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**ORIGINAL ARTICLE**

# Socioeconomic, Genetic, and Dietary Risk Factors of Ischemic Heart Disease in Pakistan. A Multicenter Case-Control Study

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## ABSTRACT

**Background:** Ischemic heart disease (IHD) is a leading cause of mortality in the world and has an overt contribution in low- and middle-income countries such as Pakistan. Traditional risk factors (hypertension, diabetes, dyslipidemia) are well known; however, the socioeconomic, dietary, and genetic determinants have not been fully explored.

**Aims and Objectives:** This study aimed to investigate the association between socioeconomic factors, dietary habits, and genetic predisposition in the development of IHD risk in Pakistan. It was specifically designed to find out if adverse socioeconomic conditions, unfavourable dietary patterns, and the presence of the APOE ε4 allele, on their own or in combination, would independently and individually increase the likelihood of IHD.

**Methods:** A Multicenter Case Control Study was conducted on n=250 participants (130 IHD patients and 130 controls) from the Punjab Institute of Cardiology (Lahore) and Chaudhry Pervaiz Elahi Institute of Cardiology (Wazirabad) from June 2022 to June 2023. Blood pressure, body mass index, lipid profile, and fasting blood glucose were measured, and comprehensive clinical evaluations were performed. Structured questionnaires were used to collect socioeconomic and dietary data, and a validated food frequency questionnaire was used to collect dietary data. Fasting blood samples were used for genomic DNA extraction, and PCR-RFLP analysis was used to genotype the APOE gene. Bivariate and multivariate logistic regression was done to determine independent predictors of IHD.

**Results:** They were older IHD patients who were known to have higher BMI, blood pressure, and adverse lipid profiles. IHD patients had lower income and educational levels, higher saturated fat intake, and lower fruit and vegetable consumption. The IHD group had a significantly higher frequency of the APOE ε4 allele.

**Conclusion:** The multifactorial interplay of clinical, socioeconomic, dietary, and genetic factors promptly in this context plays a pivotal role, and hence, an integrated preventive strategy is warranted.

**Keywords:** ischemic heart disease, socioeconomic factors, dietary habits, APOE ε4, genetic predisposition, Pakistan.

## INTRODUCTION

Ischemic heart disease (IHD) is a major cause of morbidity and mortality worldwide, but is particularly so in low- and middle-income countries such as Pakistan. IHD is a global problem, affecting nearly 18 million deaths each year (31 percent of all deaths), and in Pakistan, it accounts for approximately 30 percent of the total mortality[1]. In the past few decades, over 40 percent of Pakistan's population has lived in urban centres. Economic disparities (40 percent of Pakistanis live below the poverty line) and urban lifestyle changes have resulted in a steep rise in IHD incidence [2]. Conventional risk factors such as hypertension, diabetes, and dyslipidemia are well known in the development of IHD, but emerging data indicate the importance of other determinants. Specifically, socioeconomic status, genetics (presence of high-risk alleles in 20–30% of the population), and changing dietary habits (increased consumption of processed and high-fat foods) are important factors contributing to the increasing burden of IHD in Pakistan[3].

These socio-economic factors have a profound influence on health, primarily by affecting access to healthcare, education, and overall quality of life. People who are economically deprived and have less education in Pakistan are at a disadvantage in terms of receiving preventive care and adopting healthy behaviors[4]. Moreover, environmental stressors can worsen cardiovascular risk in this population. This is also important to understand the role of these socioeconomic disparities to identify at-risk populations and to design effective public health interventions[5].

In addition, genetic factors have also been identified for IHD risk. There are specific genetic variations that are associated with a higher propensity to atherosclerosis and subsequent cardiac events, and these are mostly related to the lipid metabolism and inflammatory processes[6]. Factors such as regional allele variations and increased rates of consanguinity may be predisposing the Pakistani population to higher cardiovascular risks, and the genetic profile of the Pakistani population may be different from the general population. It also means recognizing the genetic influences so that preventive strategies can be tailored and personalized medicine approaches developed[7].

In addition, the burden of IHD is also increased by dietary patterns. The traditional diets of Pakistan are undergoing rapid change, with an increasing intake of processed foods rich in saturated fats and sugars and decreasing intake of fruits, vegetables, and whole grains [8]. The adverse metabolic outcomes, including obesity, hypertension, and dyslipidemia, are all well-established risk factors for IHD and are associated with such changes. To prevent these cardiovascular diseases from continuing to increase in prevalence, it is necessary to address these dietary trends[9].

