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Atherogenic Index of Plasma's Association with Coronary Heart Disease Risks Among Postmenopausal Pakistani Women

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Abstract

Coronary heart disease (CHD) is a leading global cause of mortality, notably affecting postmenopausal women. Hormonal fluctuations during menopause contribute to dyslipidemia, fostering cardiovascular disease (CVD). This study explored lipid profiles among postmenopausal Pakistani women, focusing on the atherogenic index of plasma (AIP) and its association with CHD.

The data consisted of surveys from 265 women aged between 40–70 years. A STEP-wise approach, using a questionnaire from the World Health Organization, was employed for data collection. This quantitative cross-sectional study, guided by the socioecological model, examined links between AIP, age, lipid profiles, and hypertension. The AIP's association with CHD was analyzed by multiple linear regression.

Findings revealed age (β =0.406, p = 0.021), hypertension (β = 0.141, p = 0.002), and cholesterol (β = 1.557, p < 0.001) were significantly associated with AIP, while LDL (β = -1.527, p < 0.001) TG (β=0.790, pβ = -0.426, p = 0.001) were linked with AIP cholesterol.

Implications include the need for patient-centered screening initiatives and preventive measures to improve the quality of life for postmenopausal women. Monitoring and addressing dyslipidemia patterns can reduce the burden of interventional cardiology in Pakistan and enhance community health.

Keywords: *CHD, atherogenic index of plasma, postmenopausal women, dyslipidemic patterns, hypertension*

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Introduction

Hormonal fluctuations associated with menopause play a critical role in the onset of dyslipidemia (i.e., higher cholesterol levels), thereby increasing the risk of cardiovascular disease (CVD) and related complications. The cardioprotective effect observed in premenopausal women is primarily attributed to adequate levels of endogenous estrogen produced during the menstrual cycle. This hormonal influence may account for the lower incidence of coronary heart disease (CHD) in premenopausal women compared to men (Pardhe et al., 2017). Estrogen promotes cardiovascular health by elevating high-density lipoprotein cholesterol (HDL-C) levels and reducing low-density lipoprotein cholesterol (LDL-C) and triglyceride (TG) concentrations (Ryczkowska et al., 2022). The atherogenic index of plasma (AIP) is a valuable marker for assessing CVD risk, particularly among postmenopausal women. Elevated AIP values in this population suggest an increased susceptibility to atherosclerosis and cardiovascular events (Aga Khan University, 2021).

Dyslipidemia, particularly hypercholesterolemia and hypertension, remains a major CHD risk factor and a growing public health concern, especially in South Asia (Saeed et al., 2021). Menopause-related lipid disturbances often result in elevated total cholesterol, TGs, and LDL-C levels, along with reduced HDL-C levels and hypertension, with a reported prevalence of 17.9%. These are strong predictors of mortality from coronary artery disease (CAD) in women (Malik et al., 2022). The increasing prevalence of cardiovascular disease among South Asian women, particularly in Pakistan and Iran, underscores the link between dyslipidemia, AIP, and CHD risk (Hedayatnia et al., 2020). CHD is the leading cause of mortality among women, particularly in low-income settings. The relationship between AIP and CHD risk factors in postmenopausal women merits detailed investigation (Guo et al., 2020). Research conducted in Pakistan further highlighted the significant role of AIP as a predictor of adverse CHD outcomes (Shin et al., 2022). Moreover, hormonal changes during menopause, combined with adverse alterations in body composition, increase women's vulnerability to CVD (El Khoudary et al., 2018). Elevated AIP levels, particularly those within the "high AIP" range, reflect an unfavorable lipoprotein profile and are strongly associated with increased CHD risk in postmenopausal women. Issues identified in the existing literature contribute to the development of intermediate risk factors such as dyslipidemia, obesity, diabetes, and hypertension. These factors exert an indirect yet significant influence on the likelihood of CHD in postmenopausal women (Prabakaran et al., 2021).

