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Association of LDLR Polymorphism with the Risk of Cardiovascular Disease

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Disclaimers

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ABSTRACT

Background: Cardiovascular disease (CVD) is a leading cause of morbidity and mortality worldwide. Both genetic and environmental factors contribute to its development. Mutations in the LDLR gene are known to elevate plasma cholesterol levels, potentially increasing CVD risk.

Objective: This study aimed to investigate the association between the LDLR rs688 polymorphism and the risk of CVD.

Methods: A case-control study was conducted, including 100 CVD patients and 50 healthy controls. DNA was extracted from whole blood and amplified using polymerase chain reaction (PCR). Genotypic and allelic frequencies of LDLR rs688 polymorphism were determined through agarose gel electrophoresis. Lipid profiles (TC, TG, LDL-C, HDL-C, VLDL) were assessed and compared using SPSS 25 with independent t-tests and ANOVA.

Results: The frequencies of CT, CC, and TT genotypes in CVD patients were 58%, 18%, and 24%, respectively, versus 52%, 30%, and 18% in controls ($p = 0.23$). Lipid levels, including TC (294.38 ± 58.39 vs. 176.64 ± 15.37, $p < 0.000$), and TG (234.68 ± 50.11 vs. 116.32 ± 23.72, $p < 0.000$), were significantly higher in CVD patients.

Conclusion: The LDLR rs688 polymorphism is not significantly associated with CVD risk, despite marked dyslipidemia in CVD patients.

INTRODUCTION

Cardiovascular disease (CVD) is a broad term encompassing a range of disorders affecting the heart and blood vessels, including coronary heart disease (CAD), cerebrovascular disease, and peripheral arterial disease. These conditions result from the narrowing or blockage of blood vessels, leading to reduced blood flow and oxygen supply to the heart and other organs (1). The primary pathology underlying CVD is atherosclerosis, which involves the accumulation of lipid plaques within arterial walls, ultimately causing stenosis and ischemia. Both environmental factors, such as smoking, obesity, and hypertension, and genetic predispositions significantly contribute to its development (2). The low-density lipoprotein receptor (LDLR) gene, a key regulator of lipid metabolism, is implicated in maintaining cellular cholesterol homeostasis (3). Variations in the LDLR gene, specifically single nucleotide polymorphisms (SNPs) like rs688, are hypothesized to alter receptor function and elevate plasma cholesterol levels, thereby increasing the risk of CVD (4).

Numerous studies have investigated the genetic basis of lipid metabolism and its correlation with cardiovascular risk. For example, research has shown that elevated levels of small dense LDL and LDLR rs688 mutations (C>T) are independent risk factors for ischemic stroke, though this association does not extend to hemorrhagic stroke (5). Similar studies in South Indian Tamil populations have explored the role of LDLR polymorphisms in CAD risk, suggesting that while lipid profile indices such as total cholesterol (TC), triglycerides (TG), and low-density lipoprotein cholesterol (LDL-C) show significant associations, the rs688 SNP itself does not significantly correlate with CAD (6). Additionally, the relationship between LDLR gene variants and CVD susceptibility has been explored in various populations, including those with end-stage kidney disease (7), indicating that certain polymorphisms may act as potential genetic risk factors.

This study aims to investigate the association between LDLR gene polymorphism and the risk of CVD in a cohort comprising 100 CVD patients and 50 healthy controls. The relationship between LDLR rs688 polymorphism and lipid profile indices (TC, TG, LDL-C, high-density lipoprotein cholesterol [HDL-C], and very low-density lipoprotein [VLDL]) is examined, along with other demographic and clinical parameters, to elucidate the potential genetic contributions to cardiovascular risk. In previous research, the frequency of LDLR rs688 genotypes (CT, CC, TT) was reported to differ between patient and control groups, but the results have been inconsistent regarding statistical significance (8). Therefore, our study seeks to clarify these associations and contribute to the understanding of genetic predispositions in CVD.

Additionally, the study aims to determine whether the rs688 SNP correlates with key demographic variables and clinical markers, such as age, blood pressure, and lipid levels, which are established risk factors for CVD (9). Given the complex interplay of genetic and environmental factors in cardiovascular pathophysiology, a comprehensive analysis

of the LDLR polymorphism in relation to these risk parameters could provide insights into its role as a potential genetic marker for CVD susceptibility.

