



Long-Term Cardiovascular Risk Screening in Women After Preeclampsia: A Prospective Cohort Study

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ABSTRACT

Background: Preeclampsia, affecting 3-8% of pregnancies, has emerged as a significant predictor of future cardiovascular disease. Women with preeclampsia history demonstrate persistent endothelial dysfunction, metabolic abnormalities, and chronic inflammatory states extending beyond pregnancy. Despite recognition as a cardiovascular risk enhancer by major cardiology societies, systematic postpartum cardiovascular screening remains inadequately implemented, particularly in resource-limited settings.

Methods: A prospective observational cohort study enrolled 200 postpartum women (100 with previous preeclampsia, 100 age-matched controls with normotensive pregnancies) at a tertiary care center. Comprehensive cardiovascular assessment included blood pressure measurement, anthropometric evaluation, and biochemical profiling encompassing fasting glucose, complete lipid panel, high-sensitivity C-reactive protein (hsCRP), serum uric acid, and urine microalbumin-creatinine ratio. Metabolic syndrome was diagnosed using modified NCEP ATP III criteria, and 10-year atherosclerotic cardiovascular disease (ASCVD) risk was calculated using pooled cohort equations. Statistical analysis employed independent t-tests, chi-square tests, Pearson correlation, and multivariate logistic regression.

Results: Women with prior preeclampsia demonstrated significantly elevated systolic blood pressure (133.8 ± 11.6 versus 118.2 ± 9.8 mmHg, $p < 0.001$), diastolic blood pressure (86.4 ± 8.2 versus 74.6 ± 7.1 mmHg, $p < 0.001$), body mass index (27.8 ± 3.6 versus 24.7 ± 3.0 kg/m², $p < 0.001$), and waist circumference (89.6 ± 7.9 versus 80.1 ± 6.4 cm, $p < 0.001$). Biochemically, the preeclampsia group exhibited higher LDL-cholesterol (132.4 ± 27.8 versus 107.6 ± 21.4 mg/dL, $p < 0.001$), triglycerides

(168.2±42.6 versus 126.4±34.8 mg/dL, $p<0.001$), hsCRP (4.7±2.2 versus 2.0±1.2 mg/L, $p<0.001$), uric acid (5.9±1.1 versus 4.8±0.9 mg/dL, $p<0.001$), and microalbuminuria (38.6±17.4 versus 13.8±5.6 mg/g creatinine, $p<0.001$). Prevalence of chronic hypertension (44.0% versus 8.0%, $p<0.001$), metabolic syndrome (41.0% versus 17.0%, $p<0.001$), prediabetes (36.0% versus 14.0%, $p<0.001$), and intermediate-to-high ASCVD risk (28.0% versus 6.0%, $p<0.001$) was substantially elevated in the preeclampsia cohort.

Conclusion: Women with preeclampsia history demonstrate significantly increased cardiovascular and metabolic risk burden during early postpartum years. These findings underscore the critical importance of implementing structured postpartum cardiovascular screening protocols, lifestyle modification counseling, and preventive interventions to mitigate long-term cardiovascular morbidity in this high-risk population

Keywords: Preeclampsia, cardiovascular disease, metabolic syndrome, postpartum screening, atherosclerotic cardiovascular disease risk, endothelial dysfunction, microalbuminuria

INTRODUCTION

Preeclampsia, a pregnancy-specific hypertensive disorder characterized by new-onset hypertension and proteinuria or end-organ dysfunction after 20 weeks of gestation, complicates approximately 3-8% of pregnancies worldwide [1]. Traditionally conceptualized as a self-limited obstetric complication resolving with delivery, accumulating epidemiological and mechanistic evidence over the past two decades has fundamentally transformed understanding of preeclampsia from a transient pregnancy disorder to a sentinel marker of future cardiovascular disease [2].

Large-scale epidemiological studies and meta-analyses have consistently demonstrated that women with preeclampsia history face substantially elevated lifetime cardiovascular risk. A comprehensive meta-analysis incorporating data from over 3.7 million women revealed that preeclampsia confers a two-fold increased risk of developing coronary heart disease, a three-to-four-fold increased risk of chronic hypertension, and nearly double the risk of stroke during subsequent decades [3]. The magnitude of this association intensifies with disease severity, earlier gestational onset, and presence of adverse outcomes such as preterm delivery or fetal growth restriction [4].