Researchers have argued that the elevated prevalence of these metabolic risk factors intensifies the occurrence of metabolic syndrome, a constellation of conditions including hypertension, diabetes, obesity, and hyperlipidemia that collectively augment the overall risk of CHD in this population (Vaduganathan et al., 2022). Atherogenic dyslipidemia, a hallmark of metabolic syndrome, frequently arises due to postmenopausal lipid profile alterations (Ko & Kim, 2020), characterized by elevated TGs and LDL-C alongside reduced HDL-C (Wang et al., 2016). This lipid triad substantially increases atherosclerotic risk in postmenopausal women compared to premenopausal women, positioning it as a critical predictor of CHD (Ryczkowska et al., 2022). Emerging research highlighted the predictive role of the AIP in CHD development, with studies in South Asia examining the interplay between AIP, physical inactivity, and CVD risk factors among postmenopausal women (Ghaddar et al., 2024). These studies underscored its association with ischemic heart disease (IHD) and the need for lifestyle interventions in high-risk groups (Barua et al., 2018, 2019), as elevated AIP levels further exacerbate CHD susceptibility in postmenopausal women (Kamińska et al., 2023). Premature menopause, whether natural, surgical, or chemically induced before age 40, also elevates atherosclerotic cardiovascular disease (ASCVD) risk (Honigberg et al., 2019). A large cohort study of 144,260 postmenopausal women revealed a higher incidence of ASCVD (encompassing coronary artery disease, heart failure, stroke, and thromboembolism) over 7 years among women with surgical (7.6%; HR 1.87) or natural premature menopause (6.0%; HR 1.36) compared to women without premature menopause (3.9%; Yuk et al., 2023). Women face unique CHD risk factors across their lifespan, including early menarche, pre-eclampsia, preterm delivery, and menopause (Freaney et al., 2020). Stress, autoimmune diseases, and breast cancer may further elevate lipid abnormalities and AIP, compounding CVD risk (Tagoe et al., 2020). Despite CHD being the leading cause of female mortality (Centers for Disease Control and Prevention, 2024), women receive fewer diagnoses and preventive measures than men (Suman et al., 2023). Subclinical imaging techniques, such as coronary artery calcium scoring, could improve early detection (Arslan et al., 2024), particularly given the disparities in care. The 2023 multi-society guidelines, including those of the American Heart Association and American College of Cardiology (AHA, ACC), emphasized integrating female-specific risk factors such as obstetric history, lifestyle modifications, and statin use into primary prevention strategies (Virani et al., 2023). These recommendations align with a broader theoretical framework developed by the AHA, ACCA, and allied societies, which advocated for sex-specific risk factor management, reduced sedentary behavior, and enhanced diagnostic protocols to curb CHD prevalence in women.

Methods

This study aimed to examine the relationship between the AIP and various risk factors for CHD, including age at menopause, duration of menopause, physical activity, and lipid profile components. A quantitative, cross-sectional design was employed to provide a comprehensive understanding of the interplay among these factors in postmenopausal women. The independent variables included lipid profile parameters, hypertension, age, duration of menopause, physical activity, and hyperlipidemia, with AIP serving as the dependent variable.

To minimize the influence of potential confounders, control measures were applied for age at menarche, use of oral contraceptive pills, education level, income, smoking status, and the presence of diabetes mellitus. Multiple linear regression analysis was used to assess the association between AIP and key CHD risk factors, including hypertension, total cholesterol (TC), TG, LDL, and HDL. The adjusted regression model accounted for the aforementioned confounds, allowing for a more accurate evaluation of the relationships between AIP and CHD risk indicators. The use of a large sample and the absence of direct participant interaction helped minimize subjectivity and response bias, enhancing the reliability of the findings.

