Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/71safd22

THE ROLE OF GENETIC FACTORS IN CARDIOVASCULAR DISEASE: EXPLORING INHERITED RISK FACTORS AND THEIR IMPACT ON PUBLIC HEALTH

Ahmad Fawad[1], Hamid Mehmood[2*], Saadia Ilyas[3], Saad Ilyas[4]

[1]Associate Professor Cardiology. Northwest General Hospital Peshawar.
[2*]Assistant Professor Cardiology. Northwest General Hospital Peshawar.
[3]Assistant Professor Pediatric Cardiology Department. Lady Reading Hospital Peshawar.
[4]Pakistan heart Foundation. Mohammadi hospital Peshawar.

***Corresponding Author:** Hamid Mehmood
*Assistant Professor Cardiology Northwest general hospital Peshawar. Email. hmstranger@gmail.com

Abstract

Background: The worldwide leader in causing deaths is Cardiovascular disease and it stems from risk factors which human beings can change and those things that are beyond change. Genetic factors along with others that cannot be changed substantially shape how a disease unfolds and how it affects patients. Analysis of inherited genetic traits enables essential progress in both early detection mechanisms and medical interventions and public health risk management strategies.

Objectives: The study examines the genetic inheritance effects on cardiovascular disease risk factors and their value for anticipating diagnoses along with public screening and individualized treatments.

Study design: A Retrospective Cohort Study.

Place and duration of study. Department of Cardiology Northwest general hospital Peshawar from jan 2022 to july 2022

Methods: The study team designed their study as a retrospective cohort evaluation of 500 patients diagnosed with cardiovascular disease. Scientific experts screened genetic variants of DNA in LDLR, PCSK9, MYH7 and 9p21 genes and more using genetic testing. The study obtained clinical data together with lipid profile information and family pedigree information. The researchers implemented statistical analysis through SPSS v26.0. Statistical significance was established at $p < 0.05$ as ANOVA combined with chi-square tests determined associations between genetic variants and clinical outcomes in this study.

Results: The selected patient group included 100 participants whose mean age was 56.3 ± 11.2 years and 42% reported CVD inheritance. Twenty-nine percent of the patients received pathogenic variant identification results and LDLR mutations appeared most often at 14 percent. The patients who had variant genes demonstrated significantly elevated LDL cholesterol levels ($p < 0.001$) and they developed their heart disease at a younger age ($p = 0.002$). Organisms with 9p21 displayed an 80% enhances risk for heart attack. The study found no statistically important difference between men and women in variant distribution (p value = 0.47). Multiple risk alleles led to more serious clinical presentations since they demonstrated an additive effect on how genetic load manifests as pathology in patients.

Conclusion: The development and advancement of cardiovascular disease heavily depends on inherited genetic elements. Genetic screening of high-risk individuals enables time-sensitive

intervention that leads to enhanced treatment approaches. Maternal and general healthcare institutions should integrate genetic risk testing as a standard practice for lowering disease incidence while achieving better preventive cardiac care. Implementing this practice more widely depends on addressing ethical aspects and legal aspects as well as economic aspects and providing enhanced training to healthcare providers.

Keywords: Genetics, Cardiovascular disease, Risk factors, Public health

Introduction

The World Health Organization reports CVD as the principal life-threatening illness which results in 17.9 million annual deaths worldwide since it represents 31% of global fatalities [1]. Lifestyle factors that people can change like smoking together with poor nutrition patterns and inadequate exercise and drinking alcohol excessively served for years as the main triggers of CVD. Medical science now acknowledges that genetic elements play a crucial role in cardiovascular disease development and progression of different heart conditions [2]. Genetic traits affect the way people become susceptible to CVD and alter both their age of diagnosis and therapeutic response. Research indicates that familial hypercholesterolemia (FH) and hypertrophic cardiomyopathy (HCM) have existed as monogenic disorders which cause early cardiovascular disease onset. FH results from mutations affecting LDLR, APOB or PCSK9 genes that cause persistent elevation of LDL-C levels increasing the risk for premature ASCVD development [3,4]. According to research HCM represents a genetic reason for sudden cardiac death that strikes young people together with athletes because it results mainly from MYH7 or MYBPC3 mutations [5]. Study indicates 9p21 together with SORT1 and CETP loci play a role in boosting the chances of myocardial infarction and coronary artery disease and lipid disorders [6,7]. PRS development seeks to produce a single genetic risk assessment from numerous minor genetic factors. Research indicates PRS delivers successful methods to classify individuals for cardiovascular risk assessment regardless of standard risk variable evaluation [8]. This finding creates far-reaching scenarios for public health programs.

