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Levels of blood pressure, cardiovascular biomarkers and their correlations in women with previous pre-eclamptic pregnancy within 7 years postpartum: a cross-sectional study in Thailand

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ABSTRACT

Objective To assess the levels of blood pressure, cardiovascular biomarkers and their correlations measured within 7 years postpartum in women with previous pre-eclamptic pregnancies compared with women with previous normotensive pregnancies.

Design Cross-sectional study.

Setting Two tertiary hospitals in the southern region of Thailand.

Participants Women with pre-eclamptic and normotensive pregnancies in the past 7 years were enrolled from 1 October 2019 to 30 April 2021. Eligible women were interviewed, examined for body mass index (BMI) and blood pressure, and donated morning spot urine and blood samples.

Primary outcome measures Serum high-sensitivity C reactive protein, creatinine, fasting blood glucose (FBS), glycated haemoglobin (HbA1c), low-density lipoprotein (LDL) cholesterol, urine microalbumin to creatinine ratio (UACR) and sodium were measured. Group differences in biomarkers were tested using unpaired t-test, Wilcoxon rank-sum test or χ^2 test. The levels of blood pressure and biomarkers between the two study groups at <2 years, 2–4 years and >4 years were also compared. The correlations between blood pressure and biomarkers were analysed using Pearson's correlation and partial correlation methods.

Results From 206 women included in the analysis, 88 had pre-eclamptic pregnancies and 118 had normotensive pregnancies. Compared with women with previous normotensive pregnancies, women with previous pre-eclamptic pregnancies had significantly increased rates of hypertension (31.8% vs 7.6%, p<0.001) and obesity (55.7% vs 40.7%, p=0.038), as well as higher serum levels of FBS (p<0.001), HbA1c (p<0.001), LDL cholesterol (p=0.03), creatinine (p<0.001) and UACR (p<0.001). Correlation coefficients of BMI, serum creatinine and UACR with blood pressure ranged from 0.27 to 0.31.

Conclusion The risk of hypertension after a pre-eclamptic pregnancy increased. Blood pressure measurement combined with BMI, serum creatinine and UACR screening at least once during 7 years postpartum is suggested for early detection of cardiovascular risk.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ Two tertiary hospitals in the southern region of Thailand, where pre-eclampsia is common, were selected to recruit participants with heterogeneous religious and social backgrounds.
⇒ This study comprehensively assessed blood pressure and its correlations with cardiovascular biomarkers and behavioural measures during different periods following pre-eclamptic pregnancies.
⇒ This was cross-sectional in design at different periods after delivery and might not truly reflect individual longitudinal changes in blood pressure and biomarkers.
⇒ The findings might not represent women with previous pre-eclamptic pregnancies since the study took place at two tertiary hospitals located in an urban area and suffered from a low participation rate.

INTRODUCTION

Pre-eclampsia is a common hypertensive disorder in pregnancy (HDP), classically diagnosed by hypertension plus proteinuria in pregnancy,[1] affecting about 3% of pregnancies worldwide.[2] The registered incidence of pre-eclampsia was 1% in 2014, with higher rates in the central and southern regions of Thailand.[3] The pathogenesis of pre-eclampsia remains unclear; however, it is likely to be related to abnormal placentation and placenta function, endothelial injury, and systemic inflammation.[4 5] Pre-eclampsia is highly associated with increased maternal and fetal morbidity and mortality[6] and has been one of the most common, direct obstetric causes of maternal death for many decades, especially in low-income and middle-income countries.[7]

Although placental delivery usually resolves the acute clinical signs of pre-eclampsia, the health risks to pregnant women persist long

after delivery.[4] Several studies have demonstrated that women with previous pre-eclampsia are at increased risk of future hypertension, cardiovascular diseases (CVDs), diabetes mellitus and renal diseases.[8–10] These non-communicable diseases represent a global burden, particularly high systolic blood pressure, which is the largest contributor to all causes of deaths in women.[11] The mechanisms linking pre-eclampsia and future CVDs are currently unknown, and both share common risk factors or pathways related to inflammation, vascular remodelling, angiogenesis, apoptosis, haemostasis and renin–angiotensin–aldosterone system, as well as new or persistent endothelial injury after pre-eclampsia is proposed.[12–14]