Inclusion and Exclusion Criteria

For this study, we used an existing dataset available on Mendeley Data (Barua et al., 2019). The dataset originated from a cross-sectional study conducted by Barua et al. (2019) between 2016 and 2017 in a town located in the South Asian region (formerly known as East Pakistan). According to Wong et al. (2022), while many longitudinal studies on CHD span several years, the core elements (risk factors, diagnosis, prevention, and treatment) remain consistent over time. Additionally, Brown et al. (2023) provided guidelines distinguishing studies of less than ten years from those of longer durations and noted that publicly available datasets, such as those from the Centers for Disease Control and Prevention (2024), offer valuable resources for further heart disease research.

The target population for the original study consisted of postmenopausal women residing in rural South Asian areas. Barua et al. (2019) surveyed 265 postmenopausal women aged 40–70 years using a convenience sampling method. Sample size determination was based on the estimated prevalence of CVD risk. Eligibility was confirmed through self-reports, clinical histories, and medical record reviews to ensure that participants had no diagnosed CVD. Menopausal status was defined as the absence of menstrual bleeding for at least 12 consecutive months, excluding other clinical causes of amenorrhea. Women experiencing acute illness or those unwilling to participate were excluded from the study.

These criteria aligned with the study’s aim to assess CVD risk factors in otherwise healthy postmenopausal women. To collect sociodemographic and behavioral data, Barua et al. (2019) employed a modified version of the World Health Organization's (WHO) STEP-wise approach to the Surveillance of Noncommunicable

Disease Risk Factors (STEPS) questionnaire. The WHO STEPS instrument, developed in 2002 and updated regularly, is a globally standardized tool designed to capture data across three domains: Step 1 (core sociodemographic and behavioral data), Step 2 (physical measurements), and Step 3 (biochemical assessments); see Appendix. Its modular and flexible design enables comparability across countries while accommodating local contexts and available resources. The STEPS questionnaire gathers information on major noncommunicable disease (NCD) risk factors such as tobacco and alcohol use, dietary patterns, and physical activity levels. Participants in the Barua et al. study were confirmed as free of CHD based on clinical history, self-reports, and a review of medical records, ensuring the reliability of the dataset for examining early CVD risk indicators in postmenopausal women.

Data Analysis

We analyzed the data using SPSS (Version 28) and Microsoft Excel 365. The sample size of 265 was determined using G* power (Version 3.1.9.4). This procedure enabled an a priori type of statistical power analysis focused on a significance level of 0.03 and a power of 0.99 for the population effect size. We used multiple linear regression for this study. The power (1-β err prob) was 0.99. The odds ratio used was 1.65.

Results

The presented descriptive statistics provide valuable insights into the characteristics of the dataset comprising measurements from 265 Pakistani women. The average age of approximately 53.49 years indicated a diverse range of participants ranging from 30–70 years. The AIP holds an average of 0.1560, suggesting a relatively low average cardiovascular risk level. The respondents had an average age at menopause of 44.83 years and an average duration of menopause of 8.79 years. The waist–hip ratio's average of 0.8837 implies a moderate body fat distribution (see Table 1).

Table 1. *Physical and Biochemical Parameters of Cardiovascular Diseases Among the Study Population,* N = *265.*

Parameter	Mean+-SD	Median (IQR)	*N* %
BMI (kg/m2)	23.26 ± 4.74	23.05 (20.13–26.02)	
Non-obese			245(92.5)
Generalized obese (30 kg/m2)			20(7.5)
SBP (mm Hg)	120.56 ± 20.17	120 (100–140)	
DBP (mm Hg)	76.72 ± 11.49	80 (70–85)	
2-h PG (mmol/l), n =223	6.24 ± 1.97 6	5.8 (3.–16.9)	
ND			215(96.4)
Diabetic			8(3.6)
Systolic hypertension140>	120.035±20.04	118(90–180)	
TC (mmol/l)	5.23 ± 1.3	5.33 (2.48–9.28)	
Desirable to borderline high			197(74.3)
Hypercholesterolemia (6.2>mmol)			68(25.7)
HDL-C (mmol/l)	1.1 ± 0.3	1(1–1)	
Low (<1.0 mmol/l)			70 (26.4)

