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Hypertensive pregnancy complications and maternal characteristics as predictors of cardiovascular health within ten years after delivery

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ABSTRACT

Objective: To identify the combination of maternal characteristics in women with hypertensive disorders of pregnancy (HDP) associated with hypertensive and other cardiovascular diseases (CVDs) within ten years following delivery. The aim is to understand who should receive the most intensive primary cardiovascular disease prevention.
Study design: A prospective cohort study.
Main outcome: The population was the FINNPEC cohort (2008–2011), including women with (n = 1837) and without (n = 847) HDP. The main exposures were maternal hypertensive pregnancy complications linked with maternal pregnancy data from hospital records. The outcomes were hypertensive diseases and other CVDs (International Classification of Diseases, Tenth Revision).
Results: Women with de novo pre-eclampsia (PE) had an elevated risk for hypertensive diseases within ten years following delivery. The risk of CVD was increased in women with superimposed PE and chronic hypertension (CHT) only. Women with de novo PE and hypertensive diseases were more often primiparous (41.4% vs. 23.0%, $p = 0.020$), had gestational diabetes (GDM) (31.0% vs. 11.7%, $p = 0.002$), and higher pre-pregnancy body mass index (BMI) (28.7 ± 5.8 vs. 24.6 ± 4.8 kg/m^2, $p = 0.001$), compared with women who remained normotensive. Women with superimposed PE with CVD had more likely early-onset PE, preterm delivery and were older than women without later CVD.
Conclusions: Healthcare professionals should target early prevention of CVDs in women with chronic hypertension during pregnancy; of those who developed superimposed PE prior to 34th weeks of gestation and who delivered preterm. Women with de novo PE who are overweight/obese, primiparous, and with concurrent GDM need regular blood pressure monitoring.

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1. Introduction

Hypertensive disorders of pregnancy (HDP) are a group of conditions that involve high blood pressure during pregnancy [1] and are one of the leading causes of maternal and neonatal morbidity and mortality worldwide [2,3]. The prevalence is 5–10% globally [4], with the highest burden in Africa and Southeast Asia, the lowest in Western Pacific [5]. The association between HDP, particularly pre-eclampsia (PE), and subsequent cardiovascular diseases (CVDs), as well as postpartum chronic hypertension, is well established [6–10]. A recently published cohort study of over 2 million Swedish women showed that women with HDPs were 1.5–2 more likely to have ischemic heart disease compared to women without HDPs in the 10 years following delivery [11].

The correlation between the severity of HDP and future CVD risk suggests that the differences in long-term later risk for hypertension and CVD may depend on variations in the underlying maternal CVD risk profiles [12], particularly in the development of hypertension. Postpartum chronic hypertension (CHD) is likely a crucial mediator for heart failure, coronary artery disease, and cerebrovascular disease after HDP [13]. CVDs remain the leading cause of death in women worldwide [14]; HDP could be seen as an opportunity to identify high-risk women and prevent CVDs.

The objective of this study was to identify pregnancy/maternal characteristics associated with increased risk of hypertensive and other cardiovascular diseases (CVD) within ten years following delivery in women with and without HDPs. The aim is to understand who should receive the most intensive primary cardiovascular disease prevention.

2. Methods

2.1. Outcomes and exposure

The outcomes were hypertensive diseases and other CVDs within ten years following delivery and the exposures were HDPs together with maternal characteristics. The definitions of CVDs are in Supplemental Table S3. Women with CHT and superimposed PE already had pre-existing hypertension (defined from maternal antenatal records), thus their second occurrence of CVDs were analyzed.