Some studies have demonstrated that women with pre-eclamptic pregnancies have elevated biomarkers of endothelial injury and inflammation several years after delivery, including microalbuminuria[15] and high-sensitivity C reactive protein (hs-CRP),[16] respectively. Both biomarkers have also been associated with increased risk of CVD.[17 18] The association between pre-eclampsia and CVD may result from common metabolic risk factors such as insulin resistance, obesity and dyslipidaemia.[19 20] Likewise, behavioural risk factors including high sodium intake, sedentary lifestyle and sleep disturbances are related to high blood pressure in pregnant women[21–23] as well as in the general population.[24–26] Nonetheless, only a few studies have investigated these behavioural risk factors in the postpartum period. In regard to the postpartum period, breast feeding is another protective factor against hypertension and CVD.[27 28]

To date, there have been several studies concerning the level of cardiovascular biomarkers after pregnancies complicated by pre-eclampsia.[15 16 19 29–33] However, most studies were cross-sectional in design, with limited postpartum periods and specific time points. We identified few previous studies evaluating the correlations between blood pressure and biomarkers.[31 34] Comprehensive assessment of postpartum blood pressure, cardiovascular biomarkers and behavioural measures in the years following delivery can be useful, as this is a time in life when chronic hypertension may first present after previous pregnancy complications such as pre-eclampsia.[35] Hence, this study aimed to assess the levels of blood pressure, cardiovascular biomarkers and their correlations measured within 7 years postpartum in women with previous pre-eclamptic pregnancies compared with women with previous normotensive pregnancies.

MATERIALS AND METHODS

Study design and setting

A cross-sectional study was conducted in the southern region of Thailand, where pre-eclampsia is common.[3] Two tertiary hospitals from Songkhla and Narathiwat provinces were selected to recruit participants with heterogeneous religious and social backgrounds. Each hospital has in total approximately 4000 deliveries a year and is responsible for providing care to women with pre-eclampsia in either the Songkhla or Narathiwat province.

Sample size calculation

Due to the lack of previous studies, an assumed correlation coefficient between biomarkers and blood pressure of 0.5 was used to calculate the required sample size. With a type I error of 5% and a type II error of 20%, the required sample size was 29 women from each period of postpartum year slots (<2 years, 2–4 years and >4 years since last delivery).

Study participants

Delivery records of women who gave birth in the two study hospitals from 1 January 2014 to 30 June 2020 were screened for eligibility. Women were eligible if they were at least 18 years old, not currently pregnant and lived in the same province as the study hospital. Those who were non-Thai, unable to be contacted or had communication barriers were excluded. According to their most recent pregnancy, women with previous pre-eclamptic pregnancies were 1:1 matched with women with previous normotensive pregnancies using maternal age (±5 years), parity (either primipara or multipara) and duration since last delivery (±2 months). Eligible women were informed by phone and invited to participate in the study. Women were enrolled from 1 October 2019 to 30 April 2021.

Exposure assessment

Pre-eclampsia was defined as systolic blood pressure (SBP) ≥140 mm Hg and/or diastolic blood pressure (DBP) ≥90 mm Hg after 20 weeks of gestation, accompanied by proteinuria.[1] Proteinuria was defined as ≥300 mg/24 hours, protein to creatinine ratio ≥0.3 or a dipstick reading of 2+. According to the most recent pregnancy, the diagnosis recorded in the delivery records was used to define women across all forms of severity of pre-eclampsia (with or without severe features, superimposed pre-eclampsia or eclampsia). Controls were women without neither diagnosis of pre-eclampsia, gestational hypertension nor chronic hypertension during their most recent pregnancy.

Data collection

Eligible women who agreed to participate were asked to visit the outpatient department of the study hospital after fasting overnight. At the study visit, a trained research assistant interviewed the women for demographic and obstetrics information, physical activity and sleep quality. Morning spot urine and blood samples were collected from all participants after fasting overnight for 12 hours, then refrigerated and transported in cold storage to the clinical chemistry laboratory unit for analysis of biomarkers within the same day. Physical activity was evaluated using the Thai version of the Global Physical Activity Questionnaire.[36] Total physical activity, including activity for work, during transport and leisure time, was described using metabolic equivalent of task (MET) minutes per week. The WHO recommendations on

physical activity for health ≥600 MET-min per week were used. Sleep quality was assessed using the Thai version of the Pittsburgh Sleep Quality Index.[37] A global score, ranging from 0 to 21, was the sum of seven components assessing each sleep problem. Higher scores indicated worse sleep quality, and a global score >5 indicated poor sleep quality.

