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Differential Impact of Maternal Versus Paternal Coronary Artery Disease History on Cardiac Function and Angiographic Severity in Offspring: A Cross-Sectional Study.

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Abstract

Background: Parental history is an established risk factor for coronary artery disease (CAD), but the relative effects of maternal and paternal history on disease severity and cardiac function remain unclear, particularly in South Asian populations. This study compared maternal and paternal CAD history in relation to angiographic severity and left ventricular systolic function.

Methodology: This hospital-based cross-sectional study included 250 consecutive adults undergoing diagnostic coronary angiography at Hayatabad Medical Complex, Peshawar, Pakistan, from October 2025 to March 2026. Participants were classified as having paternal history only (n=65), maternal history only (n=45), both parents affected (n=24), or no parental history (n=116). CAD severity was assessed using the Gensini score, and left ventricular ejection fraction (LVEF) was measured by transthoracic echocardiography. Multivariable logistic regression adjusted for conventional cardiovascular risk factors.

Results: Patients with maternal CAD history had the greatest disease severity. Median Gensini scores were 69 (IQR 50–92) in the maternal history group, 52 (35–73) in the paternal history group, and 46 (30–66) in those without parental history ($p<0.001$). Mean LVEF was lower with maternal history (48.3 ± 7.9%) than with paternal history (52.6 ± 8.1%) or no parental history (58.7 ± 7.6%) ($p=0.03$). Maternal history independently predicted severe CAD after adjustment for age, sex, hypertension, diabetes, dyslipidemia, and smoking (adjusted OR 1.58; 95% CI 1.15–2.16; $p=0.01$).

Conclusion: Maternal CAD history was associated with greater angiographic severity and poorer left ventricular systolic function than paternal history. Incorporating sex-specific parental history into cardiovascular risk assessment may improve early identification of high-risk individuals.

Keywords

Coronary Artery Disease, Family History, Maternal History, Paternal History, Gensini Score, Angiography, Left Ventricular Ejection Fraction, South Asia.

Introduction

Coronary artery disease (CAD) remains the leading cause of morbidity and mortality worldwide and continues to impose a substantial clinical and economic burden on healthcare systems[1,2]. Although several modifiable cardiovascular risk factors including hypertension, diabetes mellitus, dyslipidemia, smoking, obesity, and physical inactivity have been extensively studied, inherited susceptibility also plays a critical role in determining an individual's lifetime risk of developing CAD[1,2]. Among the recognized non-modifiable risk factors, a positive family history of premature coronary artery disease has consistently been identified as an independent predictor of future cardiovascular events and earlier disease onset[3].

Previous epidemiological studies have demonstrated that parental history of myocardial infarction significantly increases the risk of CAD in offspring, even after adjustment for conventional cardiovascular risk factors[3]. Interestingly, several investigations have suggested that maternal history may confer a stronger cardiovascular risk than paternal history[4]. Proposed biological mechanisms include mitochondrial inheritance, epigenetic modifications, fetal programming, and intrauterine environmental influences that may alter cardiovascular development and lifelong metabolic regulation[5,6]. Maternal cardiometabolic health during pregnancy has been shown to influence placental function, fetal vascular development, lipid metabolism, and susceptibility to atherosclerosis later in life[7]. Furthermore, mothers frequently exert a greater influence on early-life dietary habits, physical activity patterns, and other health-related behaviors, which may contribute to the intergenerational transmission of cardiovascular risk[8,9].

South Asian populations experience coronary artery disease approximately 5–10 years earlier than Western populations and frequently present with more aggressive and extensive coronary atherosclerosis[10]. Conventional cardiovascular risk factors alone do not completely explain this increased disease burden, suggesting that genetic predisposition and familial influences may play a more substantial role in this population[10,11]. Studies from Pakistan have also demonstrated that a positive family history is associated with increased CAD severity; however, most have evaluated parental history as a single variable without distinguishing between maternal and paternal inheritance[12-13].

