical examination, focusing on cardiovascular symptoms, risk factors, and related conditions. Diagnostic evaluation for Group I included baseline tests such as resting echocardiography, heart rate monitoring, and chest radiography. Control subjects exhibited no signs of cardiac dysfunction or chronic illness. Individuals with genetic conditions, malignancies, allergic disorders, pregnancy, or autoimmune diseases were excluded from participation.

ANTHROPOMETRIC MEASUREMENTS, DNA ISOLATION, AND LIPID PROFILING

Body Mass Index (BMI) was determined by recording each participant's height and weight. For biochemical analysis, 3 ml of venous blood was collected following a 12-hour overnight fast, using K3EDTA-coated tubes. Plasma was separated and preserved at −20°C for lipid profiling. Fasting blood glucose (FBG), total cholesterol (TC), triglycerides (TG), and high-density lipoprotein (HDL) levels were measured using diagnostic kits from Reckon Diagnostics Pvt. Ltd., Vadodara, India. Low-density lipoprotein (LDL) concentrations were derived using Friedewald's equation (1972). Additional lipid indices—including Non-HDL (TC minus HDL), TG index (TG/FBS), and TG/HDL ratio—were computed using established formulas. CVD risk was evaluated through Castelli risk indices [CRI: TC/HDL; CRII: LDL/HDL], the Atherogenic Index of Plasma (AIP: Log10[TG/HDL]), and the Atherogenic Coefficient (AC: [TC − HDL]/HDL). Genomic DNA was isolated from whole blood using the HiPur Blood Genomic DNA Miniprep Kit [MB504, HiMedia]. DNA purity was verified by measuring the absorbance ratio at 260/280 nm using a UV–Vis spectrophotometer, and its integrity was confirmed via 0.8% agarose gel electrophoresis. Extracted DNA samples were stored at −20°C for subsequent analysis.

GENOTYPING OF RS2274908 POLYMORPHISM

The genotyping of the rs2274908 in the omentin-1 gene was carried out using the Amplification Refractory Mutation System–Polymerase Chain Reaction (ARMS-PCR) technique. The allele-specific primers and associated base pairs designed for the assay are listed in Table 1. Each PCR reaction was prepared in a 20 µl total volume, consisting of the following components-10µl of 2X PCR master buffer, 2µl of genomic DNA (approximately 50 ng), 2µl of 10µM outer primer mix, 4µl of 10µM inner primer mix, and 2 µl of nuclease-free water. Amplification was performed on an Applied Biosystems 96-well thermal cycler (California, USA) under the following cycling conditions: an initial denaturation step at 95°C for 5 minutes, followed by 35 cycles of denaturation at 95°C for 30 seconds, annealing at 59°C for 30 seconds, extension at 72°C for 30 seconds and a final elongation step was carried out at 72°C for 10 minutes. For product verification, 3µl of the PCR amplicons were subjected to electrophoresis on a 2.0% agarose gel prepared with ethidium bromide as the intercalating dye. A 50 bp DNA ladder (Himedia, India) was run in parallel to determine fragment size. The gels were subsequently visualized and documented using the Gel Doc EZ Imaging System (Bio-Rad Laboratories, California, USA).

Table 1: Primer sequence and amplicon size of the rs2274908 polymorphism

Primer	Sequence	Amplicon size
Forward Outer	TGGCCGCCTCTGCAGATCCAAAGGTGTT	
Reverse Outer	CCCTCAGCTCTCAGACAGGGAGGCTCTGGG	277 bp
Forward Inner (G)	GTGCACTTCCCACGCATGTCATTCGCG	173 bp
Reverse Inner (A)	GCTGGACCCTGGTGGCCAGCGTGAAT	156 bp

SERUM OMENTIN-1 LEVELS DETERMINATION

The serum Omentin-1 levels were estimated using the ELISA kit for human omentin-1 (Abcam Limited, UK (ab269545)) with a sensitivity of 0.21 ng/mL. All serum estimations were carried out in duplicate to ensure a percentage coefficient of Variation (CV) below 10%.

