Received: 18 November 2020 | Revised: 2 February 2021 | Accepted: 16 February 2021

DOI: 10.1111/aogs.14132

AOGS Acta Obstetricia et Gynecologica Scandinavica

ORIGINAL RESEARCH ARTICLE

Chronic hypertension in pregnancy stratified by first-trimester blood pressure control and adverse perinatal outcomes: A prospective observational study

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Abstract

Introduction: The aim of this study was to assess perinatal outcomes in women with chronic hypertension (CH) stratified into four groups according to their blood pressure (BP) control in the first trimester of pregnancy.

Material and methods: This was a prospective cohort study between January 2011 and June 2017, based in a university hospital in London, UK. The population consisted of four groups: group 1 included women without history of CH, presenting in the first trimester with BP >140/90 mmHg (n = 100). Groups 2-4 had prepregnancy CH; group 2 had BP <140/90 mmHg without antihypertensives (n = 234), group 3 had BP <140/90 mmHg with antihypertensives (n = 272), and group 4 had BP ≥140/90 mmHg despite antihypertensives (n = 194). The main outcome measures were: fetal growth restriction, admission to neonatal (NNU) or neonatal intensive care unit (NICU) for ≥2 days, composite neonatal morbidity, and composite serious adverse neonatal outcome. Outcomes were collected from the hospital databases and for up to 6 weeks postnatally. Differences between groups were assessed using chi-squared test and multivariate logistic regression was used to assess the independent contribution of the four groups to the prediction of pertinent outcomes, after controlling for maternal characteristics.

Results: There was a higher incidence of fetal growth restriction in groups 3 (17.6%) and 4 (18.2%), compared with groups 1 (10.0%) and 2 (11.1%) (P = .04). There were more admissions to the NNU for ≥2 days in groups 3 (23.2%) and 4 (25.0%), compared with groups 1 (17.0%) and 2 (13.2%) (P = .008); and more admissions to NICU for ≥2 days in groups 3 (9.2%) and 4 (9.4%), compared with groups 1 (3.0%) and 2 (3.4%) (P = .01). Composite neonatal morbidity was higher in groups 3 (22.4%) and 4 (21.4%), compared with groups 1 (17.0%) and 2 (11.5%) (P = .009). Composite serious adverse postnatal outcome was higher in groups 3 (3.3%) and 4 (4.2%), compared with groups 1 (1.0%) and 2 (0.9%) but the difference did not reach statistical significance (P = .09). These results were also observed when values were adjusted for maternal characteristics.

Conclusions: In CH adverse perinatal outcomes are worse in women who are known to have CH and need antihypertensives in the first trimester of pregnancy. Women

Abbreviations: BP, blood pressure; CH, chronic hypertension; FGR, fetal growth restriction; NICU, neonatal intensive care unit; NNU, neonatal unit; PE, preeclampsia.

with newly diagnosed CH in the first trimester have similar outcomes to those with known CH who have antihypertensive treatment discontinued.

KEYWORDS
chronic hypertension, intensive care unit, neonatal mortality, neonatal outcomes, neonatal unit, perinatal morbidity, placental abruption, pregnancy, stillbirth, stratification

1 | INTRODUCTION

Chronic hypertension (CH) complicates 1%-5% of pregnancies[1] and, compared with the general obstetrical population, it is associated with higher rates of adverse maternal and perinatal outcomes.[1,2] However, the reported rates of such adverse outcomes vary widely between studies, probably because CH was considered as a single entity and there was wide heterogeneity in study populations and definitions of outcome measures.[2]

We have previously proposed that women with CH should be stratified according to their blood pressure (BP) control and need for antihypertensive medications in the first trimester of pregnancy into the following four groups: those who were first diagnosed as being hypertensive at this visit (group 1), those known to have CH but found to have normal BP <140/90 mmHg without the need for antihypertensive medication (group 2), those known to have CH but in need of medication to remain normotensive (group 3), and those known to have CH who despite medication were hypertensive and we had to increase their medication (group 4). We reported that the rates of development of severe hypertension and superimposed preeclampsia (PE) and birth of small-for-gestational-age neonates were substantially lower in women who adapted well in the first trimester and reduced their BP obviating the need for antihypertensive treatment than in women who remained hypertensive despite treatment.[3,4]

The objective of this study is to assess perinatal outcomes in women with CH stratified into these four groups. All women were followed up prospectively in a dedicated clinic for the management of hypertension in pregnancy with a unified management protocol and standardized reporting criteria.