Body weight was measured after all heavy clothing was removed. Body mass index (BMI) was derived from weight in kilograms divided by the square of the height in metres. The BMI cut-off points for Asian populations of 23–24.9 kg/m^2 for being overweight and ≥25 kg/m^2 for obesity were used.[38] SBP and DBP were measured using an automatic cuff-oscillometric device (HEM-7300; Omron Healthcare, Kyoto, Japan) in mm Hg after women had rested for at least 15 min. Three consecutive blood pressure measurements were taken and their average was used. Current diagnosis of hypertension was defined as blood pressure at study visit of ≥140/90 mm Hg, self-reported hypertension or currently under antihypertensive treatment.

Laboratory methods

The biomarkers assessed in this study included serum hs-CRP (particle enhanced immunoturbidimetric method), creatinine (creatinine in urine and serum measured by enzymatic colourimetric method), fasting blood glucose (FBS; enzymatic hexokinase method), glycated haemoglobin (HbA1c; capillary electrophoresis method), low-density lipoprotein (LDL) cholesterol (homogeneous enzymatic colourimetric method), urine microalbumin to creatinine ratio (UACR; urine microalbumin measured by immunoturbidimetric method), urine sodium (indirect ion selective electrode method) and urine sodium to creatinine ratio. Most biomarkers were measured using a Cobas 6000 modular analyser (Roche Diagnostics, Mannheim, Germany), except HbA1c which was measured using Capillarys 3 Tera (Sebia, France), at the clinical chemistry laboratory (Songklanagarind Hospital, Prince of Songkla University, Thailand).

Statistical analysis

Demographic and obstetrics information of participants was descriptively presented. Differences in demographic and obstetrics information, physical and behavioural measures, and biomarkers between women with previous pre-eclamptic pregnancies and normotensive pregnancies were tested. For continuous data, an unpaired t-test or Wilcoxon rank-sum test was used as appropriate. For categorical data, χ^2 test was used. Due to skewed distribution, blood pressure and biomarkers between women with previous pre-eclamptic pregnancies and previous normotensive pregnancies at different periods since last delivery (<2 years, 2–4 years and >4 years) were compared using a Wilcoxon test, with Holm-Bonferroni adjustment for multiple comparisons. Correlations between biomarkers and blood pressure were calculated using Pearson's correlation method and partial correlation analysis controlling for age at postpartum study visit and pre-existing hypertension. Correlations between blood pressure and pre-eclampsia were also analysed by controlling for age at postpartum study visit, pre-existing hypertension, BMI and renal function (serum creatinine and UACR). Factors associated with hypertension at postpartum study visit were analysed using multivariate logistic regression after excluding women with pre-existing hypertension. All data were analysed using R V.4.0.4 (R Core Team 2021, Vienna, Austria).

Patients and public involvement

Patients and/or the public were not involved in the design, conduct, reporting or dissemination of results of this study.

RESULTS

A total of 1337 eligible women were identified from the delivery records of two study hospitals. Of these, 219 did not have a registered phone number in the hospital database, 581 were unable to be contacted and 2 were deceased. We invited 537 women to participate in the study, of whom 211 agreed to enrol in the study. The medical records of all enrolled women were reviewed in more detail and five did not have pre-eclampsia, resulting in 206 women included for analyses (88 women with previous pre-eclamptic pregnancies and 118 women with previous normotensive pregnancies) (online supplemental figure 1).

The demographic and obstetrics information of participating women is presented in table 1. Women with previous pre-eclamptic pregnancies were significantly older (mean±SD age: 36.0±5.9 vs 34.1±6.5) compared with women with previous normotensive pregnancies. Family history of hypertension (63.6% vs 42.4%) and CVD (26.1% vs 10.2%) was more commonly reported in women with previous pre-eclamptic pregnancies. The proportion of women reporting family history of HDP was not different between the groups. Time since the last delivery varied from 0.7 to 7 years for the total study group. The median time since delivery was similar for both previous pre-eclamptic (2.2 years, IQR 1.5–4.5) and previous normotensive (2.0 years, IQR 1.5–4.1) pregnancy groups. At their last delivery, the group of women with pre-eclamptic pregnancies were older, had higher prepregnancy BMI, higher rates of being overweight and obesity, and had a higher prevalence of preterm birth as well as low infant birth weight.