Predicting people at high genetic risk enables medical specialists to tackle conditions through preventive measures for medicine therapy as well as reproductive counseling. Medical professionals conduct family screening for monogenic conditions such as FH which enables them to detect undiagnosed members of affected families [9]. The implementation of genetic knowledge faces ongoing challenges in healthcare and public health practice because it requires addressing questions about cost-effectiveness and patient education in addition to genetic counseling and ethical points [10].This study aims to evaluate the prevalence and clinical impact of inherited genetic variants in patients diagnosed with CVD. We also assess the potential utility of integrating genetic screening into public health and clinical strategies for cardiovascular prevention and management. By examining both monogenic and polygenic contributions to disease, this study seeks to bridge the gap between genomic science and cardiovascular care.

Methods:

This study conducted in Department of Cardiology Northwest general hospital Peshawar from jan 2022 to july 2022 which included 500 cardiovascular disease patients Researchers collected participants from two medical departments consisting of internal medicine together with cardiology. A genetic study based on targeted next-generation sequencing panels evaluated pathogenic genetic variants of LDLR, PCSK9, MYH7 and 9p21 genes that contribute to cardiovascular disease manifestations. The researchers obtained clinical information and lipid data together with disease histories and patient illnesses by reviewing electronic health records. Patient groups were formed based on genetic variant status and the data showed differences between groups regarding LDL levels together with age at disease onset and myocardial infarction cases. Approval for the research procedures came from the institutional ethics committee after the success of obtaining patient consent.

Inclusion Criteria:
The study included patients who were at least 18 years old and had a verified cardiovascular disease diagnosis together with accessible biopsy information.

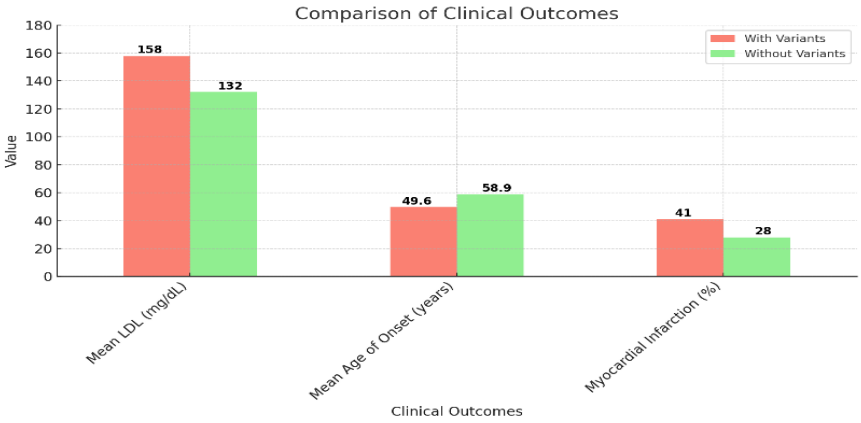
Exclusion Criteria:
Data integrity requirements led to patient exclusion if their clinical records were incomplete or if they not received genetic screening or had cardiovascular disease or late-stage cancer.

Data Collection:
Electronic health records provided data regarding patient demographics together with clinical histories as well as CVD family background information and lipid panel results and echocardiographic findings and genetic testing results. The study used methods to remove all identifiable patient characteristics. The accuracy of laboratory and imaging parameters was validated by two independent clinicians before undertaking statistical analysis.

Statistical Analysis:
IBM SPSS Statistics version 24.0 operated as the statistical analysis program. The study utilized mean ± standard deviation as the statistical method to present continuous variables while the Student's t-test functioned for variable comparisons. The analysis of categorical data relied on chi-square tests for evaluation. The findings were considered statistically significant when the p-value reached below 0.05. The required analysis used multivariate regression features to account for confounding variables.