The main objective of this study was to examine the interplay between socioeconomic conditions, genetics, and dietary habits and the risk of ischemic heart disease in Pakistan. The study aimed to delineate the relative contributions and interactions of these factors to generate insights that can inform the development of targeted, culturally appropriate public health interventions. Ultimately, this will facilitate a deeper understanding of these multifaceted determinants, which can help in reducing the incidence of IHD and in improving cardiovascular health outcomes in the entire Pakistani population[10].

## MATERIALS AND METHODS

**Study Design and Setting:** This Multicenter Case-Control Study was done from June 2022 to June 2023 at two major hospitals in Pakistan: Punjab Institute of Cardiology (PIC), Lahore, and Chaudhry Pervaiz Elahi Institute of Cardiology (CPEIC), Wazirabad. The study was intended to completely evaluate the

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relationship between socioeconomic factors, genetic predispositions, dietary exposures, and clinical biomarkers with the risk of IHD.

**Sample Size and Power Analysis, Study Population:** The participants were recruited using stratified random sampling to achieve diversity in socioeconomic groups, and a total of 250 participants were recruited. A G*Power software was used for an a priori power analysis. To determine sample size sufficient to detect significant association among study variables, based on expected medium effect size (odds ratio ~1.5), alpha level of 0.05, and power of 80%, analysis was performed and it was confirmed that for a sample size of 250 participants it was sufficient to detect significant associations.

**Inclusion and Exclusion Criteria:** Participants included residents of the study regions aged 30 through 75 years who were willing to give informed consent for their participation. It included comprehensive clinical evaluations (including blood pressure, BMI, and laboratory testing) as well as genetic testing and the completion of extensive socioeconomic and dietary assessments. Also excluded were those with congenital heart disease, severe nonischemic cardiovascular disease, advanced chronic illness (renal or hepatic failure), or currently pregnant. Subjects were also excluded if they did not wish to participate in any part of the study.

**Data Collection Procedures:** Different multiple complementary methods were used to collect data. Trained clinicians performed demographic and clinical assessments, including age, gender, and physical exam of height and weight (for BMI) and blood pressure (systolic and diastolic). Blood samples (5 ml) were drawn after an overnight fast, assayed in the laboratory, and used for genetic analysis. Fasting blood glucose and lipid profiles (total cholesterol, low-density lipoprotein [LDL], high-density lipoprotein [HDL], and triglycerides) were evaluated in certified clinical laboratories according to standard protocols.

Data from structured questionnaires were obtained on education level, monthly household income (divided into quartile), occupation type (professional, manual labor, unemployed), and residential status (urban, rural). A validated food frequency questionnaire (FFQ) designed for the local dietary pattern was used to assess dietary habits. This instrument measured frequency and portion sizes of foods with high saturated fat (processed foods and red meats) and daily serving portions of fruits, vegetables, whole grains, and sugary beverages/snacks.

A commercial kit was used for extracting genomic DNA from fasting blood samples for genetic analysis. PCR followed by RFLP analysis was used for targeted genotyping of candidate polymorphisms, particularly within the APOE gene. The IHD status was determined by a comprehensive review of self-reported medical history, clinical examinations, and diagnostic records, including Electrocardiogram (ECG) and laboratory findings.

**Statistical Analysis:** The data was entered into a secure database, and the analysis was done using SPSS version 25 (IBM Corp., Armonk, NY). Demographic details, clinical biomarkers, socioeconomic variables, dietary patterns, and genetic markers were calculated on descriptive statistics, including means, standard deviations, frequencies, and percentages. Bivariate analyses using Chi-square tests for categorical variables and t-tests for continuous variables were used to examine associations between the study variables and IHD status. Subsequently, multivariate logistic regression analyses were performed to identify independent predictors of IHD with adjustment for potential confounders such as age, gender, and BMI. The null hypothesis was considered to be statistically significant if the p-value was less than 0.05.

**Ethical Considerations:** The study was conducted by the ethical standards of the Institutional Review Board of the participating institutions. All procedures were by the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000. The research process maintained confidentiality and data integrity.

## RESULTS

A total of 250 subjects were enrolled in the study, including 130 patients with ischemic heart disease (IHD) and 120 age and sex matched controls without IHD. The demographic characteristics, clinical biomarkers, socioeconomic indices, dietary patterns, and genetic profiles were all considered in the comprehensive analysis. The study population had an overall mean age of 57.8 ± 9.6 years and an almost equal gender distribution (56.7% % 65.4% male among groups). Controls had significantly lower body mass index (BMI), blood pressure, and adverse lipid profiles than did those in the IHD group.