Key message

Chronic hypertension in pregnancy: adverse perinatal outcomes are worse in those who are known to have chronic hypertension and need antihypertensives in the first trimester of pregnancy.

2 | MATERIAL AND METHODS

2.1 | Study population

This was a prospective study conducted in the Antenatal Hypertension Clinic at King's College Hospital, London between January 2011 and June 2017. According to local protocols, pregnant women with hypertension, preexisting or newly identified at the booking visit, are referred to this dedicated clinic for the management of their pregnancy. Women were followed up until delivery at 4-week intervals and maternal, labor, and neonatal outcomes were collected prospectively from the hospital databases and for up to 6 weeks postnatally. Hypertension was defined as two consecutive BP measurements of ≥140/90 mmHg 4 hours apart and CH was defined as hypertension predating pregnancy requiring antihypertensive medication either currently or previously, or hypertension diagnosed at <20 weeks of gestation during the current pregnancy.[5] Optimal control with antihypertensive therapy was considered to be a target BP of <140/90 mmHg.[5]

The inclusion criteria for this study were singleton pregnancies with either prepregnancy CH or newly diagnosed CH before 20 weeks of gestation in the absence of renal or liver disease, resulting in the live birth or stillbirth of non-malformed, euploid babies at ≥24 weeks of gestation. Maternal data recorded routinely at booking included age, height, weight, body mass index, racial origin, parity, and history of diabetes mellitus. Pregnancy dating was based on fetal crown-rump length measured by ultrasound at 11-13 weeks of gestation and BP was measured by an automated device, validated for use in pregnancy.[6]

2.2 | Outcome measures

The definitions of maternal and neonatal outcomes are presented in Table 1.

The main outcome measures were: fetal growth restriction (FGR), admission to neonatal unit (NNU) or neonatal intensive care unit (NICU) for ≥2 days, composite of neonatal morbidity, and composite of serious adverse postnatal outcome.

In addition, we examined the following outcome measures as surrogate markers of disease severity: severe hypertension, superimposed PE, preterm birth, delivery by cesarean section, placental abruption, and perinatal death.

TABLE 1 Definitions of neonatal and pregnancy outcomes of women with chronic hypertension collected between January 2011 and June 2017, in a University hospital in London, UK

Outcome	Definition
Fetal growth restriction	Birthweight <3rd centile or birthweight between the 3rd and 10th centiles with abnormal Doppler waveforms (umbilical artery pulsatility index >95th centile, middle cerebral artery pulsatility index or cerebroplacental ratio <5th centile) and/or oligohydramnios (deepest vertical pocket <2 cm)[21,22]
Composite of neonatal morbidity	Defined by presence of any one of the following: • need for ventilation (continuous positive airway pressure or nasal continuous positive airway pressure or intubation), • use of total parenteral nutrition, • respiratory distress syndrome (need for surfactant and ventilation)[23] • jaundice (bilirubin cut-offs defined according to postnatal age),[24] and • hypoglycemia (blood glucose level <2.6 mmol/L).[25]
Composite of serious adverse postnatal outcome	Defined by the presence of any one of the following: • hypoxic ischemic encephalopathy (disturbed neurologic function with evidence of perinatal hypoxia reflected in either a 5-minute Apgar score <5 or umbilical artery cord pH <7.0 or base deficit >12 mmol/L, supported by neuroimaging evidence of acute brain injury),[26] • intraventricular hemorrhage grade >2,[27] • periventricular leukomalacia, • chronic lung disease (oxygen need at 36 weeks postmenstrual gestational age),[28] retinopathy of prematurity,[29] • necrotizing enterocolitis requiring surgical intervention,[30] and • hypotension (2.5th centile according to postnatal age).[31,32]
Severe hypertension	Systolic BP ≥160 mmHg and / or diastolic BP ≥110 mmHg[5]
Superimposed PE	As defined by the ISSHP–2018 guidelines as new-onset hypertension arising after 20 weeks of pregnancy (systolic BP ≥140 mmHg and/or diastolic BP ≥90 mmHg) with evidence of end-organ damage[5]
Preterm birth	Spontaneous or iatrogenic delivery at <37 weeks of gestation
Placental abruption	Presence of vaginal bleeding accompanied by persistent severe abdominal pain, uterine tenderness or tetanic contractions
Perinatal death	Stillbirth with delivery of a fetus that does not show any evidence of life such as breathing, beating of the heart, pulsation of the umbilical cord or definite movement of voluntary muscles at >22 weeks of gestation or death of a neonate up to 28 days after delivery