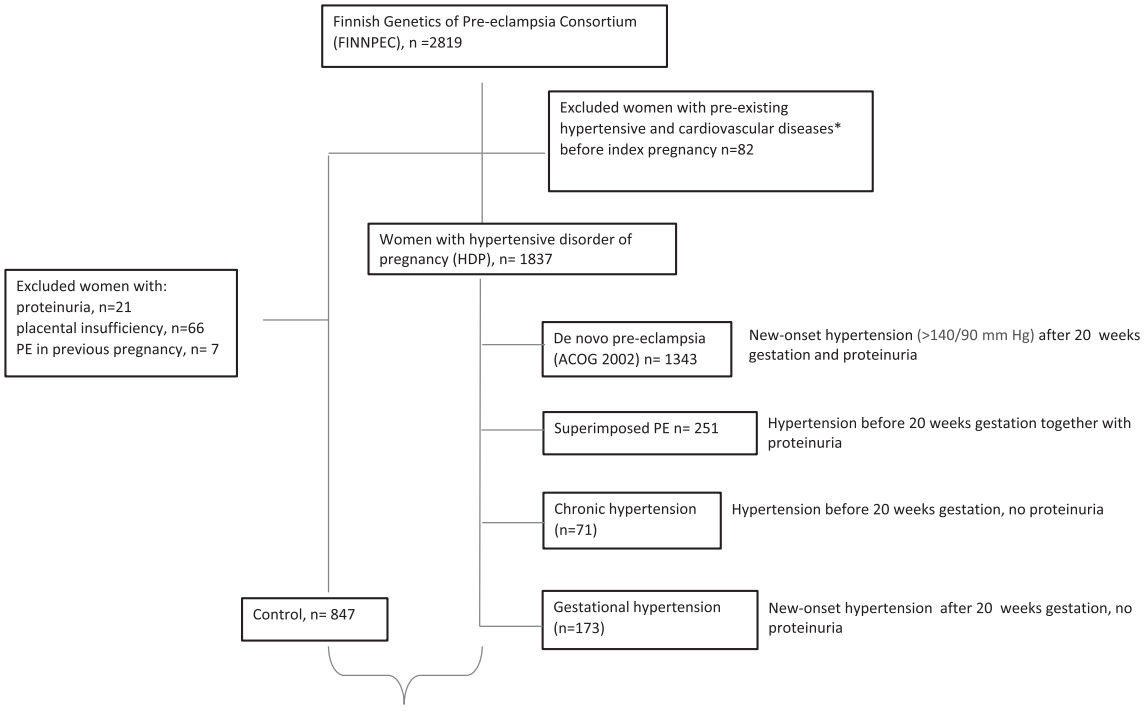
2.2. Study population and design

The FINNPEC-study.

This was a prospective cohort study. Fig. 1 illustrates the study design. The study population was the Finnish Genetics of Preeclampsia Consortium (FINNPEC) Cohort, recruited in 2008–2011 and included 2,819 women with a singleton pregnancy. There were two arms: prospective and retrospective. In the prospectively recruited arm (2008–2011) PE women (n = 923) and women without PE (n = 1,009) were identified during pregnancy on admission to any of the five university hospitals in Finland. After the recruitment of a PE woman, a woman with a non-PE pregnancy attending the same clinic was recruited as a control. The FINNPEC study cohort has been described in detail elsewhere [17]. It includes extensive information on women and their newborns.

Pre-eclampsia definition in the FINNPEC-study.

PE was defined as hypertension (systolic blood pressure $\geq$ 140 mmHg and/or diastolic blood pressure $\geq$ 90 mmHg) and proteinuria (urinary excretion of $\geq$ 0.3 g protein in a 24-hour specimen, or 0.3 g/L, or two $\geq$ 1 + readings on a dipstick in a random urine sample with no evidence of a urinary tract infection) occurring after $20^{0/7}$ weeks of gestation (gw) according to the American College of Obstetricians and Gynecologists (ACOG) 2002 criteria [15]. Each diagnosis was ascertained from hospital records and confirmed independently. PE was defined as early onset when delivery occurred before $34^{0/7}$ gw and late-onset when at $34^{0/7}$ gw or later. Preterm delivery was defined as delivery occurring before $37^{0/7}$ gw. Birth weight below − 2.0 standard deviation (SD) units were classified as small-for-gestational-age (SGA) according to Finnish standards [16]. In the retrospectively recruited arm, all women who had been diagnosed with PE or placental insufficiency during their pregnancies were identified from hospital records and invited to participate.



*The International Classification of Diseases, Tenth Revision (*ICD-10*): I10-I15, I20-I25, I46, I70-I72, I74, I60-I69, G45 (I63.6, I67.7 and G45.4 excluded) diagnosis in the Finnish Care Registry for Healthcare.

Fig. 1. Flowchart of the study design and subgroups.

2.3. Hypertensive disorders of pregnancy in the current study

Studied groups were: normotensive control (no HDP, placental insufficiency, proteinuria, or PE in a previous pregnancy), de novo PE (hypertension after 20 gw with new-onset proteinuria), superimposed PE (hypertension before 20 gw with new-onset proteinuria), chronic hypertension (CHT, hypertension before 20 gw, no proteinuria) and gestational hypertension (GHT, hypertension after 20 gw, no proteinuria) (Fig. 1). The information on CHT was obtained from the maternity cards (blood pressure $\geq$ 140/90, no proteinuria at the first antenatal visit). Gestational diabetes was diagnosed if the woman had at least one abnormal value ($\geq$5,3 mmol/l, 10,0 mmol/l and 8,7 mmol/l for fasting, one-hour and two-hour plasma glucose concentration, respectively), in a 75 g oral glucose tolerance test (OGTT).