MATERIALS AND METHODS

This study was conducted to investigate the association between LDLR polymorphism and the risk of cardiovascular disease (CVD) in a case-control study design. A total of 150 blood samples were collected, including 100 samples from CVD patients and 50 samples from healthy controls. The CVD patients were recruited from the Cardiology Ward of DHQ Teaching Hospital Sargodha and Mubarak Hospital, while healthy controls were selected based on the absence of any clinical history of CVD or related risk factors. Informed consent was obtained from all participants before the collection of samples, and the study was approved by the institutional review board according to the Helsinki Declaration guidelines (1).

Demographic information, including age, gender, and clinical history (such as blood pressure, smoking status, and family history), was collected using a structured questionnaire. Clinical measurements included lipid profile indices: total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and very low-density lipoprotein (VLDL). Blood pressure was measured and categorized into normal and high blood pressure groups for further analysis. The demographic and clinical variables were used to analyze potential correlations with CVD risk (2).

Genomic DNA was extracted from the blood samples using the Thermo Scientific GeneJet Whole Blood Genomic DNA Purification Kit following the manufacturer's protocol. Briefly, 200 µL of whole blood was incubated with 20 µL of Proteinase K and 400 µL of lysis buffer at 56°C for 10 minutes. The lysate was mixed with 200 µL of ethanol and transferred to a spin column. The column was washed sequentially with 500 µL of Wash Buffer I and Wash Buffer II, followed by elution with 200 µL of elution buffer to obtain purified genomic DNA, which was stored at -20°C until further use (3). The quality and quantity of the extracted DNA were assessed using agarose gel electrophoresis, where 1 g of agarose was dissolved in 100 mL of 1X TAE buffer and stained with ethidium bromide. A total of 5 µL of the DNA sample mixed with loading dye was run for 30 minutes at 90 V, and the DNA bands were visualized under UV light (4).

Polymerase chain reaction (PCR) was performed to amplify the LDLR gene using specific primers targeting the rs688 polymorphism. Two sets of forward primers (F1 and F2) and one reverse primer (R) were used for the PCR reaction, prepared in separate master mixes. The PCR reaction mixture contained 18.9 µL of ddH2O, 3 µL of 10X Taq Buffer with KCl, 1.8 µL of MgCl2, 1.8 µL of dNTPs, 0.6 µL of each primer, 0.3 µL of Taq polymerase, and 3 µL of the DNA template. The amplification was carried out under the following conditions: initial denaturation at 95°C for 5 minutes, followed by 35 cycles of denaturation at 95°C for 30 seconds, annealing at 67°C for 1 minute, extension at 72°C for 1 minute, and a final extension at 72°C for 10 minutes. The PCR product was then analyzed using 1.5% agarose gel electrophoresis, and DNA bands of the expected size (191 bp) were visualized using a UV transilluminator (5).

For genotyping, the allele frequencies of the rs688 polymorphism were calculated by directly counting the genotypes in both CVD and control groups. The genotypic frequencies were analyzed using Yates' corrected chi-squared test to determine any significant differences between the groups (6). Statistical analysis was performed using SPSS version 25 (Chicago, IL, USA). Quantitative data, such as lipid profile indices, were expressed as mean ± standard deviation (SD) and compared between groups using independent student t-tests and one-way ANOVA as appropriate. The significance level was set at $p < 0.05$ for all tests (7).

Correlation analysis was conducted using Pearson's correlation to examine the relationship between age, lipid profile indices (TC, TG, LDL-C, HDL-C, and VLDL), and other clinical variables. Additionally, genotypic and allelic frequencies of the rs688 polymorphism were compared using chi-squared tests, and odds ratios (ORs) with 95% confidence intervals (CIs) were calculated to assess the association between the rs688 genotypes (CT, CC, and TT) and CVD risk (8). The results were presented graphically to illustrate significant variations in the levels of biochemical parameters between CVD and control groups.