STATISTICAL ANALYSIS

The required sample size for the study was determined using G*Power software, based on a two-tailed test with an effect size of 0.40, a type I error (α) of 0.05, and a statistical power of 85% [9]. Clinical parameters were evaluated using both the student's t-test and Analysis of Variance (ANOVA). To examine Hardy-Weinberg equilibrium (HWE) for Omentin-1 gene variants in both patient and control groups, a chi-square test was conducted by comparing observed genotype frequencies with those expected. Genotypic and allelic distributions of Omentin-1 polymorphisms between cases and controls were analysed using chi-square tests based on 2x2 contingency tables. A p-value threshold of <0.025 was adopted for statistical significance in genotype and allele comparisons, following Bonferroni correction. Disease susceptibility was quantified by calculating odds ratios (OR) along with 95% confidence intervals (CI). All genotype-to-phenotype association analyses were performed exclusively in individuals with CAD. GraphPad Prism version 5 and SPSS software, version 21 for Windows (IBM Analytics, USA) were used for all statistical computations.

RESULT:

BIOCHEMICAL PARAMETERS

Clinical parameters from 100 control subjects and 100 individuals diagnosed with CAD have been described previously. Within the CAD group, further stratification based on disease severity was performed, categorizing patients into single vessel disease (SVD, n = 60), double vessel disease (DVD, n = 25), and triple vessel disease (TVD, n = 15) for comparative assessment as shown in Table 2.

Table 2: Comparison of Clinical Parameters and BMI Across CAD Subtypes Based on Affected Vessels

Parameter	1 vessel CAD (N = 60)	2 vessel CAD (N = 25)	3 vessel CAD (N = 15)	P value
Age	64 ± 14	63 ± 16	59 ± 13	0.465
Gender Male Female	 39 21	 13 12	 07 08	 0.431
Smoking Smokers Non Smokers	 16 44	 7 18	 04 11	 0.995
Alcoholic status Alcoholic Non-Alcoholic	 30 30	 11 14	 08 07	 0.866
Diabetic status Yes No	 39 21	 11 14	 13 02	 0.072
BMI	27.11 ± 4.71	27.77 ± 3.89	25.17 ± 3.94	0.191
HbA1c	7.26 ± 1.54	7.02 ± 1.33	9.28 ± 2.12	**<0.001**
FBS	158.83 ± 45.81	153.24 ± 51.41	179.06 ± 52.53	0.244
TG	186.30 ± 67.97	191.92 ± 53.43	228 ± 85.34	0.105
HDL	33.08 ± 7.66	31.96 ± 8.01	32.20 ± 7.91	0.806
TC	217.61 ± 45.76	202.60 ± 34.82	266.93 ± 42.42	**<0.001**
Non-HDL	184.53 ± 45.89	170.64 ± 36.29	234.73 ± 44.08	**<0.001**
LDL	147.27 ± 49.74	132.25 ± 39.63	189.13 ± 44.11	**0.0012**
CR I	7.01 ± 2.61	7.08 ± 3.88	9.09 ± 4.03	0.076
CR II	4.82 ± 2.48	4.81 ± 3.70	6.60 ± 3.82	0.115
AIP	0.73 ± 0.18	0.77 ± 0.16	0.83 ± 0.18	0.150
AC	6.01 ± 2.61	6.08 ± 3.88	8.09 ± 4.03	0.076
TG Index	9.48 ± 0.59	9.48 ± 0.60	9.81 ± 0.55	0.155
TG/HDL	5.95 ± 2.61	6.37 ± 2.11	7.43 ± 2.98	0.137
BNP	664.03 ± 1132.26	456.99 ± 262.76	779.27 ± 638.71	0.548
CKMB	7.26 ± 14.86	4.36 ± 2.27	22.68 ± 18.39	**0.0002**
Troponin	35.15 ± 42.33	411.15 ± 292.49	3675.54 ± 1816.33	**<0.0001**

ASSOCIATION OF RS2274908 POLYMORPHISM

The genotype and allele frequencies of the RS2274908 polymorphism are summarized in Table 3. The genotype distribution adhered to HWE with a p-value>0.05, suggesting no significant variation in genotype or allele frequencies between CAD patients and control subjects. Furthermore, analysis across various genetic models revealed no association between the rs2274908 variant and CAD, as detailed in Table 3.