2.4. Data sources and maternal characteristics

The clinical data of the FINNPEC participants enabled us to explore the HDPs and the underlying maternal characteristics. We linked the FINNPEC participants to their new-onset hypertensive diseases and CVD diagnoses in the Finnish Care Register for Health Care (HDR), which is a national population-based register held by the Finnish Institute for Health and Welfare. Age at delivery, pre-pregnancy body mass index (BMI), primiparity, blood pressure levels (first antenatal visit and highest-level during pregnancy), proteinuria, diabetes, gw at delivery, birthweight (SD) of baby, SGA status, early/late-onset PE, preterm delivery and PE in mother's family or in previous pregnancy were compared among women with and without new-onset CVDs or hypertensive diseases in the groups of HDPs (excluded GHT). We refer to high BMI as overweight (BMI between 25 and 29 kg/m^2) and obesity (BMI 30.0 kg/m^2 or higher).

2.5. Statistical methods

Statistical analyses were performed with IBM SPSS for Windows, version 25 (IBM Corp, Armonk, NY). Statistical significance was defined with p-value < 0.05. The normality of variable distributions was verified graphically and with the Kolmogorov-Smirnov test. The characteristics and diagnoses were presented as mean and standard deviation (SD), or absolute numbers and percentages. Differences between the groups were assessed with the Chi-square test, Welch's ANOVA and ANCOVA with covariates. We used the Kruskal-Wallis test with highly skewed distributions. We performed additional analysis to clarify pairwise differences with the Games-Howell post-hoc test.

Data were also analyzed using time-to-event methods: the Kaplan-Meier and Cox proportional hazard models, yielding hazard ratios (HR) with 95% confidence intervals were used. Time at risk was accumulated from entry into the cohort (delivery) until CVD event or censoring. The proportional hazard assumption was assessed by visual assessment of Kaplan Meier curves and performing log(−log) survival vs log(time) graphs. The Cox proportional hazard models were analyzed with unadjusted and adjusted models.

Maternal age at the time of delivery, pre-pregnancy BMI, preterm delivery, the onset of PE, primiparity, smoking status before/during pregnancy, diabetes, PE in mother's family, and PE in the previous pregnancy were considered as possible confounders. In the end, the Cox hazards models for hypertensive diseases were adjusted for maternal age at delivery, pre-pregnancy BMI, primiparity, and gestational diabetes. The Cox-models for CVDs were adjusted for maternal age at delivery, pre-pregnancy BMI, primiparity, gestational diabetes, and history of diabetes (type 1 or 2). BMI was included in the analyses as a continuous variable and defined as a person's weight in kilograms divided by the square of height in meters.

3. Results

3.1. New onset hypertensive diseases in women with de novo PE and GHT

Hypertensive disease diagnoses (ICD-10 I10-I15) given in specialized healthcare within ten years following delivery were more common in women with de novo PE and GHT compared to women without HDP (Table 1). The adjusted cumulative survival curves showed that women with de novo PE were seven to ten times more likely to receive I10-I15 diagnosis [early-onset HR 10.13 (95% CI 2.2–47.0), $p = 0.003$; late-onset HR 7.29 (95% CI 1.7–32.0), $p = 0.008$] compared to control women (Fig. 2). Within ten years after delivery, 7 % (n = 2) with and 0.3 % (n = 4) without new-onset hypertensive disease developed type 2 diabetes (not shown). The maternal and pregnancy characteristics of the women participating in the FINNCARE Study are presented in Supplemental Table S1, and pairwise comparisons in Supplemental Table S2.

3.2. Characteristics of women with de novo PE and new-onset hypertensive disease

The women with de novo PE and later hypertensive diseases were older at the time of delivery, had higher pre-pregnancy BMI, were more likely to be primiparous, and have GDM and pre-existing type 2 diabetes compared to de novo PE women without later hypertension (Table 2). They also had higher blood pressure values in pregnancy.