The pathophysiological mechanisms linking preeclampsia to future cardiovascular disease are complex and multifactorial. Both conditions share common underlying risk factors including obesity, insulin resistance, dyslipidemia, and chronic inflammation, suggesting that preeclampsia may unmask pre-existing subclinical cardiovascular vulnerability [5]. However, emerging evidence indicates that preeclampsia itself induces persistent pathological changes extending beyond pregnancy resolution. The characteristic endothelial dysfunction, systemic inflammatory activation, oxidative stress, and abnormal vascular remodeling occurring during preeclamptic pregnancy appear to persist postpartum in many women [6].

Studies employing flow-mediated dilation, arterial stiffness measurements, and biomarker profiling have documented ongoing endothelial dysfunction years after preeclamptic pregnancy [7]. Elevated circulating levels of inflammatory markers including high-sensitivity C-reactive protein (hsCRP), interleukin-6, and tumor necrosis factor-alpha persist in the postpartum period, reflecting chronic low-grade inflammation that promotes atherosclerotic progression [8]. Furthermore, preeclampsia-associated renal microvascular damage, evidenced by persistent microalbuminuria, indicates ongoing renal endothelial injury and predicts future cardiovascular events [9].

Metabolic derangements represent another critical mechanism linking preeclampsia to cardiovascular disease. Women with preeclampsia history demonstrate higher rates of insulin resistance, impaired glucose tolerance, dyslipidemia, and metabolic syndrome during the postpartum period [10]. These metabolic abnormalities cluster with hypertension to create a high-risk cardiovascular phenotype requiring early identification and intervention. Additionally, elevated serum uric acid, commonly observed in preeclampsia, persists postpartum and contributes to endothelial dysfunction, oxidative stress, and hypertension development [11].

Recognition of preeclampsia as a cardiovascular risk enhancer has prompted major professional organizations to recommend enhanced cardiovascular surveillance for affected women. The American

Heart Association incorporated pregnancy complications including preeclampsia into cardiovascular risk assessment guidelines, recommending that women's cardiovascular risk evaluation include detailed reproductive history [12]. Similarly, the European Society of Cardiology identifies hypertensive pregnancy disorders as risk-enhancing factors warranting intensified preventive strategies [13].

Despite these recommendations, systematic implementation of postpartum cardiovascular screening remains inadequate globally, with particularly significant gaps in low- and middle-income countries where both preeclampsia incidence and cardiovascular disease burden are highest [14]. Multiple barriers impede effective postpartum care, including fragmented healthcare systems with poor integration between obstetric and primary care services, limited patient awareness regarding long-term risks, lack of standardized screening protocols, and insufficient healthcare provider knowledge [15].

In India, where maternal mortality from hypertensive disorders remains substantial and cardiovascular disease represents the leading cause of death among women, the intersection of preeclampsia and cardiovascular risk assumes particular importance [16]. However, limited data exist characterizing cardiovascular risk profiles in Indian women following preeclampsia, and postpartum cardiovascular screening is not routinely practiced in most settings.

The postpartum period represents a critical window of opportunity for cardiovascular risk assessment and primary prevention. Women maintain contact with healthcare systems during postpartum visits, providing accessible opportunities for screening, counseling, and intervention. Early identification of modifiable risk factors including hypertension, obesity, dyslipidemia, and dysglycemia enables lifestyle modification and pharmacological interventions that can substantially reduce future cardiovascular events [17].

Therefore, this prospective cohort study was designed with the primary objective of comprehensively evaluating long-term cardiovascular and metabolic risk profiles in women 1-5 years postpartum following preeclampsia compared to women with normotensive pregnancy histories. Secondary objectives included determining the prevalence of established cardiovascular risk factors (hypertension, obesity, dyslipidemia, prediabetes), assessing markers of subclinical cardiovascular disease (microalbuminuria, elevated hsCRP), characterizing metabolic syndrome prevalence, calculating 10-year ASCVD risk scores, and identifying independent predictors of elevated cardiovascular risk in the postpartum population.

MATERIALS AND METHODS

Study Design and Setting

This prospective observational cohort study was conducted at the District Hospital, Chitradurga, Karnataka, India, in collaboration with Basaveshwara Medical College and Research Center, over a 11-month period from JANUARY 2025 to NOVEMBER 2025. The study protocol received approval from the Institutional Ethics Committee, and all participants provided written informed consent before enrollment.

Study Population and Sampling

Women attending gynecology outpatient clinics, postpartum follow-up visits, or general medicine clinics were systematically screened for eligibility based on obstetric history. Eligible women with previous preeclampsia were identified through medical record review and patient history. Age-matched control participants with normotensive pregnancy histories were recruited from the same clinical settings to minimize selection bias.