Abbreviations: BP, blood pressure; ISSHP, International Society for the Study of Hypertension in Pregnancy.

2.3 | Statistical analyses

Normality of distribution of numerical variables was assessed by the Kolmogorov-Smirnov test. Numerical data are expressed as mean (standard deviation) or median (interquartile range) for normally and non-normally distributed data, respectively. Differences in maternal booking characteristics and pregnancy outcomes were compared between the four subgroups of women with CH with the analysis of variance or Kruskal-Wallis tests (for numerical parametric or nonparametric data) with significance values adjusted for the number of comparisons with the Bonferroni post hoc test. The chi-squared test was used for the comparison of categorical variables.

Multivariate logistic regression analysis was performed to assess the independent contribution of the groups of women with CH on the prediction of pertinent maternal and neonatal outcomes, after controlling for maternal demographic characteristics.

Statistical analysis was performed using SPSS version 22 (SPSS Inc.).

2.4 | Ethics approval

The study is registered as an Audit (Registration number OA 1707, date of approval 16 November 2018). As the data collected are part of our routine clinical management, the local Research and Development Committee (King's College Hospital NHS Foundation Trust) and Research Ethics Committee (London-Dulwich, NRES Committee) advised that formal consideration was not required.

3 | RESULTS

3.1 | Population characteristics

The entry criteria were fulfilled by 798 women, including 100, 234, 272, and 192 in groups 1, 2, 3, and 4, respectively. The characteristics of the four groups are compared in Table 2. The overall population tended to be older, more likely to be obese and of black racial origin, and less likely to be nulliparous, compared with the average local pregnant population.[1] There were no statistically significant differences between the four groups in the gestational age of booking, family history of PE, and the presence of preexisting diabetes. Women in groups 3 and 4, compared with group 2, were older, heavier, less likely to be nulliparous and more likely to have had a previous history of PE or to be of black racial origin. The systolic and diastolic BPs were significantly higher in women who were hypertensive at booking (groups 1 and 4), compared with women in groups 2 and 3.

3.2 | Pregnancy and neonatal outcomes

Pregnancy outcomes in the four groups of CH are compared in Tables 3 and 4 and in the Supporting Information S1, and are illustrated in Figure 1.

The overall rate of delivering a baby with features of FGR was 14.9%, and there was a higher incidence of FGR in groups 3 (17.6%) and 4 (18.2%), compared with groups 1 (10.0%) and 2 (11.1%) (P = .04) (Table 3).

Overall, 20% of babies needed admission to the NNU for 2 days or more, of which about one-third needed admission to NICU (6.8%) (Table 3, Figure 1). There were more admissions to the NNU for ≥2 days in groups 3 (23.2%) and 4 (25.0%), compared with groups 1 (17.0%) and 2 (13.2%) (P = .008) (Table 3; Figure 1). Similarly, there were more admissions to NICU for ≥2 days in groups 3 (9.2%) and 4 (9.4%), compared with groups 1 (3.0%) and 2 (3.4%) (P = .01) (Table 3, Figure 1). The main indications for admission were prematurity (51%), hypoglycemia (19.5%), sepsis (10.4%), perinatal hypoxia (10.4%), birthweight <1.8 kg (9.8%), and jaundice (3%) (see Supplementary material, Table S1).