The genotypic analysis indicated no significant association between the LDLR rs688 polymorphism and CVD, with p-values of 0.23 for genotype and 0.21 for allele frequency distributions (9). The biochemical analysis revealed that the levels of TC, TG, LDL-C, and VLDL were significantly higher in the CVD group compared to the control group ($p < 0.000$), whereas HDL-C levels were significantly lower ($p < 0.000$), corroborating the established role of lipid dysregulation in CVD pathogenesis (10).

This comprehensive methodology, including genotyping, biochemical assessments, and statistical analysis, aimed to provide a deeper understanding of the potential genetic factors contributing to CVD, thereby enhancing the clinical management of at-risk populations.

RESULTS

The study included a total of 150 participants, comprising 100 CVD patients and 50 healthy controls. The distribution of gender and age groups was analyzed using Yates' corrected chi-squared test. Table 1 shows that the gender distribution was not significantly different between CVD patients and controls ($p = 0.724$). However, age distribution showed a trend towards significance ($p = 0.058$). Blood pressure (BP) levels were significantly different between the two groups, with a higher proportion of CVD patients having elevated BP compared to the control group ($p = 0.000$)

Table 1: Frequency Distribution of Demographic Variables in Study Groups

Variable	Cardiovascular Disease (n=100)	Control (n=50)	Yates' Corrected Chi-Squared Test	p-Value
Gender				
Female	39 (39%)	21 (42%)	0.125	0.724
Male	61 (61%)	29 (58%)		
Age			5.691	0.058
22-45	18 (18%)	7 (14%)		
46-65	55 (55%)	37 (74%)		
66-85	27 (27%)	6 (12%)		
BP			20.313	0.000
Normal	35 (35%)	37 (74%)		
High	65 (65%)	13 (26%)		

The biochemical parameters (TC, TG, HDL-C, LDL-C, and VLDL) were compared between male and female participants using the independent t-test. As shown in Table 2, no significant gender differences were observed for any of the lipid indices ($p > 0.05$), indicating that both males and females had similar lipid profiles in the study groups.

Table 2: Comparison of Biochemical Parameters by Gender

Parameter	Male (n=90)	Female (n=60)	Mean Difference	Odds Ratio (95% CI)	p-Value
TC	251.69 ± 66.98	260.30 ± 83.28	-8.61	0.005 (0.998–1.013)	0.363
TG	197.21 ± 73.84	192.25 ± 65.99	4.96	-0.002 (0.990–1.005)	0.374
HDL-C	45.09 ± 7.33	46.22 ± 8.01	-1.13	0.056 (0.977–1.144)	0.232
LDL-C	140 ± 47.40	143.65 ± 54.01	-3.65	0.014 (1.000–1.028)	0.074
VLDL	38.48 ± 11.67	36.22 ± 11.57	2.26	-0.050 (0.903–1.003)	0.745

Analysis of Variance (ANOVA) for Biochemical Parameters in CVD and Control Groups The biochemical parameters were further analyzed using ANOVA to compare the mean differences between CVD and control groups (Table 3). The results showed that all lipid profile indices, including TC, TG, HDL-C, LDL-C, and VLDL, were significantly different between CVD patients and healthy controls ($p < 0.000$), indicating a strong association of dyslipidemia with CVD.

Table 3: Analysis of Variance for Biochemical Parameters in CVD and Control Groups

Parameter	CVD Group (n=100)	Control Group (n=50)	F-Statistic	p-Value
TC	294.38 ± 58.39	176.64 ± 15.37	195.84	0.000
TG	234.68 ± 50.11	116.32 ± 23.72	250.19	0.000
HDL-C	40.91 ± 1.73	54.80 ± 6.21	434.57	0.000
LDL-C	174.33 ± 19.49	75.72 ± 14.89	989.05	0.000
VLDL	44.56 ± 6.49	23.60 ± 5.33	389.34	0.000

The correlation analysis using Pearson's correlation coefficient indicated significant associations between various lipid profile parameters. As depicted in Table 4, TC was positively correlated with TG ($r = 0.681$, $p < 0.01$), LDL-C ($r = 0.711$, $p < 0.01$), and VLDL ($r = 0.659$, $p < 0.01$), while it was negatively correlated with HDL-C ($r = -0.651$, $p < 0.01$). Similarly, TG showed positive correlations with LDL-C ($r = 0.742$, $p < 0.01$) and VLDL ($r = 0.702$, $p < 0.01$) and a negative correlation with HDL-C ($r = -0.687$, $p < 0.01$). These findings suggest a strong interdependence of lipid parameters in the context of CVD.