Despite increasing evidence supporting familial aggregation of CAD, relatively little is known about whether maternal and paternal cardiovascular histories differentially influence angiographic disease severity and cardiac function among South Asian patients. Current cardiovascular risk prediction models do not consider family history as a binary variable and do not account for the potential differences between maternal and paternal transmission of disease risk. Consequently, an important aspect of inherited cardiovascular susceptibility may remain under recognized during routine clinical risk assessment.

To our knowledge, no previous study from Pakistan has systematically compared the effects of maternal and paternal history of coronary artery disease using objective angiographic severity scoring together with assessment of left ventricular systolic function in patients undergoing coronary angiography. Therefore, the present study aimed to evaluate the differential association of maternal and paternal CAD history with angiographic disease severity, coronary vessel involvement, and left ventricular ejection fraction in a tertiary care hospital population. Clarifying these relationships may improve cardiovascular risk stratification, facilitate earlier identification of high-risk individuals, and support the development of more personalized preventive strategies for populations at increased inherited risk of coronary artery disease.

Methodology

Study Design

This hospital-based analytical cross-sectional study was conducted to evaluate the differential impact of maternal versus paternal history of coronary artery disease (CAD) on angiographic severity and cardiac function among adult patients undergoing diagnostic coronary angiography. The study

compared coronary disease burden and left ventricular systolic function across predefined parental history groups using standardized clinical, echocardiographic, and angiographic assessments.

Ethics

The study was approved by the Institutional Research and Ethics Board (IREB) of Hayatabad Medical Complex, Peshawar (Approval No. 2911). All procedures were performed in accordance with the ethical principles outlined in the Declaration of Helsinki. Written informed consent was obtained from every participant before enrollment after explaining the objectives and procedures of the study. Participants were informed that their participation was voluntary and that they could withdraw from the study at any stage without affecting their medical care. All patient information was anonymized prior to analysis, and strict confidentiality was maintained throughout the study.

Setting

The study was carried out at the Cardiology Unit of Hayatabad Medical Complex, Peshawar, Pakistan, a tertiary care referral hospital providing specialized cardiovascular services. Participant recruitment and data collection were conducted between October 2025 and March 2026. Eligible patients were recruited consecutively from the outpatient cardiology clinics and inpatient cardiology services after being scheduled for diagnostic coronary angiography.

Participants

A total of 250 adult patients (≥18 years) with suspected or established coronary artery disease who underwent diagnostic coronary angiography during the study period were enrolled. Patients with congenital heart disease, previous coronary artery bypass graft (CABG) surgery, incomplete parental cardiovascular history, or uncertain family history that could not be reasonably verified were excluded. Eligible participants were recruited using a non-probability purposive sampling technique until the required sample size was achieved.

Variables

The primary independent variable was parental history of coronary artery disease, categorized into four mutually exclusive groups, paternal history only, maternal history only, both parents affected and no parental history.

The primary outcome variable was coronary artery disease severity measured using the Gensini score[15]. Secondary outcome variables included left ventricular ejection fraction (LVEF), presence of single-, double-, or triple-vessel coronary artery disease, and severe CAD identified through angiographic findings. Potential confounding variables included age, sex, body mass index (BMI), smoking status, hypertension, diabetes mellitus, dyslipidemia, physical activity level, and current cardiovascular medication use.

Data Sources / Measurement

After obtaining informed consent, demographic and clinical information including age, sex, educational status, BMI, smoking history, physical activity, medication use, and cardiovascular risk factors were collected using a structured clinical questionnaire and review of hospital medical records. Hypertension, diabetes mellitus, and dyslipidemia were defined as either a documented physician diagnosis or current treatment with antihypertensive, antidiabetic, or lipid-lowering medications, respectively. Smoking status was recorded as current smoker or non-smoker according to participant self-report. Parental history of CAD was obtained through structured interviews. A parent was considered to have coronary artery disease if the participant reported a documented history of myocardial infarction, physician-diagnosed angina, percutaneous coronary intervention, or coronary artery bypass graft surgery. Whenever available, participant reports were cross-verified using hospital discharge summaries, medication records, or death certificates to improve the accuracy of family history information. Cardiac function was assessed using transthoracic echocardiography performed with a GE Vivid S60 echocardiography system. Left ventricular ejection fraction (LVEF) was measured using the modified biplane Simpson's method by an experienced cardiologist who was blinded to the angiographic findings. Coronary angiography was