At the postpartum study visit, women with previous pre-eclamptic pregnancies had significantly higher SBP (p<0.001), DBP (p<0.001) and BMI (p=0.017) compared with controls (table 2). More women with pre-eclamptic pregnancies were obese and diagnosed with hypertension compared with women with normotensive pregnancies (p=0.038 and p<0.001, respectively). Both study groups had similarly high rates of insufficient physical activity

Table 1 Demographic and obstetrics information of participating women (N=206)

Characteristics	Previous pre-eclamptic pregnancy (n=88)	Previous normotensive pregnancy (n=118)	P value
Age at last delivery (years), mean (SD)	33.0 (5.6)	31.2 (6.5)	0.037
Age at postpartum study visit (years), mean (SD)	36.0 (5.9)	34.1 (6.5)	0.029
Religion			0.119
Buddhism	44 (50.0)	45 (38.1)	
Islam	44 (50.0)	73 (61.9)	
Education			0.732
Lower than bachelor's degree	35 (39.8)	43 (36.4)	
Bachelor's degree or higher	53 (60.2)	75 (63.6)	
Monthly family income (US$), median (IQR)	1000 (483–1667)	833 (500–1208)	0.249
Medical history			
Pre-existing hypertension	7 (8.0)	0 (0.0)	0.002
Diabetes mellitus	5 (5.7)	2 (1.7)	0.14
Dyslipidaemia	2 (2.3)	1 (0.8)	0.577
Family history			
Hypertension	56 (63.6)	50 (42.4)	0.002
Cardiovascular disease	23 (26.1)	12 (10.2)	0.005
HDP	7 (8.0)	4 (3.4)	0.211
Prepregnancy BMI, median (IQR)	23.5 (20.6–27.0)	21.8 (19.5–25.2)	0.02
Prepregnancy BMI categories			0.019
Normal (BMI <23 kg/m^2)	38 (43.2)	73 (61.9)	
Overweight (BMI 23–24.9 kg/m^2)	19 (21.6)	13 (11.0)	
Obesity (BMI ≥25 kg/m^2)	31 (35.2)	32 (27.1)	
Characteristics of most recent pregnancy			
Parity (primipara)	41 (46.6)	46 (39.0)	0.342
Gestational diabetes	11 (12.5)	12 (10.2)	0.763
Twin pregnancy	3 (3.4)	0 (0.0)	0.076
Preterm birth (<37 weeks of gestation)	37 (42.0)	12 (10.2)	<0.001
Low infant birth weight (<2500 g)	39 (44.3)	17 (14.4)	<0.001
Postpartum duration (years)			0.544
<2	41 (46.6)	58 (49.2)	
2–4	18 (20.5)	29 (24.6)	
>4	29 (33.0)	31 (26.3)	

Data are reported as n (%) unless stated otherwise.
BMI, body mass index; HDP, hypertensive disorder in pregnancy.

(~50%) and poor sleep quality (~71%). No statistically significant difference in lactation duration was found between the two groups (median lactation time of 6 and 8 months). Figure 1 shows the SBP and DBP in women with previous pre-eclamptic pregnancies and normotensive pregnancies stratified by periods of postpartum duration. The median SBP in women with previous pre-eclamptic pregnancies was significantly higher than women with previous normotensive pregnancies at any investigated time point postparum (<2, 2–4 and >4 years postpartum : p=0.013, p=0.023 and p<0.001, respectively; figure 1A). Significant differences in DBP between women with previous pre-eclamptic pregnancies and normotensive pregnancies were detected at <2 years postpartum investigation (p=0.007) and >4 years postpartum investigation (p<0.001; figure 1B).

The levels of FBS, HbA1c, LDL cholesterol, serum creatinine and UACR were significantly higher in women with previous pre-eclamptic pregnancies (all p<0.001, except for LDL cholesterol, p=0.03; table 3). There were no significant differences in the level of hs-CRP (p=0.171), urine sodium (p=0.437) and sodium to creatinine ratio (p=0.301) between the two study groups. As shown in table 4, there were weak correlations between

Table 2 Physical and behavioural measures at postpartum study visit for the two study groups (N=206)