Sample Size Calculation

Sample size was calculated based on expected differences in mean systolic blood pressure between groups. Previous literature suggested mean systolic BP of 132 ± 14 mmHg in women with preeclampsia history versus 118 ± 12 mmHg in controls. Using the formula for comparison of two independent means with alpha error of 0.05 (two-tailed), power of 80%, and anticipated 10% non-

response rate, the minimum required sample size was calculated as 88 participants per group. To ensure adequate power for secondary analyses and subgroup comparisons, 100 participants per group (total 200) were enrolled.

Inclusion Criteria

For the preeclampsia group: (1) women aged 18-45 years; (2) singleton pregnancy; (3) 1-5 years postpartum from index pregnancy; (4) documented diagnosis of preeclampsia during index pregnancy based on American College of Obstetricians and Gynecologists criteria (blood pressure $\geq 140/90$ mmHg on two occasions after 20 weeks gestation with proteinuria ≥ 300 mg/24 hours or evidence of end-organ dysfunction). For the control group: all above criteria except having normotensive pregnancy without gestational hypertension, preeclampsia, or eclampsia.

Exclusion Criteria

Women were excluded if they had: (1) pre-existing chronic hypertension diagnosed before pregnancy or before 20 weeks gestation; (2) pre-gestational diabetes mellitus; (3) chronic kidney disease or known renal disorders before pregnancy; (4) autoimmune disorders including systemic lupus erythematosus or antiphospholipid syndrome; (5) multiple gestation during index pregnancy; (6) known cardiovascular disease including coronary artery disease, heart failure, or cerebrovascular disease; (7) current pregnancy; (8) incomplete or unavailable medical records from index pregnancy; (9) thyroid disorders or other endocrine abnormalities; (10) current use of antihypertensive or lipid-lowering medications confounding baseline assessment.

Data Collection Procedures

All participants underwent comprehensive evaluation in a single visit scheduled after overnight fasting. Trained research personnel conducted standardized interviews using structured questionnaires capturing demographic information, detailed obstetric history including gestational age at preeclampsia diagnosis, disease severity, mode of delivery, birth weight, and any maternal or neonatal complications. Medical history including interval pregnancies, development of hypertension or diabetes, cardiovascular symptoms, medication use, and family history of cardiovascular disease was systematically recorded.

Clinical Assessment

Blood pressure was measured using validated automated sphygmomanometer (Omron HEM-7120) following standardized protocol. Participants rested in seated position for 5 minutes before measurement. Three readings were obtained at 2-minute intervals from the right arm with appropriately sized cuff, and the mean of the three measurements was recorded. Hypertension was defined as systolic BP ≥ 130 mmHg and/or diastolic BP ≥ 80 mmHg or current antihypertensive medication use.

Anthropometric measurements included height measured using stadiometer to nearest 0.1 cm, weight measured using calibrated digital scale to nearest 0.1 kg, and waist circumference measured at midpoint between lowest rib and iliac crest using non-stretchable tape. Body mass index (BMI) was calculated as $\text{weight}(\text{kg})/\text{height}^2(\text{m}^2)$. Obesity was defined as BMI ≥ 30 kg/m², overweight as BMI 25-29.9 kg/m², and normal weight as BMI 18.5-24.9 kg/m².

Laboratory Investigations

Following 10-12 hours overnight fasting, venous blood samples (15 mL) were collected in appropriate vacutainers. Fasting plasma glucose was measured using glucose oxidase-peroxidase method. Prediabetes was defined as fasting glucose 100-125 mg/dL or known impaired glucose tolerance. Complete lipid profile including total cholesterol, LDL-cholesterol, HDL-cholesterol, and triglycerides was measured using enzymatic colorimetric methods on automated analyzer (Roche Cobas c311). Dyslipidemia was defined according to NCEP ATP III guidelines.

High-sensitivity C-reactive protein (hsCRP) was measured using immunoturbidimetric assay with normal reference range <3 mg/L. Elevated cardiovascular risk was defined as hsCRP >3 mg/L. Serum uric acid was measured using uricase-peroxidase method. Serum creatinine was measured using

Jaffe's kinetic method, and estimated glomerular filtration rate (eGFR) was calculated using CKD-EPI equation.

First-morning urine samples were collected for microalbumin and creatinine measurement. Urine microalbumin was measured using immunoturbidimetric assay, and microalbumin-creatinine ratio (MACR) was calculated. Microalbuminuria was defined as MACR 30-300 mg/g creatinine.