3.3. New onset cardiovascular diseases in women with HDP

Women with CHT and superimposed PE had a statistically increased risk for CVD [adjusted HR 2.68 (95% CI 1.03–6.96), $p = 0.043$; 4.59 (95% CI 1.37–15.40), $p = 0.014$, respectively] (Table 1, Fig. 2.) The risk was not significantly elevated in women with de novo PE and GHT [adjusted HR 1.38 (95% CI 0.62–3.08), $p = 0.432$; HR 0.49 (95% CI 0.06–3.91), $p = 0.502$, respectively]. The incidence of new-onset type 2 diabetes after pregnancy was small: 0.4 % in controls, 2.0 % with de novo PE, 5.9 % with superimposed PE, 0 % with CHT, and 1.2 % with GHT (not shown).

3.4. Characteristics of women with new-onset cardiovascular diseases

Women with superimposed PE and new-onset CVD were older at the time of delivery (35.5 $\pm$ 4.6 years vs. 32.0 $\pm$ 5.6 years, $p = 0.042$), were more likely to have early-onset PE (by diagnose time) (81.8% vs. 41.2%, $p = 0.008$), preterm delivery (90.9% vs. 50.2%), $p = 0.008$), pre-existing type 2 diabetes (18.2% vs. 1.8%) and had higher maximum systolic and lower first antenatal diastolic blood pressure (192.5 $\pm$ 22.5 mmHg vs. 178.3 $\pm$ 20.3 mmHg, $p = 0.024$ and 83.6 $\pm$ 11.4 mmHg vs. 89.4 $\pm$ 9.3 mmHg, $p = 0.047$, respectively) compared to women without new-onset CVD (Table 3). There were no statistically significant differences in maternal characteristics in women with de novo PE with and without new-onset CVDs. We also explored the maternal characteristics associated with CVD in group of CHT but there were no statistically significant differences between any of the characteristics. Because of the very small number of participants in this group, we do not present these results in more detail.

4. Discussion

Women with de novo PE had an elevated risk for hypertensive diseases within ten years following delivery. The risk of CVD was increased in women with superimposed PE and CHT only. We identified that women with de novo PE (hypertension after 20 gw) who were overweight/obese, primiparous, and with gestational diabetes had a

Table 1
Number and hazard ratios of hypertensive disorders of pregnancy (HDP) illustrating the new-onset cardiovascular and hypertensive diseases in women within ten years following delivery in the FINNPEC Study.

HDP	Number of diagnoses, n(%)	Cardiovascular diseases 10 year unadjusted HR (95 % CI)	*p*-value*	10 year Adjusted† HR (95% CI)	*p*-value*	Number of diagnoses, n(%)	Hypertensive diseases 10 year unadjusted HR (95 % CI)	*p*-value*	10 year Adjusted†† HR (95% CI)	*p*-value*
No HDP (n = 843)	9 (1.1)	Ref		Ref		2 (0.2)	Ref		Ref	
De novo pre-eclampsia (n = 1326)	21 (1.5)	1.45 (0.67–3.17)	0.350	1.38 (0.62–3.08)	0.432	29 (2.1)	Early: 12.60 (2.79–56.84) Late: 7.67 (1.78–33.08)	**$p = 0.001$** **$p = 0.006$**	Early: 10.13 (2.19–47.0) Late: 7.29 (1.66–31.95)	**$p = 0.003$** **$p = 0.008$**
Superimposed pre-eclampsia (n = 289)	11 (3.8)	3.60 (1.49–8.66)	**0.004**	2.68 (1.03–6.96)	**0.043**	**NA**				
CHT (n = 74)	4 (5.3)	5.08 (1.56–16.49)	**0.007**	4.59 (1.37–15.40)	**0.014**	**NA**				
GHT (n = 168)	1 (0.6)	0.54 (0.07–4.27)	0.560	0.49 (0.06– 3.91)	0.502	8 (4.6)	not performed		not performed	

Bold text shows p-values < 0.05.
* unadjusted
†Adjusted for maternal age at delivery, pre-pregnancy BMI, primiparity, gestational diabetes and history of diabetes (type 1 or 2).
†† Adjusted for maternal age at delivery, pre-pregnancy BMI, primiparity, and gestational diabetes.
CI, confidence interval; HR, hazard ratio; Ref, reference; FINNPEC, Finnish Genetics of Pre-eclampsia Consortium; CHT, chronic hypertension; GHT, gestational hypertension.
NA= pre-existing hypertension

particularly high risk for hypertensive diseases. Of the women with CHT (hypertension before 20 gw), particularly those with early diagnosed superimposed PE leading to preterm delivery had increased risk of CVDs. These groups should receive the most intensive postpartum cardiovascular risk assessment and tailored counseling for cardiovascular disease prevention.