Measures	Previous pre-eclamptic pregnancy (n=88)	Previous normotensive pregnancy (n=118)	P value
Systolic blood pressure (mm Hg), median (IQR)	121.2 (112.8–135.5)	112.0 (102.8–119.3)	<0.001
Diastolic blood pressure (mm Hg), median (IQR)	82.5 (74.3–90.8)	70.8 (64.4–80.0)	<0.001
Current diagnosis of hypertension	28 (31.8)	9 (7.6)	<0.001
BMI, median (IQR)	26.0 (22.3–29.6)	23.5 (20.8–27.7)	0.017
BMI categories			0.038
Normal (BMI <23 kg/m^2)	25 (28.4)	54 (45.8)	
Overweight (BMI 23–24.9 kg/m^2)	14 (15.9)	16 (13.6)	
Obesity (BMI ≥25 kg/m^2)	49 (55.7)	48 (40.7)	
Lactation duration (months), median (IQR)	6.0 (3.0–14.8)	8.0 (3.0–12.5)	0.678
Insufficient physical activity	45 (51.1)	57 (48.3)	0.794
Sleep quality			0.854
Good (PSQI global score ≤5)	26 (29.9)	31 (27.7)	
Poor (PSQI global score >5)	61 (70.1)	81 (72.3)	

Data are reported as n (%) unless stated otherwise.
BMI, body mass index; PSQI, Pittsburgh Sleep Quality Index.

prepregnancy BMI, postpartum BMI, serum creatinine and UACR with both SBP and DBP in Pearson's and partial correlation methods. The correlations for all biomarkers in total and the two study groups are presented in online supplemental table 1. A history of pre-eclampsia was significantly correlated with SBP and DBP (both r=0.35) and lower correlations were shown (both r=0.22) after adjusting for age, pre-existing hypertension, postpartum BMI, serum creatinine and UACR. The final model of multivariate logistic regression assessing factors associated with hypertension at postpartum study visit is shown in online supplemental table 2. Women with previous pre-eclamptic pregnancies had higher odds of having hypertension at postpartum study visit when compared with normotensive pregnancies (adjusted OR=4.32, 95% CI 1.57 to 11.84). Serum creatinine in women with previous pre-eclamptic pregnancies was significantly higher at <2 years postpartum than in the control group (p=0.011; figure 2A). Women with previous pre-eclamptic pregnancies also had a significantly elevated UACR (p=0.001; figure 2B) and BMI (p=0.003; figure 2C) measured at >4 years postpartum compared with women with previous normotensive pregnancies.

DISCUSSION

Women with previous pre-eclamptic pregnancies not only had increased blood pressure and risk of hypertension at postpartum follow-up, but also elevated BMI, FBS, HbA1c, LDL cholesterol, serum creatinine and UACR levels, compared with women with previous normotensive pregnancies. We found no significant differences in hs-CRP nor in behavioural factors (lactation duration, total physical activity, sleep quality and sodium intake). However, fair correlations between BMI, serum creatinine and UACR and blood pressure were observed.

The group of women with previous pre-eclamptic pregnancies had consistently elevated blood pressure already from the first year postpartum when compared with controls. This finding was consistent with various studies conducted in Canada, UK, Norway and USA, with follow-up durations ranging from 6 weeks to 1 year postpartum.[31 34 39 40] The increased risk of hypertension in women with previous pre-eclamptic pregnancies in our study is also supported by a systematic review from 2007 including 13 studies mostly conducted in Western, not Asian, countries.[8] Although the risk of hypertension after pre-eclampsia was relatively consistent in this review, the pathophysiology and mechanisms may vary across ethnicity and postpartum durations.

Two previous systematic reviews found similar results as ours after a pre-eclamptic pregnancy, namely higher BMI, FBS and LDL cholesterol as compared with controls.[41 42] Our finding of a small but significant elevation in HbA1c was not replicated in these aforementioned reviews. Inconsistent HbA1c findings might result from different population characteristics, with a variation in insulin resistance and obesity rates.[43] Our group of women with previous pre-eclamptic pregnancies had elevated levels of biomarkers related to kidney function (serum creatinine and UACR), which was not replicated in a systematic review.[44] Although a previous study suggested that proteinuria after pre-eclampsia might take up to 2 years to normalise, data related to creatinine levels after pre-eclampsia are lacking.[45] Detection of microalbuminuria after pre-eclampsia was hypothesised due to endothelial injury in the kidney,[46] which is also an important factor in the pathophysiology of pre-eclampsia.[4 5] Whether our