High			195 (73.6)
LDL-C (mmol/l)	3.19 ± 1.139	3(2-4)	
Optimal to borderline high			210 (79.2)
High (>4.1 mmol/l)			55 (20.8)
TG (mmol/l)	1.86 ± 1.13	2(1-2)	
Normal to borderline high			153 (57.7)
High (>2.3 mmol/l)			112 (52.3)
AIP	0.16 ± 0.25	0.13(0.03 to 0.32)	
Low risk (<0.11)			124 (47.3)
Intermediate risk (0.11-0.24)			45 (17.2)
High risk (>0.24)			93 (35.5)

Total cholesterol and LDL cholesterol averages of 5.2333 mmol/L and 3.1866 mmol/L, respectively, reflected a moderate risk factor for cardiovascular health. The variation in MET values highlights differing levels of physical activity engagement. Other parameters, such as educational status, age of menarche, smoking habits, diabetes prevalence, TG level, HDL cholesterol level, income, glucose levels, and blood pressure, further contribute to the comprehensive overview of the participants' health profile. Understanding these interpretations provides a foundation for exploring potential relationships among these variables and their implications for health and well-being.

The research question we tested was: Is there an association between CHD risk factors of hypertension (HTN), TC, TGs, LDL, HDL, and AIP in Pakistani women, after controlling for age at menarche, oral contraceptive pills, education level, income, smoking and diabetes mellitus, and can we reject the null and accept the alternative hypothesis? (See Table 2)

Table 2. *Coefficients and* p *Value of Association Between Atherogenic Index of Plasma and CHD Risk Factors*

CVD Risk Factors	Unstandardized *B*	95% CI for *B*	*p-value*
Age	.011	(0.002–0.023)	0.021
HTN	.002	(0.001–0.003)	0.002
Total cholesterol	0.291	(0.228–0.341)	<0.001
LDL cholesterol	-0.313	(-0.366– -0.243)	<0.001
Triglycerides	0.190	(0.179.–.195)	<0.001
HDL	-0.383	(-0.426– -00350)	<0.001

Age demonstrated a positive and statistically significant association with the AIP, with an unstandardized coefficient (*B*) of 0.011 (p = .016). This indicates that holding all other variables constant, each additional year of age corresponds to a 0.011 increase in AIP. Unstandardized beta coefficients were used in the analysis due to their practical utility for prediction and interpretation.

Systolic blood pressure, serving as an indicator of hypertension, was also significantly and positively associated with AIP (B = 0.002, p = .006), suggesting that higher systolic pressure is linked to increased atherogenic risk. Furthermore, total cholesterol exhibited a strong positive relationship with AIP (B = 0.291, p < .001), where each unit increase in cholesterol was associated with a 0.291 unit rise in the AIP score. In contrast, LDL-C demonstrated a significant negative association with AIP (B = -0.313, p < .001), suggesting that higher LDL-C levels were linked to lower AIP values in this cohort. Similarly, HDL-C was inversely associated with AIP (B = - 0.383, p < .001), reinforcing its well-established cardioprotective role. TGs also showed a significant positive relationship with AIP (B = 0.190, p < .001), indicating that increased TG levels are associated with higher atherogenic risk.

The confidence intervals for all significant predictors did not include zero, underscoring the statistical robustness of these associations. These findings highlight the critical role of age, blood pressure, and various components of the lipid profile in determining atherogenic risk among postmenopausal women.

Based on the results of the multiple linear regression analysis, the null hypothesis can be rejected. The analysis confirms a statistically significant relationship between CHD risk factors (namely, age, systolic blood pressure, total cholesterol, LDL-C, HDL-C, and TGs) and AIP among Pakistani postmenopausal women. These relationships remained significant even after controlling for confounding variables such as age at menarche, use of oral contraceptive pills, educational attainment, income level, smoking, and diabetes mellitus.