Table 3: Genotype, allele distribution and association of rs2274908 polymorphism with CAD under different genetic model.

Genotype/ Genetic model	Group I (CAD)	Group II (Control)	P for HWE	P for association	Odds ratio	95% CI
GG	20	18				
GA	78	80	0.936	0.717	0.877	0.431– 1.783
AA	02	02		0.920	0.900	0.114–7.067
G	118	116	$\chi 2$ =			
A	82	84	0.130	0.839	0.959	0.644–1.428
Dominant model (GA+AA vs GG)				0.718	0.878	0.432–1.781
Co-dominant model (GA vs GG+AA)				0.728	1.128	0.570–2.229
Recessive model (AA vs GG+GA)				1.000	1.000	0.138–7.242

ASSOCIATION OF RS2274908 WITH BMI AND CLINICAL PARAMETERS

No significant association was observed between the three rs2274908 genotypes and BMI or other clinical parameters in individuals diagnosed with CAD, as presented in Table 4.

Table 4: Association Between Clinical Parameters and rs2274908 Genotypes in the Study Population

Parameters	GG	GA	AA	P Value
BMI	26.66 ± 4.76	27.12 ± 4.43	24.97 ± 2.72	0.751
HbA1c	6.36 ± 1.67	6.35 ± 1.74	6.02 ± 0.71	0.928
FBS	122.15 ± 47.60	123.91 ± 51.55	125.50 ± 54.14	0.979
TG	139.60 ± 65.65	146.13 ± 73.52	135.50 ± 111.71	0.856
HDL	40.26 ± 10.84	40.81 ± 10.61	38.25 ± 15.17	0.866
TC	185.02 ± 54.95	185.47 ± 53.63	188.50 ± 30.44	0.992
Non-HDL	144.76 ± 61.23	144.65 ± 59.58	150.25 ± 41.59	0.983
LDL	116.84 ± 58.10	115.43 ± 53.15	123.15 ± 38.03	0.953
CR I	5.33 ± 3.39	5.19 ± 3.12	5.78 ± 2.92	0.913
CR II	3.51 ± 3.05	3.37 ± 2.76	3.76 ± 2.01	0.928
AIP	0.51 ± 0.29	0.51 ± 0.29	0.48 ± 0.48	0.973
AC	4.33 ± 3.39	4.19 ± 3.12	4.78 ± 2.92	0.913
TG Index	8.87 ± 0.77	8.90 ± 0.81	8.76 ± 1.14	0.921
TG/HDL	4.09 ± 2.89	4.12 ± 2.76	5.08 ± 6.20	0.802
BNP	317.81 ± 876.67	328.72 ± 654.62	681.50 ± 1162.95	0.613
CKMB	9.18 ± 16.96	6.00 ± 9.98	11.25 ± 15.82	0.240
Troponin	345.07 ± 1045.85	350.05 ± 1102.81	16.65 ± 8.77	0.831

SERUM OMENTIN-1 LEVELS AND ITS ASSOCIATION WITH RS2274908 POLYMORPHISM

The serum omentin-1 levels showed a significant decrease in expression among CAD patients, as shown in Figure 1a. However, no statistically significant variation in omentin-1 levels was observed across different BMI categories (Figure 1b). Additionally, analysis revealed no correlation between serum omentin-1 expression and the three genotypes of the rs2274908 polymorphism (Figure 1c).