Metabolic Syndrome and ASCVD Risk Assessment

Metabolic syndrome was diagnosed using modified NCEP ATP III criteria requiring presence of three or more of the following: (1) waist circumference >80 cm for Asian women; (2) triglycerides ≥ 150 mg/dL or specific treatment; (3) HDL-cholesterol <50 mg/dL or specific treatment; (4) blood pressure $\geq 130/85$ mmHg or antihypertensive treatment; (5) fasting glucose ≥ 100 mg/dL or diabetes treatment. Ten-year atherosclerotic cardiovascular disease (ASCVD) risk was calculated using the American College of Cardiology/American Heart Association Pooled Cohort Equations, incorporating age, sex, race, total cholesterol, HDL-cholesterol, systolic blood pressure, diabetes status, smoking status, and antihypertensive treatment. Risk categories were defined as low (<5%), borderline (5-7.4%), intermediate (7.5-19.9%), and high ($\geq 20\%$).

Statistical Analysis

Data were entered into Microsoft Excel and analyzed using Statistical Package for Social Sciences (SPSS) version 26.0. Normality of continuous variables was assessed using Shapiro-Wilk test and visual inspection of histograms and Q-Q plots. Continuous variables with normal distribution were expressed as mean $\pm$ standard deviation and compared between groups using independent samples Student's t-test. Non-normally distributed variables were expressed as median (interquartile range) and compared using Mann-Whitney U test.

Categorical variables were presented as frequencies and percentages and compared using chi-square test or Fisher's exact test when expected cell frequencies were <5. Pearson correlation coefficient was calculated to assess linear relationships between continuous variables. Multivariate logistic regression analysis was performed to identify independent predictors of elevated ASCVD risk (>7.5%), with results presented as odds ratios with 95% confidence intervals. Variables with $p < 0.10$ in univariate analysis were included in multivariate models. Statistical significance was set at two-tailed p -value <0.05 for all analyses.

RESULTS

Study Population Characteristics

During the study period, 124 women with previous preeclampsia were screened, of whom 100 met inclusion criteria and consented to participation. Twenty-four were excluded (8 currently pregnant, 6 with pre-existing chronic hypertension, 4 with incomplete records, 3 with autoimmune disorders, 2 with chronic kidney disease, 1 declined participation). One hundred age-matched controls with normotensive pregnancy histories were similarly enrolled. All 200 participants completed the comprehensive cardiovascular assessment protocol.

Baseline Demographic and Clinical Characteristics

Table 1 presents baseline demographic characteristics and obstetric history. The groups were well-matched for age, with mean ages of 29.6 ± 4.3 years in the preeclampsia group versus 29.2 ± 4.1 years in controls ($p = 0.508$). The mean interval from index pregnancy to study assessment was similar between groups (2.8 ± 1.2 versus 2.7 ± 1.1 years, $p = 0.562$). Among women with previous preeclampsia, 62% had severe disease, mean gestational age at diagnosis was 33.4 ± 3.6 weeks, and 54% delivered preterm (<37 weeks).

Table 1: Baseline Demographic Characteristics and Obstetric History

Parameter	Preeclampsia Group (n=100)	Control Group (n=100)	p-value
Age (years)	29.6 ± 4.3	29.2 ± 4.1	0.508
Years postpartum	2.8 ± 1.2	2.7 ± 1.1	0.562

Education (≥12 years), n (%)	54 (54.0)	58 (58.0)	0.566
Rural residence, n (%)	68 (68.0)	64 (64.0)	0.547
Family history CVD, n (%)	42 (42.0)	28 (28.0)	0.040
Current smoking, n (%)	2 (2.0)	1 (1.0)	0.562
Parity (median, IQR)	2 (1-2)	2 (1-2)	0.684
Severe preeclampsia, n (%)	62 (62.0)	-	-
GA at PE diagnosis (weeks)	33.4 ± 3.6	-	-
Preterm delivery, n (%)	54 (54.0)	8 (8.0)	<0.001
Cesarean delivery, n (%)	72 (72.0)	38 (38.0)	<0.001
Low birth weight, n (%)	48 (48.0)	12 (12.0)	<0.001

Family history of cardiovascular disease was significantly more prevalent in the preeclampsia group (42.0% versus 28.0%, $p=0.040$), suggesting shared genetic or familial risk factors.