Table 1 describes the baseline demographic and clinical characteristics. Patients with IHD had a mean age (59.2 ± 9.4 vs. 56.1 ± 9.7 years, $p = 0.012$) and BMI (28.3 ± 4.1 vs. 26.7 ± 3.8 kg/m², $p = 0.003$) that was higher than normal. IHD patients also had elevated systolic blood pressure (SBP) (146.5 ± 15.2 mmHg vs 132.8 ± 12.6 mmHg, $p < 0.001$) and diastolic blood pressure (DBP) (89.4 ± 10.1 mmHg vs 82.2 ± 8.5 mmHg, $p < 0.001$). Moreover, the lipid profile showed considerable difference in total cholesterol, LDL, and triglyceride levels with higher values in the IHD group and lower values of HDL (all $p < 0.001$). Also, IHD patients had significantly elevated fasting blood glucose ($p = 0.002$).

Household income, educational attainment, and employment status were assessed through structured questionnaires that were used to assess socioeconomic status. In Table 2, 60.0% of the IHD patients were from the lowest income quartile ($p < 0.001$), and 55.4% of the IHD had low educational attainment ($p = 0.002$) compared to 35.0% and 33.3% of controls, respectively. The employment patterns were such that 50.0% of IHD patients were either unemployed or engaged in manual work, as opposed to 37.5% of controls ($p = 0.050$). The two groups did not significantly differ in terms of residential status (urban versus rural).

A locally validated food questionnaire was used to perform dietary assessments. Table 3 shows that IHD patients consumed significantly more saturated fats (40.5 ± 8.2 g/day versus 32.1 ± 7.5 g/day, $p < 0.001$), and less fruits (1.8 ± 0.9 versus 2.5 ± 1.1 servings/day, $p < 0.001$) and vegetables (2.0 ± 1.0 versus 3.1 ± 1.2 servings/day, $p < 0.001$) than controls.

Genetic profiling focused on the APOE ε4 allele, a well-established genetic marker associated with cardiovascular risk. The APOE ε4 allele frequency was significantly elevated in the IHD group at 35.4% compared with 20.0% in controls ($p = 0.005$), as detailed in Table 4.

A multivariate logistic regression model was constructed to predict IHD independent of confounding variables like age, gender, and BMI. Finally, the final model (Table 5) showed that independent predictors of IHD were low socioeconomic status (adjusted OR = 1.95; 95% CI: 1.30–2.93; $p = 0.001$), presence of APOE ε4 allele (adjusted OR = 2.15; 95% CI: 1.35–3.43; $p = 0.002$), and high saturated fat intake (adjusted OR = 1.75; 95% CI: 1.10–2.79; $p = 0.019$). After adjustment, this association did not reach statistical significance (adjusted OR = 1.30; 95% CI: 0.85–2.00; $p = 0.210$).

The results conclude that patients with IHD in this study were older and had higher BMI, higher blood pressure, and an adverse lipid profile than the controls. Specifically, unfavorable dietary habits, including high saturated fat intake, and socioeconomic and genetic predisposition conferred by the APOE ε4 allele independently contributed to the risk of IHD. These results from robust clinical, biochemical, socioeconomic, dietary, and genetic data emphasize the multifactorial etiology of ischemic heart disease and the need for integrated public health strategies to address these modifiable risk factors.

Table 1. Baseline Demographic and Clinical Characteristics of Study Participants

| Parameter | IHD (n = 130) | Non-IHD (n = 120) | p-value |
|---|---|---|---|
| Age (years), mean ± SD | 59.2 ± 9.4 | 56.1 ± 9.7 | 0.012 |
| Male, n (%) | 85 (65.4%) | 68 (56.7%) | 0.183 |
| Female, n (%) | 45 (34.6%) | 52 (43.3%) | 0.183 |
| BMI (kg/m²), mean ± SD | 28.3 ± 4.1 | 26.7 ± 3.8 | 0.003 |
| SBP (mmHg), mean ± SD | 146.5 ± 15.2 | 132.8 ± 12.6 | <0.001 |
| DBP (mmHg), mean ± SD | 89.4 ± 10.1 | 82.2 ± 8.5 | <0.001 |
| Total Cholesterol (mg/dL), mean ± SD | 228.4 ± 35.7 | 198.6 ± 30.1 | <0.001 |
| LDL (mg/dL), mean ± SD | 146.2 ± 28.9 | 118.4 ± 24.5 | <0.001 |
| HDL (mg/dL), mean ± SD | 38.7 ± 7.8 | 44.9 ± 8.3 | <0.001 |
| Triglycerides (mg/dL), mean ± SD | 175.3 ± 42.5 | 142.7 ± 38.6 | <0.001 |
| Fasting Glucose (mg/dL), mean ± SD | 112.5 ± 15.8 | 104.3 ± 12.6 | 0.002 |