performed according to standard institutional protocols. Coronary artery disease severity was independently evaluated by two experienced cardiologists blinded to the participants' clinical information. Coronary vessel involvement was classified as single-vessel, double-vessel, or triple-vessel disease based on ≥50% luminal stenosis in major epicardial coronary arteries. Disease severity was further quantified using the Gensini scoring system, which assigns weighted scores according to both the percentage of luminal stenosis and the anatomical importance of the affected coronary segment[15].

Bias

Several strategies were implemented to minimize potential sources of bias. Consecutive recruitment of all eligible patients during the study period reduced selection bias. To minimize information bias, standardized data collection procedures were used for all participants. Family history information obtained through structured interviews was verified against available clinical records whenever possible. Participants with uncertain or unverifiable parental history were excluded to reduce misclassification.

Observer bias was minimized by ensuring that echocardiographic and angiographic assessments were independently interpreted by experienced cardiologists who were blinded to each other's findings and to the participants' clinical characteristics and parental history. Although recall bias regarding parental medical history could not be completely eliminated, efforts to verify reported information and exclude uncertain cases helped reduce its impact, consistent with approaches adopted in previous family history studies such as the INTERHEART study[14].

Study Size

Sample size estimation was performed using G*Power version 3.1, assuming a one-way ANOVA with four comparison groups, a medium effect size (Cohen's f = 0.25), two-sided significance level of 0.05, and statistical power of 80%.

The calculated minimum sample size was 180 participants. To improve statistical precision, account for subgroup comparisons, and reduce the influence of incomplete observations, a total of 250 eligible participants were included in the final analysis.

Statistical Methods

Data were entered, checked for completeness, cleaned, and analyzed using Statistical Package for the Social Sciences (SPSS) version 26.0. Normality of continuous variables was assessed using the Shapiro-Wilk test. Normally distributed continuous variables were expressed as mean ± SD and compared among the four parental history groups using one-way analysis of variance (ANOVA).

Non-normally distributed continuous variables, including the Gensini score, were reported as median (interquartile range) and compared using the Kruskal-Wallis test. Categorical variables were presented as frequencies and percentages and compared using the Chi-square test. Multivariable logistic regression analysis was performed to identify independent predictors of severe coronary artery disease after adjustment for conventional cardiovascular risk factors, including age, sex, hypertension, diabetes mellitus, dyslipidemia, and current smoking status. Adjusted odds ratios (ORs) with corresponding 95% confidence intervals (CIs) were calculated. Statistical significance was defined as a two-sided p-value of <0.05.

Results

Participants

A total of 250 patients undergoing diagnostic coronary angiography were enrolled and included in the final analysis. Participants were categorized according to parental history of coronary artery disease (CAD) into four groups: paternal history only (n = 65, 26.0%), maternal history only (n = 45, 18.0%), both parents affected (n = 24, 9.6%), and no parental history (n = 116, 46.4%). All recruited participants fulfilled the eligibility criteria, completed the required clinical assessments, and were included in the statistical analyses.

Descriptive Data

The baseline demographic and clinical characteristics of the study population are summarized in Table 1. The overall mean age of the participants was 58.3 ± 9.6 years, and 68% were male. No statistically

significant differences were observed among the four parental history groups with respect to age (p = 0.24), sex distribution (p = 0.78), body mass index (BMI) (p = 0.19), or current smoking status (p = 0.79), indicating that these baseline characteristics were generally comparable across groups. In contrast, significant differences were observed for several cardiometabolic risk factors. Participants with a maternal history of CAD or both parents affected demonstrated a higher prevalence of hypertension, diabetes mellitus, and dyslipidemia compared with those having only paternal history or no parental history (p = 0.04, p = 0.03, and p = 0.01, respectively). The use of statins and antiplatelet medications was comparable among the study groups and did not differ significantly (p > 0.05). Overall, these findings suggest that offspring with maternal or combined parental CAD history exhibited greater clustering of conventional cardiovascular risk factors (Table 1).