Cardiovascular Risk Factors and Anthropometric Measurements

Table 2 demonstrates comprehensive cardiovascular risk factor profiles and anthropometric measurements. Women with previous preeclampsia exhibited significantly elevated blood pressure parameters, with mean systolic BP of 133.8 ± 11.6 mmHg versus 118.2 ± 9.8 mmHg in controls ($p<0.001$), and mean diastolic BP of 86.4 ± 8.2 mmHg versus 74.6 ± 7.1 mmHg ($p<0.001$). Chronic hypertension prevalence was substantially higher in the preeclampsia group (44.0% versus 8.0%, $p<0.001$).

Anthropometric indicators of obesity demonstrated significant between-group differences. Mean BMI was 27.8 ± 3.6 kg/m² in the preeclampsia group versus 24.7 ± 3.0 kg/m² in controls ($p<0.001$). Obesity prevalence (BMI ≥ 30 kg/m²) was 32.0% versus 12.0% ($p=0.001$), and overweight/obesity combined affected 76.0% versus 48.0% ($p<0.001$). Central obesity, measured by waist circumference, was markedly increased (89.6 ± 7.9 cm versus 80.1 ± 6.4 cm, $p<0.001$).

Table 2: Cardiovascular Risk Factors and Anthropometric Measurements

Parameter	Preeclampsia Group (n=100)	Control Group (n=100)	p-value
Systolic BP (mmHg)	133.8 ± 11.6	118.2 ± 9.8	<0.001
Diastolic BP (mmHg)	86.4 ± 8.2	74.6 ± 7.1	<0.001
Chronic hypertension, n (%)	44 (44.0)	8 (8.0)	<0.001
Body mass index (kg/m ²)	27.8 ± 3.6	24.7 ± 3.0	<0.001
Obesity (BMI ≥ 30), n (%)	32 (32.0)	12 (12.0)	0.001
Overweight/Obese, n (%)	76 (76.0)	48 (48.0)	<0.001
Waist circumference (cm)	89.6 ± 7.9	80.1 ± 6.4	<0.001

Metabolic syndrome, n (%)	41 (41.0)	17 (17.0)	<0.001
Prediabetes, n (%)	36 (36.0)	14 (14.0)	<0.001
Type 2 diabetes, n (%)	8 (8.0)	2 (2.0)	0.053
Current medication use, n (%)	38 (38.0)	6 (6.0)	<0.001

Metabolic syndrome was diagnosed in 41.0% of women with preeclampsia history compared to 17.0% of controls ($p<0.001$). Prediabetes prevalence was significantly elevated (36.0% versus 14.0%, $p<0.001$), though type 2 diabetes prevalence showed a trend without reaching statistical significance (8.0% versus 2.0%, $p=0.053$).

Biochemical and Laboratory Parameters

Table 3 presents comprehensive biochemical profiles. Metabolic parameters demonstrated significant derangements in the preeclampsia group. Mean fasting plasma glucose was elevated (98.4 ± 13.8 mg/dL versus 88.6 ± 9.8 mg/dL, $p<0.001$), though mean values remained in the normal range for both groups.

Lipid profiles revealed significant atherogenic patterns in women with preeclampsia history. Mean LDL-cholesterol was markedly elevated (132.4 ± 27.8 mg/dL versus 107.6 ± 21.4 mg/dL, $p<0.001$), with 58.0% demonstrating LDL ≥ 130 mg/dL compared to 22.0% of controls ($p<0.001$). Mean HDL-cholesterol was significantly lower (43.8 ± 7.4 mg/dL versus 51.6 ± 8.2 mg/dL, $p<0.001$), with 64.0% having HDL <50 mg/dL versus 28.0% of controls ($p<0.001$). Mean triglycerides were substantially elevated (168.2 ± 42.6 mg/dL versus 126.4 ± 34.8 mg/dL, $p<0.001$).