The overall rate of composite neonatal morbidity was 18.3% and the incidence was higher in groups 3 (22.4%) and 4 (21.4%), compared with groups 1 (17.0%) and 2 (11.5%) (P = .009, Table 3). A detailed analysis of composite neonatal morbidity is presented in the Supplementary material (Table S1).

The overall rate of severe adverse outcome was 2.5%. The incidence was higher in groups 3 (3.3%) and 4 (4.2%), compared with groups 1 (1.0%) and 2 (0.9%), but the difference did not reach statistical significance (P = .09), Table 3). A detailed analysis of severe adverse outcome is presented in the Supplementary material (Table S1).

The overall rates of severe hypertension, superimposed preeclampsia, and preterm birth, and the rate of delivering by cesarean section were 26%, 33%, 16%, and 46.9%, respectively, and the rates were significantly higher in groups 3 and 4 compared with groups 1 and 2 (Table 3; Figure 1).

In the whole cohort, there were 12 (1.5%) perinatal deaths and 12 cases complicated by placental abruption (1.5%). As a result of the small number of cases, the differences between groups were not

TABLE 2 Characteristics of the study population

Characteristic	Group 1 (n = 100)	Group 2 (n = 234)	Group 3 (n = 272)	Group 4 (n = 192)	*P* value
Age (years)	34.3 (4.9)	34.0 (5.6)	35.1 (4.8) **	35.2 (5.5) **	.002
Body mass index (kg/m^2)	30.5 (26.2-36.1)	29.4 (25.2-34.1)	31.2 (26.4-35.7) **	33.0 (28.5-37.6) ***	<.0001
Booking gestational age (weeks)	10.9 (9.7-13.4)	10.3 (9.4-12.0)	10.1 (9.3-12.1)	10.5 (9.1-12.3)	.052
Systolic blood pressure (mmHg)	140 (132-148) *** †††	122 (118-130)	125 (120-130)	142 (135-152) *** †††	<.0001
Diastolic blood pressure (mmHg)	90 (80-91) *** †††	78 (70-81)	80 (72-82)	90 (80-96) *** †††	<.0001
Nulliparous, n (%)	36 (36.0) ††	102 (43.6)	57 (21.0) ***	56 (29.2) ** †	<.0001
Family history of PE, n (%)	16 (16.0)	29 (12.4)	31 (11.4)	26 (13.5)	.674
Previous history of PE, n (%)	35 (35.0) †	58 (24.8)	131 (48.2) ***	79 (41.4) ***	.001
Racial origin					
White, n (%)	38 (38.0) †† $	89 (38.0)	60 (22.1) ***	48 (25.0) **	<.0001
Black, n (%)	55 (55.0) † $	121 (51.7)	186 (68.4) ***	132 (68.8) ***	<.0001
South-East Asian, n (%)	2 (2.0)	9 (3.8)	14 (5.1)	1 (0.5) * ††	.031
Mixed, n (%)	5 (5.0)	14 (6.0)	12 (4.4)	11 (5.7)	.852
Diabetes mellitus, n (%)	3 (3.0)	10 (4.3)	19 (7.0)	7 (3.6)	.424

Data presented for 798 women with CH, collected between January 2011 and June 2017, in a university hospital in London, UK. The table provides the overall *P* values of the analysis of variance, Kruskal-Wallis tests, or chi-squared tests. The between group comparisons are indicated within individual cells.

Abbreviation: PE, preeclampsia.

Group 1: new onset, Group 2: not treated and controlled, Group 3: treated and controlled, Group 4: treated not controlled.

Statistical significance when compared with: Group 2: * <.05, ** <.01, *** <.001; Group 3: † <.05, †† <.01, ††† <.001; Group 4: $ <.05, $$ <.01, $$$ <.001.