Outcome Data

The angiographic findings according to parental history are presented in Table 2. Triple-vessel coronary artery disease was observed most frequently among participants with a maternal history of CAD (42.2%), followed by those with both parents affected (41.7%), paternal history only (40.0%), and no parental history (28.5%). Although differences in vessel involvement were not statistically significant (p = 0.29), a clear trend toward more extensive coronary disease was observed among individuals with maternal or combined parental history.

Assessment of angiographic disease severity using the Gensini score demonstrated significant differences between the study groups. Participants with a maternal history of CAD had the highest median Gensini score 69 (IQR 50–92), followed by those with both parents affected 65 (47–88), paternal history only 52 (35–73), and no parental history 46 (30–66) (p < 0.001), indicating substantially greater coronary atherosclerotic burden among individuals with maternal familial history (Table 2).

Cardiac systolic function assessed by transthoracic echocardiography is summarized in Table 3. Mean left ventricular ejection fraction (LVEF) differed significantly among the groups (p = 0.03), with the lowest mean LVEF observed in participants with maternal CAD history (48.3 ± 7.9%), followed by those with both parents affected (50.2 ± 7.5%), paternal history only (52.6 ± 8.1%), and no parental history (58.7 ± 7.6%).

Similarly, reduced left ventricular systolic function (LVEF <50%) was more prevalent among participants with maternal (48.9%) and combined parental history (41.7%) compared with those having paternal history only (35.4%) or no parental history (28.4%), approaching statistical significance (p = 0.05) (Table 3).

Main Results

The multivariable logistic regression model evaluating independent predictors of severe coronary artery disease is illustrated in Figure 1. After adjustment for conventional cardiovascular risk factors, including age, sex, hypertension, diabetes mellitus, dyslipidemia, and current smoking, maternal history of CAD remained an independent predictor of severe angiographic coronary artery disease (adjusted OR = 1.58, 95% CI: 1.15–2.16, p = 0.01).

In contrast, paternal history (adjusted OR = 1.12) and history of CAD in both parents (adjusted OR = 1.27) showed positive but statistically non-significant associations with severe CAD (p > 0.05).

Among the conventional cardiovascular risk factors, increasing age (adjusted OR = 1.02 per year; 95% CI: 1.00–1.05; p = 0.04), hypertension (adjusted OR = 1.36; 95% CI: 1.05–1.76; p = 0.02), and diabetes mellitus (adjusted OR = 1.44; 95% CI: 1.10–1.89; p = 0.01) were also identified as significant independent predictors of severe coronary artery disease. Male sex, dyslipidemia, and current smoking were not independently associated with disease severity after multivariable adjustment (Figure 1).

Table 1: Baseline clinical characteristics stratified by parental history of CAD (N = 250).

Variables	Paternal only (n=65) N(%)	Maternal only (n=45) N(%)	Both parents (n=24) N(%)	None (n=116) N(%)	p-value
Age (years); Mean ± SD	59.1 ± 9.4	60.3 ± 8.7	58.4 ± 9.1	57.6 ± 10.2	0.24
Male	46 (70.8%)	28 (62.2%)	17 (70.8%)	78 (67.2%)	0.78
BMI (kg/m²); Mean ± SD	28.3 ± 3.9	28.9 ± 4.1	29.2 ± 4.3	27.9 ± 3.7	0.19
Current smoker	20 (30.8%)	12 (26.7%)	8 (33.3%)	30 (25.9%)	0.79
Hypertension	39 (60.0%)	33 (73.3%)	18 (75.0%)	63 (54.3%)	0.04*
Diabetes mellitus	24 (36.9%)	22 (48.9%)	11 (45.8%)	33 (28.4%)	0.03*
Dyslipidemia	37 (56.9%)	33 (73.3%)	17 (70.8%)	51 (44.0%)	0.01*
Statin use	49 (75.4%)	36 (80.0%)	18 (75.0%)	88 (75.9%)	0.86
Antiplatelet use	55 (84.6%)	40 (88.9%)	21 (87.5%)	101 (87.1%)	0.92

Data are presented as mean ± SD or n (%).
*p<0.05 is considered statistically significant.