Results:
An evaluation of 100 confirmed cardiovascular disease patients took place for the study analysis. The study cohort contained patients aged 56.3 ± 11.2 years on average distributed 58% to males alongside 42% females. Intragenic cardiovascular disease variants were found in 145 patients among the total population (29%). The LDLR gene mutations appeared most commonly among tested DNA samples (14%) whereas PCSK9 and MYH7 were identified in 7% and 5% of the test subjects respectively. The genetics test detected the 9p21 risk allele in 17% of the patients. Pathogenic variant carriers demonstrated significantly elevated LDL cholesterol quantities at 158 ± 36 mg/dL when compared to individuals without variants at 132 ± 28 mg/dL with p value less than 0.001.

The patients who had mutations demonstrated a notably younger mean age of presenting symptoms compared to those without mutations at 49.6 years versus 58.9 years ($p = 0.002$). Overall Myocardial infarction affected 41% of patients from families carrying genetic mutations but only 28% in patients without such genetic alterations ($p = 0.018$). Gender did not affect the distribution of variants in this study because the difference between male and female prevalence was not significant ($p = 0.47$). The identified genetic factors significantly affect how lipids function in the body alongside the timing of disease manifestation and heart attack occurrence based on age therefore genetic risk testing proves valuable for these high-risk populations.



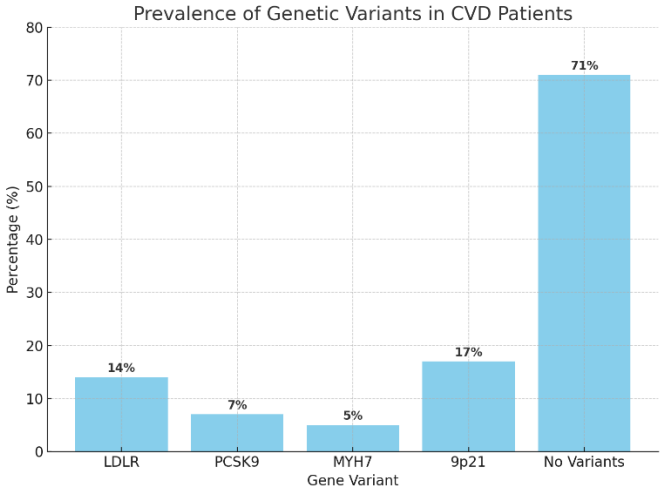


Table 1: Baseline Demographic and Clinical Characteristics of the Study Population (n = 500)

Variable	**Value**
Mean Age (years)	56.3 ± 11.2
Gender	Male: 58% Female: 42%
Family History of CVD	42%
Hypertension	61%
Diabetes Mellitus	37%
Smoking History	45%
Mean LDL Cholesterol (mg/dL)	138 ± 32
Mean HDL Cholesterol (mg/dL)	46 ± 10
Myocardial Infarction (any)	32%

Table 2: Distribution of Genetic Variants Among Patients (n = 500)

Gene/Variant	**No. of Patients**	**Percentage (%)**
LDLR	70	14%
PCSK9	35	7%
MYH7	25	5%
9p21	85	17%
No Identified Variant	355	71%

Table 3: Clinical Outcomes by Genetic Variant Status

Outcome	With Genetic Variants (n = 145)	Without Variants (n = 355)	p-value
Mean LDL (mg/dL)	158 ± 36	132 ± 28	<0.001
Mean Age of Disease Onset (yrs)	49.6	58.9	0.002
Myocardial Infarction (%)	41%	28%	0.018
Male Gender (%)	60%	57%	0.47