Discussion

In low- and middle-income countries (LMICs), noncommunicable diseases contribute to nearly half of the total disease burden (Mendis, n.d.). In 2019, CHD alone accounted for approximately 30% of global mortality (Mendis, n.d.). Although CHD is more prevalent among men up to the age of 50, its incidence increases significantly in women after this age, likely due to the loss of the cardioprotective effects of estrogen post-menopause (Bucciarelli-Ducci et al., 2020). This shift underscores the importance of screening menopausal women for early identification and prevention of CHD (Adedinsewo et al., 2022), especially in LMICs such as Pakistan, where women constitute over half the population (Mendis, n.d.).

The present study identified a significant association between the AIP and key CHD risk factors, hypertension, TC, TGs, LDL-C, and HDL-C. These findings align with prior research demonstrating the direct relationship between lipid profiles, hypertension, and elevated AIP levels, thereby increasing CHD risk. Although Nansseu et al. (2016) did not establish a direct link between AIP and CHD, studies by Cai et al. (2017), Barua et al. (2019), and Wu et al. (2018) found a significant association between AIP values (ranging from 0.24 to 1.1) and CHD, which remains a leading cause of global mortality. Cai et al. (2017) reported similarly significant associations between lipid levels, hypertension, and AIP (p < .05). Barua et al. (2019) also found significant associations between AIP and several CHD predictors, such as duration of menopause (B = 0.606, p = .043), TC (B = 1.082, p < .001), and LDL-C (B = 1.044, p < .001). Consistent with these findings, our study reaffirmed AIP as a strong predictor of CHD risk in postmenopausal women.

Expanding on prior work by Wu et al. (2018), who established AIP as a reliable risk indicator for CHD in clinical populations, this study analyzed a cohort of 265 postmenopausal women while controlling for confounding variables such as age at menarche, use of oral contraceptive pills, education, income, smoking status, and diabetes mellitus. The results revealed statistically significant associations across all key variables, affirming the predictive power of AIP about CHD risk.

The study further emphasized that hypertension is a particularly influential predictor of CHD when combined with other factors, including elevated AIP. Given the widespread implications of hypertension for public health, these findings call for immediate attention from healthcare policymakers and practitioners. While age and sex are established risk factors for CHD, Zhu et al. (2019) noted that most patients also exhibit at least one modifiable risk factor. However, the utility of screening and targeted intervention for certain emerging risk factors remains under investigation. A study by Chen et al. (2022) using a nationally representative sample of Chinese postmenopausal women found that reproductive characteristics also influence cardiovascular risk. Specifically, later age at menarche was associated with a 10.6% increased risk of CVD, while each additional year of reproductive lifespan reduced CVD risk by 3.8%. Among women with comorbid conditions, each year of delayed menopause reduced CVD risk by 6.2%.

Compared to data on Indian postmenopausal women (Barua et al., 2019), this study found the rate of smokeless tobacco use to be substantially higher (4% vs. 45%). Moreover, dietary patterns in rural populations reflected excessive caloric intake, corroborating findings by Coleman et al. (2023). These behavioral risk factors, when left unmanaged, contribute to intermediate risks such as obesity, diabetes, and dyslipidemia (Hayden, 2023).

The literature also reflects ongoing debate regarding HDL-C levels in postmenopausal women. While some studies have reported a decline in HDL-C following menopause, others have noted increases, aligning with this study's findings (Li et al., 2023). Consistently, this study observed positive correlations between AIP and TC, TG, and LDL-C, while HDL-C was negatively correlated with AIP in postmenopausal women.

Given these findings, further investigation is warranted into the physiological and behavioral mechanisms driving AIP variation in postmenopausal women. Gender-specific research and tailored interventions are essential to understanding and mitigating cardiovascular risk. Future studies should adopt longitudinal designs to monitor changes in AIP across time and evaluate the influence of hormonal aging. Additionally, the significance of early cardio-metabolic risk factors in youth warrants emphasis, particularly regarding the relationship between atherogenic dyslipidemia, obesity, and metabolic syndrome.