Our results are in line with previous studies reporting that women with de novo PE and GHT have higher risk for hypertension after delivery [6,8,18,19]. In our study, women with de novo PE who developed later hypertensive disease had PE in their first pregnancy more often compared to those who remained normotensive. According to a longitudinal follow-up study, non-recurrent PE was associated with elevated CVD and hypertension risk but not as much as recurrent PE [20]. Interestingly, the risk was close to or higher with some CVD endpoints for women with PE and one delivery compared to women with recurrent PE [20]. Future pregnancies might have affected the risk for hypertensive diseases in our study population. Furthermore, many women have high blood pressure without them knowing it. In addition, a registry study concluded that the risk of death due to CVD was higher in women with PE in their first pregnancy, particularly in one-child mothers, compared to those who had PE in later pregnancies [21]. Primiparous PE pregnancy could be a potential signal of the need for special attention in primary care.

The overall prevalence of GDM in women with de novo PE was close to the average among women in Northern Europe [22], but it was higher in women with subsequent hypertensive diseases compared to women who remained normotensive. This could be explained by the higher pre-pregnancy BMI in women with subsequent hypertensive disease because obesity is an important risk factor for GDM and HDP [23]. GDM strongly predicts future type 2 diabetes [24] but is also associated with an increased risk for hypertension [25]. Furthermore, the combined effect of GDM and PE on the development of post-partum hypertension is high [26], as in our study. Our finding is further supported by a recent case-control study of Swedish female population which concluded that having both PE and GDM is a major risk factor for future CVD, regardless of BMI [27]. Considering that both GDM and PE are common pregnancy-related conditions, special attention should be targeted to blood pressure management and CVD prevention in this group.

In contrast to several studies that show an increased risk of CVDs approximately three to fourfold higher in PE women [9,28–30] we did not find a significantly increased risk of CVD other than later hypertensive diseases in women with de novo PE or GHT within ten years following delivery. The shorter follow-up time and young maternal age in our study likely explain contradictory results. Also, different kind of criteria for PE might also explain the differences in CVD risk. For example, in one study [28] PE and superimposed PE were grouped together and the definition for superimposed PE was broader compared to FINNPEC. Nevertheless, a recent registry-based study demonstrated that Finnish women with a history of PE have a same-fold CVD risk as those reported from other countries [31]. They utilized the same HDR registry as used in our study, but they had a mean follow-up of 33.4 years and a sample size of 120 000 women. Our study supports the hypothesis that the risk for hypertension is present within the first ten years after PE pregnancy, possibly mediating the future CVD risk. Thus, it would be of interest to re-analyze CVDs in FINNPEC cohort in the future as well.

The incidence of new-onset CVD was small, and the risk was significantly increased only in women with superimposed PE and CHT. Previously women with superimposed PE have been reported to have a higher risk for CVD than women with CHT [32,33] but in our study, women with CHT had the highest risk for future CVD. One possible explanation could be that in the current study, more women with superimposed PE were treated with medication for hypertension before 20 gw: their blood pressure is managed and followed better leading to fewer CVD events. Also, women with CHT might have been exposed to elevated blood pressure longer than women with superimposed PE,