Table 3: Biochemical and Laboratory Parameters

Parameter	Preeclampsia Group (n=100)	Control Group (n=100)	p-value
Fasting glucose (mg/dL)	98.4 ± 13.8	88.6 ± 9.8	<0.001
Total cholesterol (mg/dL)	198.6 ± 36.4	172.4 ± 28.6	<0.001
LDL-cholesterol (mg/dL)	132.4 ± 27.8	107.6 ± 21.4	<0.001
HDL-cholesterol (mg/dL)	43.8 ± 7.4	51.6 ± 8.2	<0.001
Triglycerides (mg/dL)	168.2 ± 42.6	126.4 ± 34.8	<0.001
hsCRP (mg/L)	4.7 ± 2.2	2.0 ± 1.2	<0.001
hsCRP >3 mg/L, n (%)	62 (62.0)	18 (18.0)	<0.001
Serum uric acid (mg/dL)	5.9 ± 1.1	4.8 ± 0.9	<0.001
Hyperuricemia, n (%)	38 (38.0)	12 (12.0)	<0.001
Serum creatinine (mg/dL)	0.9 ± 0.2	0.8 ± 0.2	0.002
eGFR (mL/min/1.73m ²)	94.6 ± 14.2	102.4 ± 12.8	<0.001
MACR (mg/g creatinine)	38.6 ± 17.4	13.8 ± 5.6	<0.001
Microalbuminuria, n (%)	46 (46.0)	8 (8.0)	<0.001
ASCVD risk $\geq 7.5\%$, n (%)	28 (28.0)	6 (6.0)	<0.001
Mean ASCVD risk	5.8 ± 4.2	2.4 ± 1.8	<0.001

score (%)			
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Inflammatory markers showed marked elevation in the preeclampsia cohort. Mean hsCRP was significantly elevated (4.7 ± 2.2 mg/L versus 2.0 ± 1.2 mg/L, $p < 0.001$), with 62.0% demonstrating levels > 3 mg/L indicative of high cardiovascular risk compared to only 18.0% of controls ($p < 0.001$).

Serum uric acid remained significantly elevated years after pregnancy (5.9 ± 1.1 mg/dL versus 4.8 ± 0.9 mg/dL, $p < 0.001$), with hyperuricemia (> 6.0 mg/dL) present in 38.0% versus 12.0% ($p < 0.001$). Renal function parameters showed subtle but significant differences, with mean eGFR lower in the preeclampsia group (94.6 ± 14.2 versus 102.4 ± 12.8 mL/min/1.73m², $p < 0.001$).

Microalbuminuria, an important marker of endothelial dysfunction and cardiovascular risk, was substantially elevated in women with preeclampsia history. Mean microalbumin-creatinine ratio was 38.6 ± 17.4 mg/g creatinine versus 13.8 ± 5.6 mg/g in controls ($p < 0.001$), with 46.0% meeting criteria for microalbuminuria compared to 8.0% of controls ($p < 0.001$).

Ten-year ASCVD risk assessment revealed significantly elevated cardiovascular risk in the preeclampsia group. Mean calculated ASCVD risk was $5.8 \pm 4.2\%$ versus $2.4 \pm 1.8\%$ in controls ($p < 0.001$). Importantly, 28.0% of women with preeclampsia history demonstrated intermediate-to-high risk ($\geq 7.5\%$) compared to only 6.0% of controls ($p < 0.001$), indicating that more than one-quarter of previously preeclamptic women warranted intensive cardiovascular risk reduction strategies based on current guidelines.

Correlation and Regression Analyses

Pearson correlation analysis revealed significant positive correlations between years since preeclampsia diagnosis and current systolic BP ($r = 0.284$, $p = 0.004$), BMI ($r = 0.312$, $p = 0.002$), and LDL-cholesterol ($r = 0.268$, $p = 0.007$), suggesting progressive cardiovascular risk accumulation over time.

Multivariate logistic regression analysis identified independent predictors of elevated ASCVD risk ($\geq 7.5\%$). After adjusting for age, family history, BMI, and smoking, preeclampsia history remained a strong independent predictor (OR 4.82, 95% CI 1.86-12.48, $p = 0.001$). Other independent predictors included metabolic syndrome (OR 3.64, 95% CI 1.42-9.32, $p = 0.007$), microalbuminuria (OR 2.86, 95% CI 1.18-6.94, $p = 0.020$), and elevated hsCRP > 3 mg/L (OR 2.54, 95% CI 1.06-6.08, $p = 0.037$).

DISCUSSION

This prospective cohort study demonstrates that women with preeclampsia history exhibit substantially elevated cardiovascular and metabolic risk profiles 1-5 years postpartum compared to women with normotensive pregnancy histories. The comprehensive cardiovascular assessment revealed significant elevations in blood pressure, anthropometric obesity markers, atherogenic lipid profiles, inflammatory biomarkers, microalbuminuria, and calculated 10-year ASCVD risk. These findings provide compelling evidence supporting the implementation of structured postpartum cardiovascular screening protocols for women following preeclampsia.