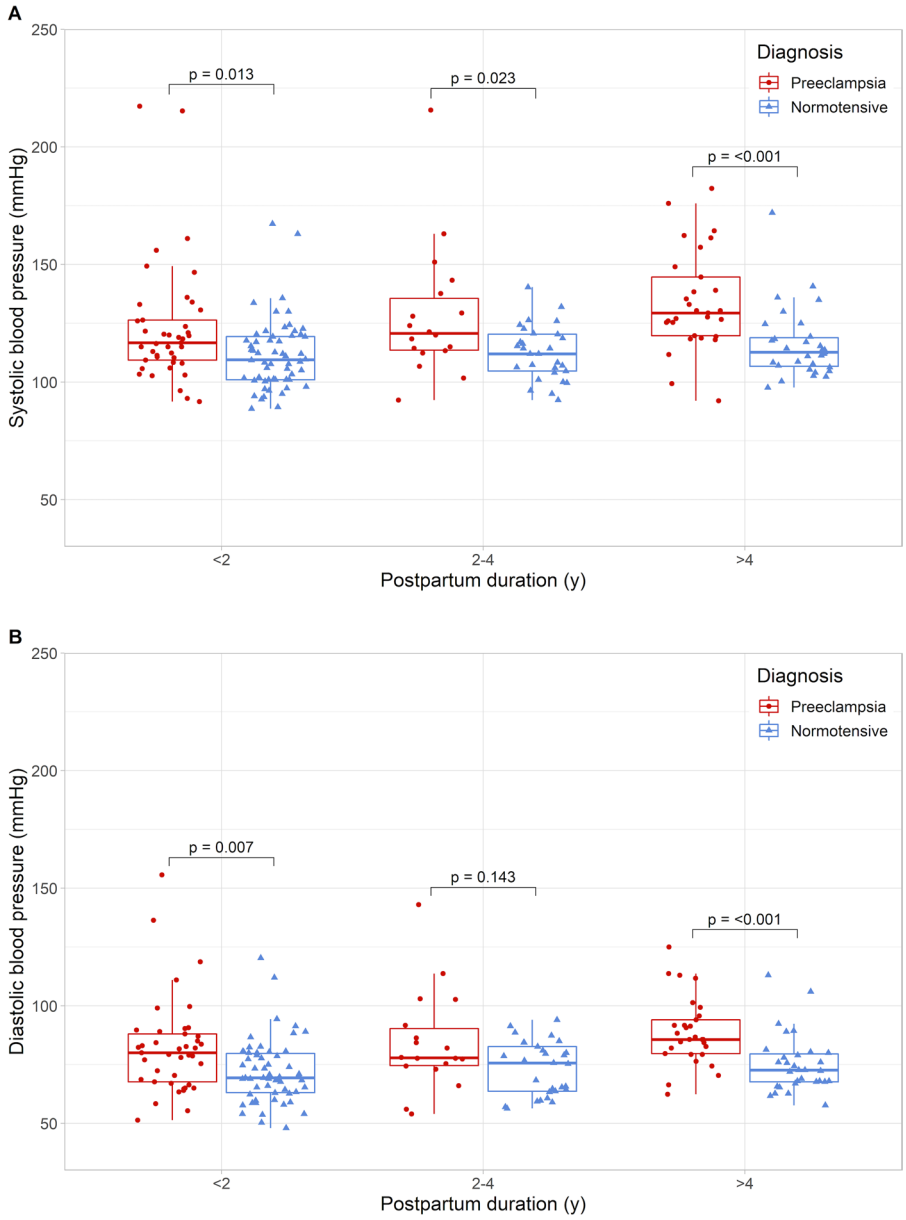

Figure 1 Boxplot of systolic blood pressure (A) and diastolic blood pressure (B) for the two study groups (N=206) at <2 years, 2–4 years and >4 years postpartum.

group of previous pre-eclamptic women had abnormal kidney function also prior to their pre-eclamptic pregnancy is however not known.

Our finding of unaltered hs-CRP in women with previous pre-eclamptic pregnancies was similar to the findings of two studies that followed up women with pre-eclampsia and HDP at 1 year postpartum.[39 40] However, a significant association between HDP and higher CRP levels was shown when the follow-up duration was up to 20 years postpartum in previous studies.[30 47] This suggests that increased inflammation (measured as elevated hs-CRP) may develop over time after pre-eclampsia and possibly linked to other evidence of metabolic dysregulation.