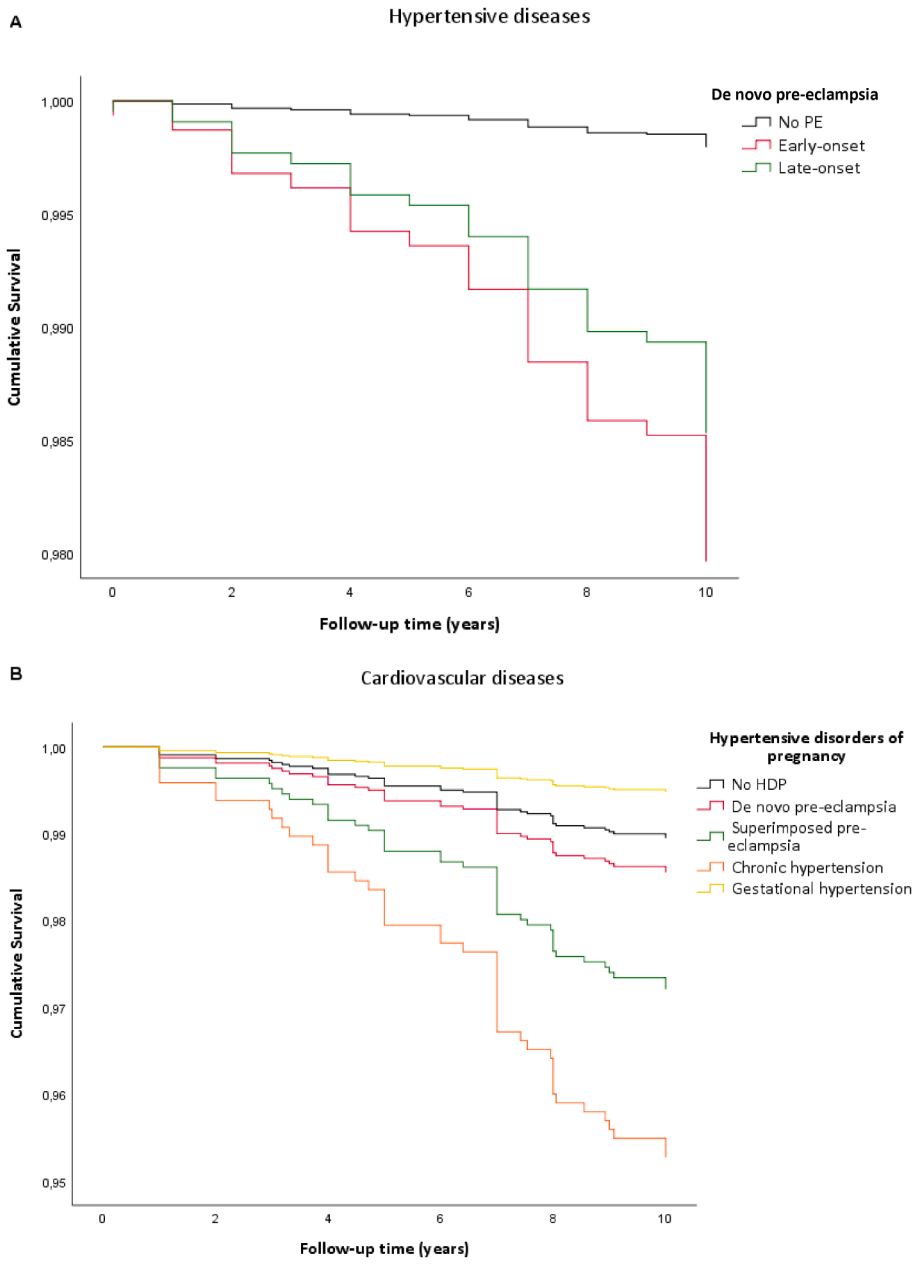


Fig. 2. Cumulative survival curves of hypertensive diseases in women with de novo pre-eclampsia (late/early-onset) (A), and cardiovascular diseases in women with hypertensive disorders of pregnancy (B) within ten years following delivery. A: Adjusted for maternal age at delivery, pre-pregnancy BMI, primiparity, and gestational diabetes. B: adjusted maternal age at delivery, pre-pregnancy BMI, primiparity, gestational diabetes, and history of diabetes before pregnancy (type 1 or 2).

possibly causing more endothelial harm, an essential element of both PE and CVD [34]. Since most women with CHT and superimposed PE did not have medication for hypertension and none had ICD10 I0-I15 or other CVD diagnoses before pregnancy, elevated blood pressure was most likely detected first time in early pregnancy in this relatively young group of women. This highlights the importance of antenatal blood pressure measurements. We were not able to determine the onset of hypertension before pregnancy.

Women with superimposed PE and subsequent CVD had more often early-onset PE and preterm delivery than women with superimposed PE without CVD. This agrees with previous data showing that both early-onset PE [12] and preterm delivery [35] are associated with increased CVD risk. Most of the women with superimposed PE and CHT were overweight or obese already before pregnancy suggesting that a high pre-pregnancy BMI was a contributing factor to the increased risk of developing CVD in these women.

5. Strengths

A major strength of this study is its detailed clinical data from hospital records combined with data from HDR. We were also able to include women with chronic hypertension, the group of women that previous studies have often overlooked [13,29,36–38]. Furthermore, the HDR registry has good validity with ICD-10 codes concerning CVDs [39]. Both the occurrence of PE and CVD varies between geographical regions in Finland [40,41] and the FINNPEC recruitment covers several of these.