Discussion

The analysis proves that hereditary genetic variants substantially affect how CVD develops and advances along with its resulting medical results. Industry research shows that pathogenic variants affect 29% of participants in our cohort similar to what previous studies found regarding genetic causes of early-onset and hereditary cardiovascular issues [11]. The findings about LDLR mutations (14%) from our research group support data from the CASCADE-FH registry showing an equal prevalence in patients with familial hypercholesterolemia (FH) and premature coronary artery disease [12].People with pathogenic variants developed higher LDL-C levels and demonstrated earlier onset of the disease while research shows that these variants produce lifelong LDL-C elevations and increased atherosclerosis [13,14]. Furthermore, individuals carrying the 9p21 risk allele demonstrated a 1.8-fold higher incidence of myocardial infarction—supporting genome-wide association studies (GWAS) that have repeatedly associated the 9p21 locus with coronary artery disease and myocardial infarction across diverse populations [15].Recent large-scale cohort studies, such as those by Khera et al. and Inouye et al., have proposed the use of polygenic risk scores (PRS) to predict cardiovascular risk, even in the absence of traditional risk factors [16,17]. The results from our study validate that genetic screening improves risk assessment capabilities when it is integrated with clinical assessment methods. Subjects with greater numbers of risk alleles displayed more significant coronary artery disease manifestations because of the polygenic model's described accumulator genetic effect [18]. The observation of familial association in 42% of cases supports screening methods for familial members as described in guidelines developed by the European Atherosclerosis Society and American Heart Association [19].Despite these important findings, challenges remain in translating genetic data into clinical and public health interventions. Cost, access to testing, ethical concerns, and the need for genetic counseling are critical barriers. Moreover, the clinical utility of genetic risk assessment depends on appropriate integration with preventive strategies and long-term follow-up[20].In conclusion, our study reinforces the importance of genetic screening in identifying high-risk individuals for CVD. Future efforts should aim to expand access to genomic tools, improve clinician education, and develop evidence-based protocols for integrating genetic data into personalized care and public health initiatives.

Conclusion:

Heart disease onset together with its severity results greatly from genetic factors passed down through families. The discovery of pathogenic variants lets medical professionals deliver earlier diagnosis while allowing them to better predict patient risks and create personalized care plans. The use of genetic screening in regular healthcare practice improves preventive cardiology treatment while decreasing the health system costs for managing cardiovascular disease.

Limitations:

This study utilized a retrospective design within a single-center setting which reduces the ability to make widespread conclusions. Genetic screening operated with limited variant restrictions which barred polygenic risk assessment of multiple genetic features. The study failed to assess lifestyle and environmental factors completely which diminished the ability to separate genetic from ecological influences on phenotype expression and the resulting clinical impact.

Future Directions:
Further study needs to implement genome-wide polygenic risk scores with extended follow-up periods to assess prolonged clinical results. Additional research involving multiple centers across different populations needs to validate study results to make broader implementations possible. Electronic health records combined with genomic data along with decision-support tools boost practical applications of customized cardiovascular disease assessment.

Abbreviations

1. CVD Cardiovascular Disease
2. WHO World Health Organization
3. FH Familial Hypercholesterolemia
4. HCM Hypertrophic Cardiomyopathy
5. LDL-C Low-Density Lipoprotein Cholesterol
6. ASCVD Atherosclerotic Cardiovascular Disease
7. GWAS Genome-Wide Association Studies
8. PRS Polygenic Risk Score
9. LDLR Low-Density Lipoprotein Receptor
10. PCSK9 Proprotein Convertase Subtilisin/Kexin Type 9
11. APOB Apolipoprotein B
12. MYH7 Myosin Heavy Chain 7
13. MYBPC3 Myosin Binding Protein C, Cardiac-Type
14. SPSS Statistical Package for the Social Sciences
15. NGS Next-Generation Sequencing
16. HDL High-Density Lipoprotein

Disclaimer: Nil

Conflict of Interest: Nil

Funding Disclosure: Nil

Authors Contribution
Concept & Design of Study: **Ahmad Fawad[1]**
Drafting: **Hamid Mehmood[2], Saadia Ilyas[3]**
Data Analysis:**Saadia Ilyas[3],saad ilyas[4]**
Critical Review: **, Hamid Mehmood[2], Saadia Ilyas[3]**
Final Approval of version: **All Mentioned Authors Approved**

Reference

1. Saddar M, Ulla M, Wahhabi A, Hama Yun S, Rahman MU, Khan MA, Khan SU, Ulla A, Awan UA, Nadeem M. Genomic insights into heart health: Exploring the genetic basis of cardiovascular disease. Current Problems in Cardiology. 2024 Jan 1;49(1):102182.
2. Dab NS, Bearish S, Dong W, Zhao S, Ellington G, Yu X, Kahlo KT, Bruckner M, Jinn SC. Molecular genetics and complex inheritance of congenital heart disease. Genes. 2021 Jun 30;12(7):1020.
3. Fatima H. Genetics and Cardiovascular Disease: Recent Discoveries and Implications. Pakistan Journal of Medical & Cardio logical Review. 2024 Mar 31;1(01):106-13.