In our study, a slightly longer lactation duration was found in women with previous normotensive pregnancies compared with previous pre-eclamptic pregnancies, but this difference was not statistically significant. In normal pregnancy, two cohort studies have reported lower blood pressure during lactation at 1 or 5 months postpartum.[48 49] Sodium intake, reflected by spot urine sodium to creatinine ratio, did not differ between women with previous pre-eclamptic and normotensive pregnancies and only correlated weakly with postpartum blood pressure, which was in line with a previous study from ≥8 months postpartum.[50] This is also consistent with blood pressure not necessarily being affected by levels of sodium intake, but by intrinsic salt sensitivity in pre-eclampsia.[51 52]

Our participating women had moderate rates of physical activity, with no difference in median values between the two study groups. A previous study reported a higher percentage (62%) of women meeting the recommendations on physical activity at 3 and 6 months after

Table 3 Comparison of biomarkers at postpartum study visit for the two study groups (N=206)

Biomarkers	Previous pre-eclamptic pregnancy (n=88)	Previous normotensive pregnancy (n=118)	P value
Serum FBS (mg/dL), median (IQR)	86.5 (82.1–92.7)	82.8 (76.4–88.8)	<0.001
Serum HbA1c (%), median (IQR)	5.5 (5.3–5.7)	5.2 (5.1–5.5)	<0.001
Serum LDL cholesterol (mg/dL), mean (SD)	140.4 (36.4)	129.8 (33.1)	0.03
Serum creatinine (mg/dL), median (IQR)	0.7 (0.6–0.8)	0.6 (0.6–0.7)	<0.001
Serum hs-CRP (mg/L), median (IQR)	2.3 (0.9–4.2)	1.7 (0.6–3.7)	0.171
UACR (mg/g Cr), median (IQR)	7.3 (4.5–23.8)	4.9 (3.3–8.1)	<0.001
Urine sodium (mmol/L), mean (SD)	144.8 (57.8)	151.1 (58.3)	0.437
Urine sodium to creatinine ratio, median (IQR)	13.7 (8.7–20.0)	16.8 (10.0–21.0)	0.301

Cr, creatinine; FBS, fasting blood sugar; HbA1c, glycated haemoglobin; hs-CRP, high-sensitivity C reactive protein; LDL, low-density lipoprotein; UACR, urine microalbumin to creatinine ratio.

pre-eclampsia[53]; however, this study used a different questionnaire for physical activity. Of the women in our study, 70% experienced poor sleep quality, regardless of their pre-eclamptic status during pregnancy. The prevalence of poor sleep quality was higher than previously reported at 2 months postpartum.[54] Women participating in our study might have underlying sleep problems, leading to worsening of sleep disruption normally occurring during the postpartum period.[55]

Only three of the investigated biomarkers were fairly correlated with blood pressure: BMI, serum creatinine and UACR. Elevated BMI has previously been shown to represent a risk factor for incident hypertension during the postpartum period.[56] In the general population, a correlation between blood pressure, creatinine and microalbuminuria is already known.[57 58] We suggest that these biomarkers could be useful for early detection of high blood pressure, and subsequently guide lifestyle modification in postpartum women with previous pre-eclampsia.

Table 4 Pearson's correlation and partial correlation coefficients of SBP and DBP with clinical measures and biomarkers for the total study group (N=206)

	Correlation coefficient (r)		Partial correlation coefficients (r)‡	
Variables†	SBP	DBP	SBP	DBP
Prepregnancy BMI	0.23**	0.25***	0.21**	0.22**
BMI	0.28***	0.31***	0.28***	0.31***
Serum HbA1c	0.15*	0.16*	0.18**	0.22**
Serum creatinine	0.31***	0.28***	0.25***	0.21**
UACR	0.27***	0.31***	0.22**	0.20**

†Only variables with significant correlation coefficients shown: *p value<0.05; **p value<0.01; ***p value<0.001. Full results presented in online supplemental table 1.
‡Partial correlation coefficients adjusted by age at the postpartum study visit and pre-existing hypertension.
BMI, body mass index; DBP, diastolic blood pressure; HbA1c, glycated haemoglobin; SBP, systolic blood pressure; UACR, urine microalbumin to creatinine ratio.

To date, there have been few studies focusing on blood pressure levels and cardiovascular biomarkers after pre-eclampsia in Asia, as most studies have been conducted in Europe and North America. Our study comprehensively examined blood pressure and their correlations with cardiovascular biomarkers and behavioural measures during different periods following delivery. Another advantage of our study is that detailed information on the diagnosis of pre-eclampsia was checked from medical records using prespecified criteria, thus preventing misclassification of study exposure.