6. Limitations

The main limitation is the different group sizes of HDPs. The FINNPEC protocol was focused on PE and non-PE women, consequently, women with GHT and CHT were not recruited separately, and the

Table 2
Maternal and pregnancy characteristics of women with de novo PE with or without a new-onset hypertensive disease within ten years following delivery in the FINNPEC Study.

Characteristics	New-onset hypertensive disease (ICD10 I10-I15) No (n = 1328)	Yes (n = 29)	*p*-value*	adjusted p-value**
Age at delivery, year	29.7 ± 5.4	32.7 ± 4.7	**0.003**	
BMI, kg/m2§	24.6 ± 4.8	28.7 ± 5.8	**0.001**	
Primiparous	305 (23.0)	12 (41.4)	**0.020**	
SBP at first antenatal visit, mm Hg	121.3 ± 10.3	127.4 ± 7.9	**0.002**	**0.025**
DBP at first antenatal visit, mm Hg	75.2 ± 8.2	80.6 ± 6.7	**0.001**	**0.018**
Highest SBP, mm Hg	164.1 ± 17.5	174.3 ± 16.6	**0.002**	**0.002**
Highest DBP, mm Hg	108.3 ± 8.5	111.9 ± 6.7	**0.020**	**0.040**
Proteinuria (maximum), g/24 h, med(IQR)	3.1 (4.8)	2.3 (4.0)	0.318	
Gestational diabetes mellitus	155 (11.7)	9 (31.0)	**0.002**	
Type 2 diabetes, pre-pregnancy	4 (0.3)	1 (3.4)	**0.006**	
Early onset pre-eclampsia (gestational week < 34 + 0)				
Diagnosis	359 (27.1)	11 (37.9)	0.193	
Delivery	225 (17.1)	5 (17.2)	0.981	
Premature delivery (<37^{+0})	473 (35.6)	11 (37.9)	0.797	
PE in mother's family#	106 (8.0)	4 (13.8)	0.257	
PE in previous pregnancy	107 (8.1)	3 (10.3)	0.655	
Gestational weeks at delivery	36.6 ± 3.4	36.5 ± 3.7	0.863	
Relative birth weight (SD)	−1.0 ± 1.3	−1.1 ± 1.3	0.750	

Bold text shows p-values < 0.05. Frequencies: n (%), continuous data: mean ± standard deviation, unless stated otherwise. * Unadjusted, ** Adjusted with BMI.
§ Based on weight and height before pregnancy, self-reported at first antenatal visit.
# Self-reported in questionnaire.
FINNPEC, Finnish Genetics of Pre-eclampsia Consortium; BMI, body mass index; SBP, systolic blood pressure: DBP, diastolic blood pressure; med, median; IQR, interquartile range.

number of these women remained small. In addition, our study might have minor misclassification because the diagnostic criteria for PE changed in 2014 [42]. Our study probably underestimates the incidence of hypertension because it often remains undiagnosed. In addition, data from primary and occupational healthcare is not included in the HDR register. The true prevalence of hypertension is probably high. The participants represented women with PE who were referred to university hospitals and thus may represent a more severe end of the disease.

6.1. Implications to the prevention of CVD

Clinicians in obstetrics, general practitioners, and other healthcare personnel working with women have a responsibility to comprehend the diverse nature of hypertensive disorders of pregnancy and how they have far-reaching implications for a woman's future health. Comprehensive education should encompass recognizing risk factors, identifying early signs, and understanding the implications of different subtypes of HDP. This knowledge equips healthcare providers to offer more targeted care and interventions. Adapting global guidelines, like the best practice advice presented by FIGO [43], to local contexts

Table 3
Maternal and pregnancy characteristics of women with de novo PE and superimposed PE with or without new-onset cardiovascular diseases within ten years following delivery in the FINNPEC Study.