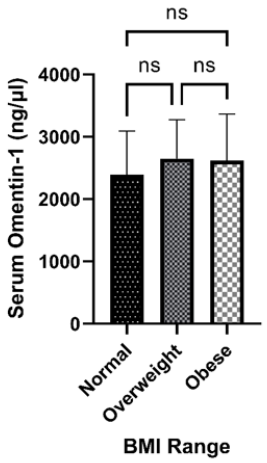

Figure 1

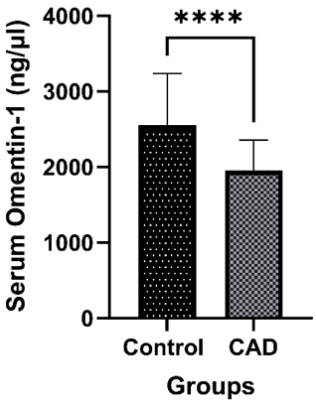

Figure 2

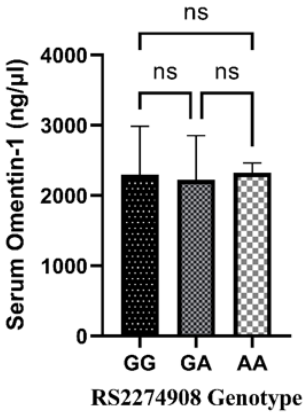

Figure 3

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DISCUSSION

Few studies have examined the involvement of omentin-1 in the pathogenesis of CAD, and the current study specifically aimed to evaluate the genetic contribution of the rs2274908 SNP to CAD susceptibility within the Tamil Nadu population. Findings from this research indicated no significant association between the rs2274908 variant and CAD development. These results align with previous observations reported in Arabic and broader Asian cohorts.7,8 Additionally, the study revealed no significant association of the rs2274908 polymorphism with BMI and other clinical parameters among CAD individuals, which was in accordance with the previous studies7. The rs2274908 SNP is located in exon 4 of the omentin-1 gene and results in a synonymous substitution—histidine remains unchanged despite a nucleotide shift from G to A at position 86. Although such silent mutations are generally considered functionally neutral, they may influence RNA transcription dynamics and adipokine expression. Yang et al. (2003) demonstrated that synonymous variants in the adiponectin gene could affect mRNA splicing or stability; however, similar regulatory effects were not evident for the omentin-1 rs2274908 variant.10

In terms of protein expression, serum omentin-1 levels were significantly reduced in CAD patients, as shown in this study. This contrasts with earlier longitudinal research in diabetic cohorts, which linked elevated omentin-1 concentrations to increased risk of cardiovascular events, stroke, and mortality.11 Saely et al. (2016) also reported that higher plasma omentin-1 levels were predictive of adverse cardiovascular outcomes in CAD patients 12. Conversely, a study involving 300 CAD patients from Pakistan found markedly lower plasma omentin-1 levels, supporting the current findings.13 Notably, studies reporting elevated omentin-1 levels were conducted in predominantly White populations, whereas those showing reduced levels—including the present study—were based in Asian populations. This suggests that ethnicity may play a critical role in modulating omentin-1 expression and its relevance to CAD risk. The observed decline in circulating omentin-1 may stem from impaired translational efficiency or reduced mRNA/protein stability. Some evidence also suggests that adiponectin may be a potential upstream regulator of omentin-1 expression. Nonetheless, further research is warranted to elucidate these molecular interactions. The diminished omentin-1 levels may contribute to CAD progression, and mechanistic studies—particularly in vivo—are needed to explore the differential regulation of mRNA and protein expression. In conclusion, while circulating omentin-1 shows promise as a biomarker for CAD in the Tamil Nadu population, the rs2274908 polymorphism does not appear to influence disease susceptibility. The findings from the present study may be useful in assisting the clinicians in accurately identifying CAD in South Indian population, and further could contribute to improved patient outcomes and support the advancement of precision medicine in cardiovascular care. However, larger cohort studies are essential to validate these findings and further the effect of other SNP in the omentin-1 genes need to be explored. Although genotyping methods are not infallible, this study employed ARMS-PCR and allele-specific PCR—techniques recognized for their speed, simplicity, and reliability in SNP detection. In spite of these limitations, the current research has public health importance as CAD has become the major contributor to global mortality and morbidity.