Table 2: Coronary angiographic disease burden by parental history.

Variables	Paternal only (n=65) N(%)	Maternal only (n=45) N(%)	Both parents (n=24) N(%)	None (n=116) N(%)	p-value
Single-vessel disease	21 (32.3%)	10 (22.2%)	6 (25.0%)	47 (40.5%)	0.29[1]
Double-vessel disease	18 (27.7%)	16 (35.6%)	8 (33.3%)	36 (31.0%)	0.29[1]
Triple-vessel disease	26 (40.0%)	19 (42.2%)	10 (41.7%)	33 (28.5%)	0.29[1]
Gensini score; median (IQR)	52 (35-73)	69 (50-92)	65 (47-88)	46 (30–66)	<0.001[2]*

[1]Chi-square test for categorical vessel disease distribution. [2]Kruskal-Wallis test for Gensini score.
*p<0.05 is considered statistically significant.

Table 3: Echocardiographic parameters by parental history.

Variables	None (n=116) N(%)	Paternal only (n=65) N(%)	Maternal only (n=45) N(%)	Both parents (n=24) N(%)	p-value
LVEF % (mean ± SD)	58.7 ± 7.6	52.6 ± 8.1	48.3 ± 7.9	50.2 ± 7.5	0.03*
LVEF < 50%, n (%)	33 (28.4%)	23 (35.4%)	22 (48.9%)	10 (41.7%)	0.05*

LVEF = left ventricular ejection fraction. P-values reflect overall group differences by ANOVA or χ^2 as appropriate.
*p<0.05 is considered statistically significant.