There were some limitations to our study. First, our study was cross-sectional in design at different periods after delivery and might not truly represent individual longitudinal changes in blood pressure and biomarkers. Second, our study suffered from a low participation rate, especially in women with previous pre-eclamptic pregnancies. Third, seven women in previous pre-eclamptic pregnancy had pre-existing hypertension and continued antihypertensive medication during participation in our study, which may affect blood pressure and its correlation with the studied biomarkers. However, the same findings were identified when the subgroup analysis excluding these women was explored. Finally, our study took place at two tertiary hospitals that provided healthcare to people only in urban and suburban areas; hence, women living within the same district as the study hospitals were more likely to participate in the study. This might have affected the external validity of our study, as women who did not participate in the study might have different socioeconomic status and disease severity.

In conclusion, women with previous pre-eclamptic pregnancies more often had hypertension, as well as higher levels of BMI, FBS, HbA1c, LDL cholesterol, serum creatinine and UACR, within 7 years postpartu. Our findings suggest that women with previous pre-eclamptic pregnancies should have their blood pressure checked at least once during the first year after delivery. Measurements of BMI, serum creatinine and UACR could provide additional benefit in targeting women at high risk of

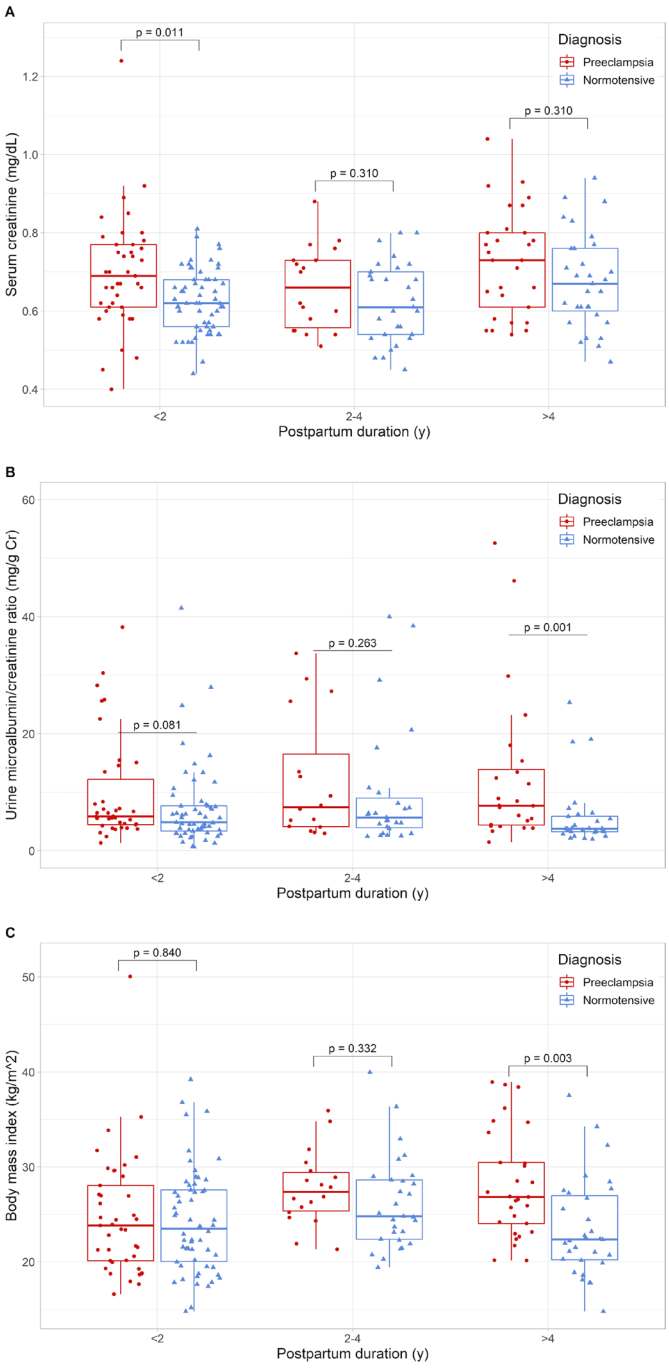

Figure 2 Boxplot of creatinine (A), urine microalbumin to creatinine ratio (B) and body mass index (C) for the two study groups (N=206) at <2 years, 2–4 years and >4 years postpartum. Fifteen outliers in (B) were removed for better visualisation. Cr, creatinine.

hypertension and offering them an early consultation about future cardiovascular risk and lifestyle intervention as well as risk monitoring strategies. Further research on optimal follow-up content and timing after pre-eclamptic pregnancies, in order to optimise early intervention and reduce the risk of long-term CVDs, is still required.

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