Table 2. Socioeconomic Characteristics of Study Participants

| Socioeconomic Variable | IHD (n = 130) | Non-IHD (n = 120) | p-value |
|---|---|---|---|
| Lowest Income Quartile, n (%) | 78 (60.0%) | 42 (35.0%) | <0.001 |
| Low Educational Attainment, n (%) | 72 (55.4%) | 40 (33.3%) | 0.002 |
| Unemployed/Manual Worker, n (%) | 65 (50.0%) | 45 (37.5%) | 0.050 |
| Urban Residence, n (%) | 100 (76.9%) | 90 (75.0%) | 0.700 |

Table 3. Dietary Characteristics of Study Participants

| Dietary Parameter | IHD (n = 130) | Non-IHD (n = 120) | p-value |
|---|---|---|---|
| Saturated Fat Intake (g/day), mean ± SD | 40.5 ± 8.2 | 32.1 ± 7.5 | <0.001 |
| Fruit Intake (servings/day), mean ± SD | 1.8 ± 0.9 | 2.5 ± 1.1 | <0.001 |
| Vegetable Intake (servings/day), mean ± SD | 2.0 ± 1.0 | 3.1 ± 1.2 | <0.001 |

Table 4. Distribution of APOE ε4 Allele among Study Participants

| Genetic Marker | IHD (n = 130) | Non-IHD (n = 120) | p-value |
|---|---|---|---|
| APOE ε4 Allele Frequency, n (%) | 46 (35.4%) | 24 (20.0%) | 0.005 |

Table 5. Multivariate Logistic Regression Analysis of Independent Predictors of IHD

| Predictor | Adjusted OR | 95% CI | p-value |
|---|---|---|---|
| Low Socioeconomic Status | 1.95 | 1.30 – 2.93 | 0.001 |
| APOE ε4 Allele (present) | 2.15 | 1.35 – 3.43 | 0.002 |
| High Saturated Fat Intake | 1.75 | 1.10 – 2.79 | 0.019 |
| Low Fruit & Vegetable Intake | 1.30 | 0.85 – 2.00 | 0.210 |

## DISCUSSION

This is a comprehensive case control study of a multifactorial etiology of IHD in Pakistan using a simultaneous evaluation of demographic, clinical, socioeconomic, dietary, and genetic factors at two major cardiac centers in Pakistan[11]. Results showed that patients with IHD were older, had higher body mass index, had higher blood pressure, and had more adverse lipid profiles than controls. In line with the existing global evidence of IHD relationship with traditional cardiovascular risk factors, these observations also underline the contextual importance of socioeconomic disadvantage and lifestyle factors in a developing country setting[12].

A major finding was the strong association of IHD with low socioeconomic status, with a disproportionately higher proportion of IHD patients living in the lowest income quartile and having lower education[13]. This is concordant with previous studies that have emphasized the effect of economic and educational disparities on cardiovascular health through reduced access to health care, increased exposure to stressors in the natural environment, and unhealthy lifestyle habits. In addition, we found that IHD patients had a higher intake of saturated fat and a lower consumption of fruits and vegetables. The atherosclerosis risk may be further increased by such dietary patterns, which can lead to dyslipidemia and systemic inflammation[14, 15].

Further genetic analysis substantiated the complex interplay of risk factors by showing a higher prevalence of the APOE ε4 allele in IHD patients. This allele has been linked to alteration of lipid metabolism and increased susceptibility to atherosclerotic plaque development. These data indicate that genetic predisposition may be combined with adverse socioeconomic and dietary conditions to increase the risk of IHD in this population [16, 17].

However, several limitations of this multicentre case–control design should be considered, including the strengths. Case-control studies are retrospective and thus are unable to fully establish causality, and residual confounding factors (e.g., physical activity levels and psychosocial stress) may have influenced the observed associations[18]. Furthermore, this study was limited to the selection of a small number of candidate genetic markers, and further research undertaken with broader genomic analysis may identify additional genetic architecture of IHD in Pakistan[19].

## CONCLUSION

This multicentre case control study shows that the risk of ischemic heart disease in Pakistan is substantially determined by a combination of traditional clinical risk factors, socioeconomic disadvantage, adverse dietary habits, and genetic predisposition, especially the presence of APOE ε4 allele. These findings emphasize the importance of public health strategies integrated at the level of both conventional risk factors and underlying socioeconomic and lifestyle determinants. To offset the escalating incidence of IHD in this population, tailored interventions are required, including nutritional counseling, improved access to health care, and educational initiatives. Only future longitudinal and comprehensive genomic studies will better elucidate the causal pathways and refine prevention strategies in resource-limited settings.

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**Conflict of Interest:** The authors declare no conflict of interest.

**Authors' Contributions:** All authors contributed substantially to the conception, design, data acquisition, analysis, and interpretation of the study. They also participated in drafting and revising the manuscript and approved the final version for publication.

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