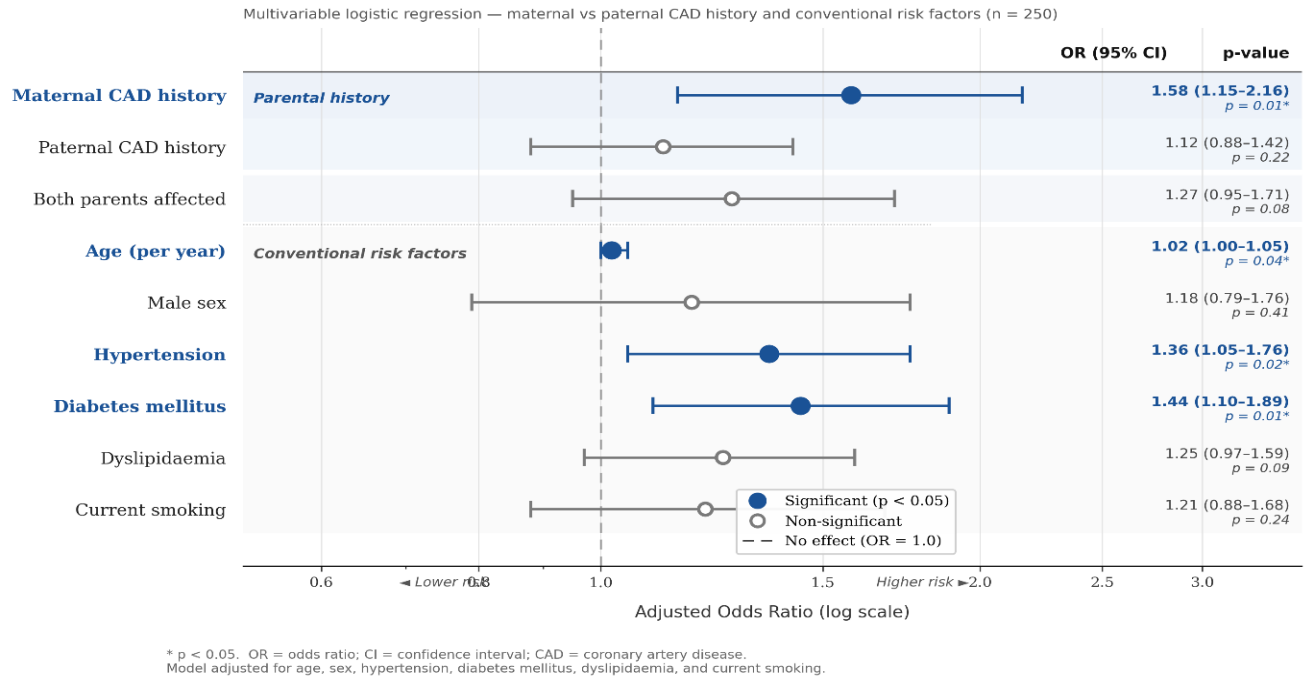


Figure 1: Adjusted odds ratios (95% CI) for severe angiographic CAD from the multivariable logistic regression model. Covariates include maternal history of CAD, paternal history of CAD, both parents affected, hypertension, diabetes, and dyslipidemia. The x-axis is on a log scale; the dashed line indicates OR=1.

Discussion

The present cross-sectional study evaluated the differential association of maternal and paternal history of coronary artery disease (CAD) with angiographic disease severity and left ventricular systolic function among patients undergoing coronary angiography. The principal finding of this study is that a maternal history of CAD was associated with significantly greater coronary atherosclerotic burden, reflected by higher Gensini scores, lower left ventricular ejection fraction (LVEF), and an increased likelihood of severe CAD after adjustment for conventional cardiovascular risk factors. Although the prevalence of triple-vessel disease was numerically higher among participants with maternal history, differences in vessel distribution were not statistically significant. Collectively, these findings suggest that maternal familial history may represent a stronger indicator of disease severity than paternal history and should receive greater consideration during cardiovascular risk assessment.

Our findings are consistent with previous epidemiological studies demonstrating that parental cardiovascular disease is an important determinant of CAD risk, while extending this evidence by showing that maternal history is associated not only with disease occurrence but also with greater angiographic severity and impaired cardiac function[16]. A systematic review and meta-analysis reported that offspring of mothers with premature cardiovascular disease experience a greater risk of developing CAD than those with paternal history alone[16]. Similarly, Muchira et al. demonstrated that maternal cardiovascular health was a stronger predictor of cardiovascular disease-free survival among offspring than paternal cardiovascular health, emphasizing the importance of maternal influences on long-term cardiovascular outcomes[17]. Recent comprehensive reviews have likewise highlighted that maternal transmission of CAD risk may equal or exceed paternal transmission, particularly when maternal cardiovascular disease occurs at a younger age[18].

Our results are also supported by studies showing that offspring of mothers with cardiovascular disease experience approximately a two-fold greater hazard of developing cardiovascular disease compared with offspring of mothers without cardiovascular disease, whereas the corresponding paternal association is comparatively weaker[19]. These observations suggest that inherited cardiovascular risk is unlikely to be explained solely by shared nuclear genetics or common environmental exposures. Importantly, our study contributes additional evidence from a South Asian population by demonstrating that maternal history is associated not only with increased angiographic disease burden but also with reduced left ventricular systolic function, a clinically meaningful indicator of myocardial damage and adverse cardiovascular prognosis. This aspect has received relatively limited attention in previous studies[20].

Nevertheless, the existing literature remains somewhat heterogeneous. The INTERHEART study demonstrated that any parental history of myocardial infarction substantially increased the risk of acute myocardial infarction but did not identify a major difference between maternal and paternal transmission after accounting for conventional cardiovascular risk factors[14]. Likewise, other contemporary studies suggest that overall family history remains an important predictor of cardiovascular risk irrespective of parental sex[21,22]. Differences between our findings and these studies may reflect variations in study populations, ethnicity, environmental exposures, prevalence of conventional cardiovascular risk factors, sample size, definitions of parental history, or methods used to quantify coronary artery disease severity.