The 44% prevalence of chronic hypertension observed in our preeclampsia cohort within 1-5 years postpartum is consistent with international literature. A large Norwegian population-based study demonstrated that women with preeclampsia had a 4.7-fold increased risk of developing chronic hypertension within 5 years compared to women with normotensive pregnancies [1]. Similarly, Brown et al. in a systematic review reported that preeclampsia increased hypertension risk by 3-4 fold [2]. The elevated blood pressure persisting years after pregnancy likely reflects both unmasking of pre-existing predisposition and pregnancy-induced vascular damage that fails to fully resolve.

The mechanisms underlying persistent hypertension post-preeclampsia are multifactorial. Endothelial dysfunction, characterized by impaired nitric oxide-mediated vasodilation and increased oxidative stress, persists years after preeclamptic pregnancy [3]. Studies using flow-mediated dilation have documented ongoing endothelial impairment in women with preeclampsia history [4]. Additionally, arterial stiffness, measured by pulse wave velocity, remains elevated postpartum, indicating permanent vascular remodeling [5]. Renal microvascular damage, evidenced by persistent microalbuminuria in 46% of our preeclampsia cohort, contributes to hypertension through impaired

sodium handling and activation of the renin-angiotensin-aldosterone system.

The significantly higher BMI and waist circumference in women with preeclampsia history, with 32% meeting obesity criteria, represents an important modifiable risk factor. Whether obesity represents a shared risk factor for both preeclampsia and cardiovascular disease, or whether pregnancy-related weight retention contributes to obesity development, remains debated. A prospective study by Fraser et al. demonstrated greater postpartum weight retention among women with preeclampsia [6]. Regardless of directionality, obesity amplifies cardiovascular risk and represents a critical intervention target.

The 41% prevalence of metabolic syndrome in our preeclampsia cohort is alarmingly high and consistent with previous reports. Hermes et al. found metabolic syndrome in 38% of women with preeclampsia history compared to 10% of controls at 6-12 months postpartum [7]. Similarly, Sandvik et al. reported metabolic syndrome in 32% of women 5-8 years after preeclamptic pregnancy [8]. The clustering of hypertension, central obesity, dyslipidemia, and dysglycemia creates a particularly high-risk cardiovascular phenotype. Metabolic syndrome confers 2-3 fold increased risk of cardiovascular events and type 2 diabetes [9].

Our finding of elevated prediabetes prevalence (36% versus 14%) aligns with evidence linking preeclampsia to future diabetes risk. A large Danish cohort study demonstrated that preeclampsia increased type 2 diabetes risk by 1.8-fold [10]. The shared pathophysiology includes insulin resistance, with preeclampsia unmasking subclinical metabolic dysfunction. Importantly, progression from prediabetes to diabetes is preventable through lifestyle interventions, emphasizing the value of early identification [11].

The atherogenic lipid profiles observed in our preeclampsia cohort, characterized by elevated LDL-cholesterol, reduced HDL-cholesterol, and elevated triglycerides, contribute substantially to atherosclerotic cardiovascular disease risk. Previous studies have documented persistent dyslipidemia following preeclampsia. A systematic review by Cusimano et al. found that women with preeclampsia history had significantly higher total cholesterol and LDL-cholesterol levels years after pregnancy [12]. The underlying mechanisms include insulin resistance-mediated hepatic overproduction of VLDL particles and altered lipoprotein lipase activity.

The markedly elevated hsCRP levels (mean 4.7 mg/L) in our preeclampsia group indicate ongoing chronic low-grade inflammation, a key driver of atherosclerotic progression. hsCRP independently predicts cardiovascular events, with levels >3 mg/L conferring high risk [13]. The persistent inflammation may reflect ongoing endothelial activation, adipose tissue inflammation associated with obesity, or residual immunological activation from preeclamptic pregnancy. Importantly, lifestyle modifications including weight loss and exercise effectively reduce CRP levels [14].

Persistent hyperuricemia in 38% of women with preeclampsia history represents an underappreciated cardiovascular risk factor. Elevated uric acid contributes to endothelial dysfunction through multiple mechanisms including reduced nitric oxide bioavailability, oxidative stress generation, and inflammatory pathway activation [15]. A meta-analysis by Li et al. demonstrated that hyperuricemia increased cardiovascular disease risk by 1.3-1.8 fold [16]. Furthermore, uric acid promotes hypertension development and progression, creating a vicious cycle of vascular damage.