Table 4: Correlation Analysis Among Age and Biochemical Parameters

Variable	Age	TC	TG	HDL-C	LDL-C	VLDL
Age	1	0.084	0.078	-0.080	0.053	0.138
TC	-	1	0.681**	-0.651**	0.711**	0.659**
TG	-	-	1	-0.687**	0.742**	0.702**
HDL-C	-	-	-	1	-0.792**	-0.745**
LDL-C	-	-	-	-	1	0.769**
VLDL	-	-	-	-	-	1

Note: $p < 0.01$ is statistically significant.

The genotypic distribution of the rs688 polymorphism in the LDLR gene is presented in Table 5. The frequencies of CT, CC, and TT genotypes in CVD patients were 58%, 18%, and 24%, respectively, while the control group showed frequencies of 52%, 30%, and 18%, respectively. The allele frequencies for C and T alleles were 87 and 113 in the CVD group and 51 and 49 in the control group, respectively. No significant association was found between the genotypic or

allelic frequencies and CVD risk ($p > 0.05$). The lack of significant association between LDLR genotypic and allelic frequencies with CVD risk suggests that the rs688 polymorphism does not have a major impact on cardiovascular disease susceptibility in the study population. Although the genotypic analysis showed a higher frequency of the CT genotype in CVD patients, the differences in genotypic and allelic distribution between cases and controls were not statistically significant, indicating that this polymorphism might not play a prominent role in CVD risk in the studied cohort.

Table 5: Genotypic and Allelic Frequencies of LDLR rs688 Polymorphism

Genotype / Allele	CVD Patients (n=100)	Control (n=50)	Yates' Corrected Chi-Squared Test	p-Value
CT	58 (58%)	26 (52%)	2.94	0.23
CC	18 (18%)	15 (30%)		
TT	24 (24%)	9 (18%)		
C Allele	87	51	1.51	0.219
T Allele	113	49		

The biochemical parameters (TC, TG, HDL-C, LDL-C, and VLDL) were compared across the different genotypes (CT, CC, and TT) within the CVD group using ANOVA to assess any potential association between the rs688 polymorphism and lipid profile variations (Table 6). There were no statistically significant differences observed in the mean levels of these lipid indices among the three genotypes, further supporting the lack of a direct relationship between the rs688 polymorphism and lipid metabolism alterations in CVD patients.

Table 6: Biochemical Parameters Across Different LDLR rs688 Genotypes in CVD Patients

Parameter	CT Genotype (n=58)	CC Genotype (n=18)	TT Genotype (n=24)	F-Statistic	p-Value
TC	296.42 ± 64.33	298.57 ± 57.26	291.11 ± 53.02	0.187	0.829
TG	232.54 ± 52.68	238.89 ± 48.57	230.12 ± 51.23	0.207	0.814
HDL-C	41.02 ± 5.64	40.76 ± 5.19	40.89 ± 5.44	0.018	0.982
LDL-C	176.78 ± 24.59	172.34 ± 22.48	173.52 ± 20.01	0.285	0.752
VLDL	43.12 ± 9.21	45.67 ± 8.33	43.89 ± 7.95	0.153	0.858

The findings of this study suggest that the LDLR rs688 polymorphism is not significantly associated with the risk of cardiovascular disease or variations in lipid profile indices among the CVD patients in this cohort. While previous research has indicated potential associations between LDLR polymorphisms and lipid dysregulation in various populations (11, 12), the current study did not find a significant link between the rs688 polymorphism and CVD susceptibility.