CONCLUSION

The current investigation indicates that the rs2274908 polymorphism in the omentin-1 gene does not exhibit a significant association with CAD susceptibility. However, individuals diagnosed with CAD showed markedly reduced serum omentin-1 concentrations.

REFERENCES

1. Stark B, Johnson C, Roth GA. Global prevalence of coronary artery disease: an update from the global burden of disease study. J Am Coll Cardiol. 2024;83(13):2320. doi:10.1016/S0735-1097(24)04310-9
2. Shannawaz M, Rathi I, Shah N, Saeed S, Chandra A, Singh H. Prevalence of CVD Among Indian Adult Population: Systematic Review and Meta-Analysis. Int J Environ Res Public Health. 2025;22(4):539. doi:10.3390/ijerph22040539
3. Blüher M. Clinical Relevance of Adipokines. Diabetes Metab J. 2012;36(5):317. doi:10.4093/dmj.2012.36.5.317
4. de Souza Batista CM, Yang RZ, Lee MJ, et al. Omentin Plasma Levels and Gene Expression Are Decreased in Obesity. Diabetes. 2007;56(6):1655-1661. doi:10.2337/db06-1506
5. Yang RZ, Lee MJ, Hu H, et al. Identification of omentin as a novel depot-specific adipokine in human adipose tissue: possible role in modulating insulin action. American Journal of Physiology-Endocrinology and Metabolism. 2006;290(6):E1253-E1261. doi:10.1152/ajpendo.00572.2004
6. Yan P, Liu D, Long M, Ren Y, Pang J, Li R. Changes of Serum Omentin Levels and Relationship between Omentin and Adiponectin Concentrations in Type 2 Diabetes Mellitus. Experimental and Clinical Endocrinology & Diabetes. 2011;119(04):257-263. doi:10.1055/s-0030-1269912
7. Al-Barqaawi MA, Al-Kashwan TA, Mahdi AG, Mirza TJ, Amber KI, Hussain MK. The impact of omentin-1 gene polymorphisms (rs2274907 and

rs2274908) on serum lipid concentrations and coronary artery disease in a sample of Iraqi individuals (A pilot study). Clin Biochem. 2022;100:29-34. doi:10.1016/j.clinbiochem.2021.11.005

8. Jha CK, Mir R, Elfaki I, et al. Evaluation of the Association of Omentin 1 rs2274907 A>T and rs2274908 G>A Gene Polymorphisms with Coronary Artery Disease in Indian Population: A Case Control Study. J Pers Med. 2019;9(2). doi:10.3390/jpm9020030
9. Faul F, Erdfelder E, Lang AG, Buchner A. G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences. . Behav Res Methods. 2007;39:175-191.
10. Yang WS, Tsou PL, Lee WJ, et al. Allele-specific differential expression of a common adiponectin gene polymorphism related to obesity. J Mol Med. 2003;81(7):428-434. doi:10.1007/s00109-002-0409-4
11. Niersmann C, Carstensen-Kirberg M, Maalmi H, et al. Higher circulating omentin is associated with increased risk of primary cardiovascular events in individuals with diabetes. Diabetologia. 2020;63(2):410-418. doi:10.1007/s00125-019-05017-2
12. Saely CH, Leiherer A, Muendlein A, et al. Coronary patients with high plasma omentin are at a higher cardiovascular risk. Data Brief. 2016;6:158-161. doi:10.1016/j.dib.2015.11.065
13. Bai P, Abdullah F, Lodi M, et al. Association Between Coronary Artery Disease and Plasma Omentin-1 Levels. Cureus. Published online August 21, 2021.