The high prevalence of microalbuminuria (46%) in our preeclampsia cohort is particularly concerning as this marker predicts not only renal disease progression but also cardiovascular events. Microalbuminuria reflects generalized endothelial dysfunction affecting both glomerular capillaries and systemic vasculature. Previous studies have documented persistent microalbuminuria years after preeclampsia. McDonald et al. found microalbuminuria in 40% of women 1-2 years post-preeclampsia [17]. Importantly, microalbuminuria is reversible with blood pressure control, RAAS blockade, and lifestyle modification, providing intervention opportunities.

The finding that 28% of women with preeclampsia history demonstrated intermediate-to-high 10-year ASCVD risk ($\geq 7.5\%$) has important clinical implications. Current guidelines recommend statin therapy and intensive risk factor modification for individuals with ASCVD risk $\geq 7.5\%$ [18]. Our results indicate that more than one-quarter of previously preeclamptic women would qualify for intensive preventive interventions based solely on traditional risk calculation, without even accounting for the additional risk conferred by preeclampsia history itself.

The clinical implications of our findings are substantial. Current postpartum care focuses primarily on immediate pregnancy-related recovery, with insufficient attention to long-term health. Women with preeclampsia history require structured cardiovascular surveillance including regular blood pressure monitoring, annual comprehensive metabolic assessment, lifestyle counseling emphasizing weight management and physical activity, and individualized pharmacological interventions when indicated. The American Heart Association recommends that preeclampsia be considered a risk-enhancing factor when calculating cardiovascular risk [18].

Several strengths enhance the validity of our study. The prospective design with comprehensive standardized assessment minimized bias. Inclusion of matched controls from the same population reduced confounding. Detailed obstetric history verification through medical records ensured accurate preeclampsia classification. Comprehensive biochemical profiling including novel markers provided multidimensional risk assessment. Use of validated ASCVD risk calculation enabled comparison with established guidelines.

However, several limitations warrant acknowledgment. The cross-sectional assessment at single time point precludes evaluation of longitudinal risk evolution. The modest sample size may have limited power for detecting associations with less common outcomes. Single-center design may limit generalizability to populations with different demographics or healthcare systems. Absence of pre-pregnancy baseline data prevents distinguishing pre-existing risk factors from preeclampsia-induced changes. Selection bias may exist if healthier women were more likely to participate. Finally, the relatively short follow-up duration (1-5 years) limits assessment of long-term cardiovascular events.

Future research should include prospective longitudinal studies following women from pregnancy through decades to characterize cardiovascular disease incidence and mortality, intervention trials evaluating whether postpartum screening and risk factor modification reduce cardiovascular events, investigation of optimal screening intervals and biomarker panels, cost-effectiveness analyses of various screening strategies, identification of genetic and epigenetic markers predicting highest-risk subgroups, and studies evaluating implementation strategies to integrate cardiovascular screening into routine postpartum care.

CONCLUSION

This prospective cohort study provides comprehensive evidence that women with preeclampsia history demonstrate substantially elevated cardiovascular and metabolic risk profiles during the early postpartum years. Compared to women with normotensive pregnancy histories, those with previous preeclampsia exhibit significantly higher rates of chronic hypertension, obesity, metabolic syndrome, prediabetes, atherogenic dyslipidemia, chronic inflammation, and microalbuminuria. More than one-quarter of previously preeclamptic women demonstrate intermediate-to-high 10-year cardiovascular risk, warranting intensive preventive interventions.

These findings underscore the critical importance of recognizing preeclampsia not merely as a pregnancy complication but as a sentinel marker identifying women at high risk for future cardiovascular disease. The postpartum period represents a crucial window of opportunity for cardiovascular risk assessment, patient education, and preventive intervention. Implementation of structured postpartum cardiovascular screening protocols, including blood pressure monitoring, metabolic assessment, and lifestyle counseling, is essential for this high-risk population.

Healthcare systems must develop integrated care models bridging obstetric and primary care services to ensure continuity of cardiovascular surveillance for women following preeclampsia. Primary care physicians and cardiologists should routinely inquire about pregnancy complications during cardiovascular risk assessment. Women with preeclampsia history should receive comprehensive counseling regarding their elevated long-term cardiovascular risk and the importance of healthy lifestyle behaviors including weight management, regular physical activity, healthy diet, and smoking avoidance.

Early identification and aggressive management of modifiable risk factors including hypertension, obesity, dyslipidemia, and dysglycemia in this population has the potential to substantially reduce future cardiovascular morbidity and mortality. By recognizing pregnancy as a natural stress test revealing women's cardiovascular vulnerability and implementing appropriate postpartum

surveillance and prevention strategies, we can transform preeclampsia from a predictor of future disease into an opportunity for life-saving early intervention

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