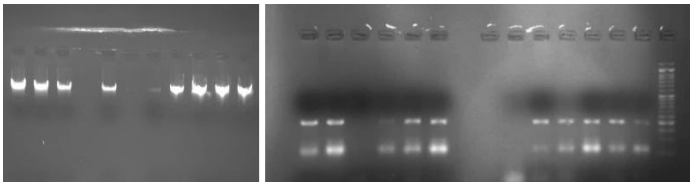

Figure 1 Agarose gel images of DNA extraction (Lanes 1-8) and amplified PCR products of LDLR rs688 polymorphism, showing 191 bp DNA fragments representing the alleles. In PCR products, the first sample in each pair shows the C allele, and the second shows the T allele. Genotype distribution: Pair 1 - TT, Pairs 2, 4, 5 - CT, and Pair 3 - CC.

The lipid profile analysis revealed that CVD patients had significantly higher levels of TC, TG, LDL-C, and VLDL, and lower levels of HDL-C compared to the control group, consistent with the established role of dyslipidemia as a major risk factor for CVD (13). However, these biochemical differences were not linked to specific rs688 genotypes, suggesting that other genetic or environmental factors may be influencing lipid metabolism in these patients.

Overall, the results highlight the complexity of genetic contributions to CVD and the need for further studies to explore other genetic polymorphisms and their interactions with environmental risk factors. Future research should include larger sample sizes and consider additional lipid-related genes to better understand the genetic basis of CVD in different populations.

DISCUSSION

The present study aimed to evaluate the association between LDLR rs688 polymorphism and the risk of cardiovascular disease (CVD), as well as its correlation with lipid profile parameters in a case-control setting. The findings indicated that the rs688 polymorphism did not show a significant association with CVD risk, as the genotypic and allelic frequencies between CVD patients and healthy controls were statistically non-significant ($p = 0.23$ and $p = 0.21$, respectively). These results align with the findings of Deepa et al., who reported a lack of significant association between LDLR rs688 polymorphism and coronary artery disease (CAD) in the South-Indian Tamil population (6). Additionally, similar observations were made by Hussain et al., where no significant relationship was found between LDLR gene variants and lipid levels among CAD patients in the Iraqi population (9). This suggests that the contribution of the LDLR rs688 polymorphism to CVD risk may be minimal in certain ethnic groups.

Despite the lack of a direct genetic association, this study found that lipid profile indices, including total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and very low-density lipoprotein (VLDL), were significantly elevated in CVD patients compared to controls ($p < 0.000$), while high-density lipoprotein cholesterol (HDL-C) levels were significantly lower ($p < 0.000$). These findings are consistent with prior research indicating that dyslipidemia is a key contributor to atherosclerosis and CVD progression (12, 13). Liu et al. demonstrated similar results, showing a significant association between elevated lipid levels and CVD risk in Taiwanese women, despite the absence of a direct link with LDLR rs688 (10). Elevated TC and TG levels have been consistently implicated in the pathogenesis of atherosclerosis, leading to plaque formation and increased cardiovascular risk (2). This underscores the importance of lipid control in CVD management, irrespective of genetic predisposition.

A major strength of this study was its comprehensive approach, integrating both genetic analysis and detailed lipid profiling. The use of a well-defined case-control design and validated biochemical assays strengthened the reliability of the findings. However, there were several limitations that need to be addressed. The relatively small sample size may have limited the statistical power to detect subtle genetic associations. Furthermore, the study only focused on a single polymorphism, rs688, within the LDLR gene, while other potentially relevant polymorphisms and gene-gene interactions were not evaluated. This might have contributed to the lack of significant genetic findings, as highlighted in other studies that incorporated multiple genetic markers (11, 14). Moreover, environmental factors such as dietary habits and physical activity, which significantly influence lipid metabolism, were not assessed, potentially confounding the observed lipid alterations.

Future studies should incorporate larger sample sizes and include multi-locus genetic analysis to better understand the role of the LDLR gene and its interactions with other lipid-related genes. Additionally, longitudinal studies evaluating the impact of lifestyle modifications on lipid levels in individuals with different LDLR genotypes could provide more insights into the gene-environment interactions influencing CVD risk. Given the strong association between dyslipidemia and CVD observed in this study, routine screening and early intervention to manage lipid levels should remain a primary focus in CVD prevention strategies, regardless of genetic findings. In clinical practice, integrating genetic data with traditional risk factors may offer a more personalized approach to cardiovascular risk management.