Limitations

The research, despite its large sample size, focused primarily on postmenopausal women's susceptibility to coronary artery disease (CAD). Potential reliability issues may arise from participants' recall limitations. The growing interest in the AIP and its impact on CHD is noted, but cultural and social factors could affect the study's dependability. The findings are based solely on responses from the South Asian region, collected using a modified WHO STEPS questionnaire, with physical activity levels measured via a Microsoft Excel template.

Conclusion

This study provided important insights into the relationship between various independent variables and the AIP among postmenopausal women in Pakistan. The regression analysis identified statistically significant associations between AIP levels and several cardiovascular risk factors, emphasizing the index's value as a predictive marker for cardiovascular health outcomes in this population. These findings contribute to a growing body of evidence supporting the utility of AIP in clinical and public health settings and establish a foundation for future quantitative research and targeted interventions aimed at reducing CVD risk in postmenopausal women.

The 2023 guidelines from the American College of Cardiology, American Heart Association, American College of Clinical Pharmacy, American Society for Preventive Cardiology, National Lipid Association, and the Preventive Cardiovascular Nurses Association acknowledged several female-specific factors, such as preeclampsia, early menopause, and autoimmune diseases, as contributors to elevated CVD risk. These guidelines recommend that in cases where these risk factors are present in individuals at borderline or intermediate risk, clinicians should consider initiating statin therapy as part of a comprehensive risk management strategy. Additionally, dietary modification and lifestyle changes are strongly encouraged, particularly in postmenopausal women presenting with multiple risk factors.

Given these recommendations, AIP may serve as a practical and informative tool for assessing atherosclerotic risk in community-based populations. Among postmenopausal women in Pakistan, elevated AIP levels are consistently associated with established CHD risk factors, highlighting the need for personalized, preventive lifestyle interventions. Integrating AIP screening into routine clinical assessments may support earlier identification of cardiovascular risk and promote more effective strategies for CVD prevention and management in this high-risk group.

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Appendix

The WHO STEPS Q-by-Q Guide for Noncommunicable Disease (NCD) Risk Factor Surveillance provides a standardized framework to collect, analyze, and use data on NCD risk factors. It outlines a three-step approach:

1. Questionnaire (Step 1). Initially, self-reported demographics, behavioral risk factors (e.g., tobacco and alcohol use, physical inactivity, dietary habits), and chronic disease history are collected.

2. Physical measurement (Step 2): Evaluation of physical parameters such as height, weight, waist circumference, and blood pressure to determine unbiased risk factors for obesity and hypertension.

3. Step 3: Conduct biochemical assessments. Laboratory testing for biomarkers, such as blood glucose and cholesterol levels, can detect diabetes and hyperlipidemia.

The guide provides step-by-step instructions for implementing each stage, ensuring consistency and reliability in data collection. It emphasizes simplicity, standardization, and flexibility, enabling countries to adapt the protocol to their local contexts while maintaining global comparability of NCD risk factor data.

The WHO STEP-wise approach to NCD risk factor surveillance (STEPS) is a simple, standardized system for gathering, analyzing, and sharing data on critical NCD risk factors at the country level. The study focuses on important behavioral risk factors, such as tobacco and alcohol use, physical inactivity, and poor diets, as well as critical biological risk factors, including overweight and obesity, high blood pressure, raised blood glucose, and abnormal blood lipid levels.

Additional modules may be added to the survey tool to cover issues such as dental health, sexual health, and road safety. STEPS allows governments to track population changes and compare statistics across borders using standardized questionnaires and methods. The method emphasizes frequent collection of small, actionable data sets to support effective monitoring and timely interventions.

Tool link: https://www.who.int/teams/noncommunicable-diseases/surveillance/systems-tools/steps

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