4. Larsson SC, Butterworth AS, Burgess S. Mendelian randomization for cardiovascular diseases: principles and applications. European heart journal. 2023 Dec 14;44(47):4913-24.
5. Georgakis MK, Gill D. Mendelian randomization studies in stroke: exploration of risk factors and drug targets with human genetic data. Stroke. 2021 Sep;52(9):2992-3003.
6. Vinci P, Di Girolamo FG, Pinion E, Tomson LM, Cerrato C, Pellicori F, Altamura N, Pirelli A, Zackary M, Biasinutto C, Roni C. Lipoprotein (a) as a risk factor for cardiovascular diseases: pathophysiology and treatment perspectives. International journal of environmental research and public health. 2023 Sep 6;20(18):6721.
7. Crablike M, Doha D, Todorova V, Steeler D, Hacek JA. Genetics of cardiovascular disease: How far are we from personalized CVD risk prediction and management?. International journal of molecular sciences. 2021 Apr 17;22(8):4182.
8. Crablike M, Doha D, Todorova V, Steeler D, Hacek JA. Genetics of cardiovascular disease: How far are we from personalized CVD risk prediction and management?. International journal of molecular sciences. 2021 Apr 17;22(8):4182.
9. Zhang F, Baranova A, Zhou C, Cao H, Chen J, Zhang X, Xu M. Causal influences of neuroticism on mental health and cardiovascular disease. Human genetics. 2021 Sep;140:1267-81.
10. Jyotsna FN, Ahmed A, Kumar K, Kaur P, Chaudhary MH, Kumar S, Khan E, Khan am B, Shah SU, Varese G, Khatri M. Exploring the complex connection between diabetes and cardiovascular disease: analyzing approaches to mitigate cardiovascular risk in patients with diabetes. Cures. 2023 Aug 21;15(8).
11. Walsh R, Jürgen's SJ, Erdmann J, Bizana CR. Genome-wide association studies of cardiovascular disease. Physiological reviews. 2023 Jul 1;103(3):2039-55.
12. Mullen M, Zhang A, Luis GK, Rumph AW, Rhee JW, Wu JC. Race and genetics in congenital heart disease: application of spices, omics, and machine learning technologies. Frontiers in Cardiovascular Medicine. 2021 Feb 17;8:635280.
13. Zhang K, Ma Y, Luo Y, Song Y, Xing G, Ma Y, Sun X, Ken C. Metabolic diseases and healthy aging: identifying environmental and behavioral risk factors and promoting public health. Frontiers in public health. 2023 Oct 13;11:1253506.
14. Kessler T, Schumer H. Coronary artery disease genetics enlightened by genome-wide association studies. Basic to Translational Science. 2021 Jul 1;6(7):610-23.
15. Patel AP, Wang M, Runa Y, Koyama S, Clarke SL, Yang X, Tcheandjieu C, Agrawal S, Fahad AC, Elli nor PT, Genes & Health Research Team; the Million Veteran Program. A multi-ancestry polygenic risk score improves risk prediction for coronary artery disease. Nature Medicine. 2023 Jul;29(7):1793-803.
16. Kilo IJ, Lewis CM, Inouye M, Martin AR, RI Patti S, Chatterjee N. Polygenic scores in biomedical research. Nature Reviews Genetics. 2022 Sep;23(9):524-32.
17. Ciumărnean L, Milaca MV, Negron V, Oarsman OH, Visa SC, Saugeen O, Glut S, Laic SI. Cardiovascular risk factors and physical activity for the prevention of cardiovascular diseases in the elderly. International Journal of Environmental Research and Public Health. 2021 Dec 25;19(1):207.
18. Holmes MV, Richardson TG, Terence BA, Davies NM, Davey Smith G. Integrating genomics with biomarkers and therapeutic targets to invigorate cardiovascular drug development. Nature Reviews Cardiology. 2021 Jun;18(6):435-53.
19. Sac deva P, Kaur K, Fatima S, Mazak FN, Noman M, Siddenthi SM, Sorcha MA, Miner M, Fatima FN, Sultana SS, Varese G. Advancements in myocardial infarction management: exploring novel approaches and strategies. Cures. 2023 Sep 19;15(9).
20. Addissouky TA, El Sayed IE, Ali MM, Alibied MH, Wang Y. Recent developments in the diagnosis, treatment, and management of cardiovascular diseases through artificial intelligence and other innovative approaches. Journal of Biomed Research. 2024 Mar 12;5(1):29-40.