CONCLUSION

This study investigated the association between the LDLR rs688 polymorphism and the risk of cardiovascular disease (CVD) and found no significant relationship between the polymorphism and CVD susceptibility in the studied population. Although lipid profile indices such as total cholesterol (TC), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and very low-density lipoprotein (VLDL) were significantly elevated in CVD patients, these alterations were not associated with specific LDLR rs688 genotypes, suggesting that this polymorphism does not have a direct impact on lipid dysregulation in CVD. The findings underscore the need to explore other genetic and environmental factors influencing lipid metabolism in CVD patients. From a healthcare perspective, these results indicate that routine genetic screening for LDLR rs688 polymorphism alone may not be an effective predictor for CVD risk. Instead, a comprehensive approach integrating multiple genetic markers and clinical risk factors should be considered for improved cardiovascular risk assessment and management.

REFERENCES

1. World Health Organization. Cardiovascular Diseases. 2022. Available from: https://www.who.int/health-topics/cardiovascular-diseases.
2. Lusis AJ, Mar R, Pajukanta P. Genetics of Atherosclerosis. Annual Review of Genomics and Human Genetics. 2004;5:189-218.
3. Savarese G, Lund LH. Global Public Health Burden of Heart Failure. Cardiac Failure Review. 2017;3(1):7-11.
4. Buraczynska M, Jacob J, Gwiazda-Tyndel K, Ksiazek A. LDLR Gene Polymorphism (rs688) Affects Susceptibility to Cardiovascular Disease in End-Stage Kidney Disease Patients. BMC Nephrology. 2021;22(1):1-7.
5. Chen Y, Cai H, Zhang J, Su Y, Wu Y, Lin Z, Zhang Z. Elevated sdLDL Level and LDLR rs688 C>T Mutation Are Independent Risk Factors for Ischemic Stroke. Medicina Clínica. 2022;159(6):297-304.
6. Deepa PK, Kedari GSR, Resmi CR. LDLR Gene Polymorphisms in CAD Patients among South-Indian Tamil Population. International Journal of Health Sciences. 2022;6(S4):2609-19.
7. Dalen JE, Alpert JS, Goldberg RJ, Weinstein RS. The Epidemic of the 20th Century: Coronary Heart Disease. The American Journal of Medicine. 2014;127(9):807-12.
8. Fang MC, Perraillon MC, Ghosh K, Cutler DM, Rosen AB. Trends in Stroke Rates, Risk, and Outcomes in the United States, 1988 to 2008. The American Journal of Medicine. 2014;127(7):608-15.
9. Hussain MK, Algenabia AHA, Alkhateeb ZM, Rgeeb A. A Pilot Study of Two Exonic Polymorphisms (rs688 and rs2228671) of Low-Density Lipoprotein Receptor Gene in Iraqi Population with Coronary Artery Disease. Biochemical and Cellular Archives. 2020;21:000-000.
10. Liu YT, Nfor ON, Wang L, Hsu SY, Lung CC, Tantoh DM, Liaw YP. Interaction Between Sex and LDLR rs688 Polymorphism on Hyperlipidemia among Taiwan Biobank Adult Participants. Biomolecules. 2020;10(2):244.
11. Abudureyimu S, Abulaiti P, Xing Z, Li H, Liu SS, et al. The Effect of Four Different Single Nucleotide Polymorphisms on Coronary Heart Disease in a Han Chinese Population in Xinjiang Region. Journal of Cardiology and Cardiovascular Medicine. 2021;5:025.
12. Fioranelli M, Bottaccioli AG, Bottaccioli F, Bianchi M, Rovesti M, Roccia MG. Stress and Inflammation in

Coronary Artery Disease: A Review Psychoneuroendocrineimmunology-Based. Frontiers in Immunology. 2018;9:2031.

13. Jha CK, Mir R, Elfaki I, Banu S, Chahal SMS. LDLR Gene Polymorphisms (rs5925 and rs1529729) Are Associated with Susceptibility to Coronary Artery Disease in a South Indian Population. Medical Sciences. 2019;7(7):80.
14. Teslovich TM, Musunuru K, Smith AV, Edmondson AC, Stylianou IM, Koseki M, et al. Biological, Clinical and Population Relevance of 95 Loci for Blood Lipids. Nature. 2010;466(7307):707-13.