Characteristics	De novo PE Cardiovascular diseases No (n = 1336)	Yes (n = 21)	*p*-value*	Superimposed PE No (n = 279)	Yes (n = 11)	*p*-value*
Age at delivery, year	29.8 ± 5.4	31.1 ± 6.3	0.280	32.0 ± 5.6	35.5 ± 4.7	**0.042**
BMI, kg/m2§	24.6.2 ± 4.8	25.8 ± 7.0	0.261	27.9 ± 6.1, n = 278	28.3 ± 4.7	0.864
Primiparous	1023 (76.6)	14 (66.7)	0.302	181 (64.9)	7 (63.6)	1.000
SBP at first antenatal visit, mm Hg	121.4 ± 10.3 (n = 1284)	123.3 ± 13.1 (n = 1)	0.432	139.7 ± 14.0, n = 267	143.2 ± 17.1	0.417
DBP at first antenatal visit, mm Hg	75.3 ± 8.2, n = 1283	76.0 ± 8.4, n = 20	0.736	89.4 ± 9.3, n = 267	83.6 ± 11.4	**0.047**
Highest SBP, mm Hg	164.3 ± 17.6, n = 1335	165.3 ± 13.2, n = 21	0.796	178.3 ± 20.3, n = 279	192.5 ± 22.5	**0.024**
Highest DBP, mm Hg	108.3 ± 8.5	108.7 ± 9.7	0.860	117.2 ± 10.0, n = 279	114.0 ± 8.9	0.304
Proteinuria (maximum), g/24 h, med(IQR)	3.0(4.8), n = 1164	3.6(3.0), n = 19	0.641	3.0(4.7), n = 248	4.6(7.7), n = 10	0.147
Gestational diabetes mellitus	165 (12.4)	1 (4.8)	0.501	58 (20.8)	2 (18.2)	1.000
Type 2 diabetes, pre-pregnancy	5 (0.4)	0 (0.0)	1.000	5 (1.8)	2 (18.2)	**0.025**
Early onset pre-eclampsia (gestational week < 34 + 0)						
Diagnosis	367 (27.5)	5 (23.8)	0.708	115(41.2)	9 (81.8)	**0.008**
Delivery	231 (17.4)	3 (15.0)	1.000	77 (27.8), n = 277	5 (45.5)	0.304
Premature delivery (<37^{+0})	479 (35.9)	9 (42.9)	0.507	140 (50.2)	10 (90.9)	**0.008**
PE in mother's family#	107 (8.0%)	2 (9.5)	0.683	35 (12.5)	2 (18.2)	0.637
PE in previous pregnancy	111 (8.3)	2 (9.5)	0.692	44 (15.8)	2 (18.2)	0.830
Gestational weeks at delivery	36.5 ± 3.4	36.2 (3.1)	0.681	35 ± 4.2	33.6 (2.2)	**0.043**
Relative birth weight (SD)	−1.0 ± 1.3	−1.2 ± 1.2	0.493	−1.2 ± 1.3	−1.2 ± 1.3	0.902

Bold text shows p-values < 0.05. Frequencies: n (%), continuous data: mean ± standard deviation, unless stated otherwise. *Unadjusted.
§ Based on weight and height before pregnancy, self-reported at first antenatal visit.
# Self-reported in questionnaire.
FINNPEC, Finnish Genetics of Pre-eclampsia Consortium; BMI, body mass index; SBP, systolic blood pressure: DBP, diastolic blood pressure; med, median; IQR, interquartile range.

healthcare providers can contribute to reducing the CVD mortality of the female population globally.

7. Conclusions

In the current FINNPEC study, we analyzed the combination of pregnancy/maternal characteristics associated with hypertensive diseases and other CVDs within ten years following delivery after HDP pregnancy. Based on the results, the women with prior HDP should not be regarded as a homogenous group when assessing the risk for hypertension and other CVDs later in life. Women with de novo PE who are overweight/obese, primiparous, and have GDM are an important risk group for CVD; they enter pregnancy with normal blood pressure but have a high risk of developing hypertensive diseases in the years following delivery. Women with hypertension before 20 gw, particularly those accompanied with PE diagnosed before 34 gw leading to preterm delivery need early and individually tailored CVD prevention because of high risk of CVDs within the early postpartum years.

Participant *meta*-analysis of studies with extensive clinical data of women with HDPs would broaden the understanding of the specific risk groups. Moreover, there is an urgent need for randomized, controlled trials that evaluate the effectiveness of a behavioral lifestyle intervention to reduce the risk of hypertension and CVD in women with HDPs.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Contribution to authorship

Design: AK, TJ, SH, HL, KK, JK, EK were involved in design. AK performed the literature search, performed the statistical analyses, and wrote the first and later versions of the manuscript. All authors contributed to the interpretation of the results and read and commented the final version before submission.

Details of ethical approval

All subjects provided written informed consent and the FINNPEC study protocol was approved by the coordinating Ethics Committee of the Hospital District of Helsinki and Uusimaa (permit number 149/E0/07).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.preghy.2023.09.001.

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