Several biological mechanisms may explain the stronger association observed with maternal cardiovascular history. Unlike nuclear DNA, mitochondrial DNA is inherited exclusively through the maternal lineage and plays a fundamental role in myocardial energy production, oxidative phosphorylation, and cellular responses to oxidative stress. Variations in mitochondrial function have been implicated in the development and progression of coronary artery disease[23,24]. In addition, maternal cardiometabolic disorders during pregnancy may adversely influence fetal cardiovascular development through placental dysfunction, altered nutrient delivery, inflammation, and epigenetic programming, thereby increasing susceptibility to cardiovascular disease later in life[25]. Maternal obesity, hypertension, diabetes, and dyslipidemia may induce persistent alterations in vascular structure, endothelial function, lipid metabolism, and inflammatory pathways that predispose offspring to premature atherosclerosis[26]. Furthermore, mothers often exert a greater influence on childhood nutrition, physical activity, lifestyle behaviors, and health-related habits, which may further contribute to intergenerational cardiovascular risk transmission[8,9].

From a clinical perspective, these findings have important implications for cardiovascular prevention and risk stratification. Current cardiovascular risk prediction models generally consider family history as a single dichotomous variable without distinguishing between maternal and paternal inheritance. Our findings suggest that obtaining a detailed, sex-specific parental cardiovascular history may improve identification of individuals at increased risk for severe coronary artery disease. Recognition of maternal CAD history could justify earlier cardiovascular screening, more aggressive modification of traditional risk factors, and closer clinical surveillance among high-risk individuals, particularly in South Asian populations where coronary artery disease frequently develops at younger ages and with greater severity.

Strengths and Limitations

The present study possesses several important strengths. It is among the first hospital-based studies from Pakistan to directly compare maternal and paternal history of coronary artery disease using objective measures of angiographic severity and cardiac function. Coronary artery disease severity was quantified using the validated Gensini scoring system, while left ventricular systolic function was assessed using standardized

transthoracic echocardiography, providing objective evaluation of both anatomical and functional cardiovascular outcomes. The use of blinded assessment by experienced cardiologists reduced observer bias, and adjustment for major conventional cardiovascular risk factors strengthened the validity of the observed associations. However, several limitations should be acknowledged. First, the cross-sectional study design precludes establishment of temporal or causal relationships between parental cardiovascular history and disease severity. Second, parental history was primarily obtained through participant self-report and, despite verification using available medical records whenever possible, some degree of recall or misclassification bias may remain. Third, the study was conducted at a single tertiary care center using purposive sampling, which may limit the generalizability of the findings to the broader Pakistani population or other ethnic groups. Fourth, important biological factors including genetic variants, mitochondrial DNA alterations, epigenetic markers, inflammatory biomarkers, and detailed maternal pregnancy history were not evaluated and therefore the underlying mechanisms could not be directly explored. Finally, residual confounding from unmeasured variables such as socioeconomic status, dietary habits, psychosocial stress, environmental exposures, medication adherence, and lifetime physical activity cannot be completely excluded. Future multicenter prospective cohort studies incorporating genomic, epigenetic, biomarker, and maternal health data are warranted to further elucidate the biological pathways responsible for the stronger maternal influence observed in this study and to determine whether incorporating sex-specific parental history improves existing cardiovascular risk prediction models.

Conclusion

This study demonstrates that maternal history of coronary artery disease is associated with greater angiographic disease severity, higher Gensini scores, reduced left ventricular systolic function, and an increased likelihood of severe coronary artery disease compared with paternal or no parental history. These findings suggest that maternal cardiovascular history may represent a stronger marker of inherited cardiovascular susceptibility than paternal history in this South Asian population. Incorporating sex-specific parental history into routine cardiovascular risk assessment may enhance early identification of individuals at increased risk for severe coronary artery disease and facilitate more personalized preventive strategies. Larger multicenter prospective studies incorporating genetic, epigenetic, and maternal health data are needed to validate these findings, clarify the underlying biological mechanisms, and determine their clinical utility in improving cardiovascular risk prediction and preventive care.

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