TABLE 3 Pregnancy outcomes in women with chronic hypertension, collected between January 2011 and June 2017, in a university hospital in London, and stratified according to blood pressure control at first hospital visit

Outcome measure	Total (n = 798)	Group 1 (n = 100)	Group 2 (n = 234)	Group 3 (n = 272)	Group 4 (n = 192)	*P* value
Perinatal outcomes						
Gestational age at delivery (weeks)	38.9 (37.7-39.9)	39.0 (38.0-40.0) † $	39.2 (38.1-40.0)	38.7 (37.4-39.6) ***	38.7 (37.0-39.6) **	<.0001
Perinatal death, n (%)	12 (1.5)	0 (0)	3 (1.3)	6 (2.2)	3 (1.6)	.472
Birthweight centile	36.0 (10.7-64.1)	41.6 (19.5-71.0) $	40.2 (15.3-66.7)	33.3 (7.8-82.8)	28.4 (8.5-58.9) *	.004
Fetal growth restriction, n (%)	119 (14.9)	10 (10.0)	26 (11.1)	48 (17.6) *	35 (18.2) *	.041
Delivery before 37 weeks, n (%)	129 (16.2)	15 (15.0)	21 (9)	48 (17.6) *	45 (23.4) ***	.001
Admission to NNU for ≥2 days, n (%)	159 (19.9)	17 (17)	31 (13.2)	63 (23.2) **	48 (25) **	.008
Admission to NICU for ≥2 days, n (%)	54 (6.8)	3 (3) † $	8 (3.4)	25 (9.2)	18 (9.4) **	.010
Composite of neonatal morbidity	146 (18.3)	17 (17)	27 (11.5)	61 (22.4) *	41 (21.4) *	.009
Composite severe adverse outcome	20 (2.5)	1 (1.0)	2 (0.9)	9 (3.3)	8 (4.2)	.091
Maternal and pregnancy outcomes						
Severe hypertension, n (%)	212 (26.6)	16 (16) $$$	26 (11.1)	68 y *** $$$	102 (53.1)***	<.0001
Superimposed preeclampsia, n (%)	267 (33.5)	27 (27.0) $ †	54 (23.1)	105 (38.6) ***	81 (42.2) ***	<.0001
Placental abruption, n (%)	12 (1.5)	0 (0.0)	4 (1.7)	6 (2.2)	2 (1.0)	.433
Delivery by cesarean section, n (%)	374 (46.9)	38 (38.0) $ ††	85 (36.3)	152 (55.9) ***	99 (51.6) **	<.0001

Group 1: new onset, Group 2: not treated and controlled, Group 3: treated and controlled, Group 4: treated not controlled.

Overall *P* value of the chi-squared test is provided in the last column of the table and post hoc between group comparisons were as follows: statistical significance when compared with: Group 2: * <.05, ** <.01, *** <.001; Group 3: † <.05, †† <.01, ††† <.001; Group 4: $ <.05, $$ <.01, $$$ <.001.

significant. The perinatal deaths included 10 stillbirths and two neonatal deaths. The presumed cause of death in the stillbirths was placental insufficiency in seven cases and placental abruption in three. Apart from one placental abruption, all cases were preterm, and half occurred before 32 weeks of gestation. Three of them were lethal.

3.3 | Multivariate logistic regression analysis

Multivariate logistic regression analysis demonstrated that the stratification of the four CH groups was an independent predictor for FGR, composite neonatal morbidity, maternal severe hypertension, superimposed PE, delivery before 37 weeks of gestation, and delivery by cesarean section after controlling for maternal age, body mass index, nulliparity, history of previous PE, and racial origin (Table 4).

4 | DISCUSSION

The results of this study confirm that pregnancies of women with CH have high rates of adverse perinatal outcomes, with perinatal death, FGR, admission to NNU and NICU and composite neonatal morbidity and composite adverse outcome complicating 1.5%, 14.9%, 19.9%, 6.8%, 18.3%, and 2.5% of pregnancies, respectively. However, these outcomes are disproportionally distributed according to the BP control at the first-trimester booking visit. Women with known CH who are on antihypertensive medication in the first trimester of pregnancy have higher rates of all adverse outcomes including FGR, admission to NNU and NICU, and composite neonatal morbidity. Furthermore, women who are newly diagnosed with CH in the first trimester have high rates of adverse perinatal outcomes, approximating those of women with known CH who remain normotensive without the need for treatment.

A novel finding of our study is that, similar to the maternal adverse outcomes, perinatal outcomes are dissimilar between the four groups of women with CH, reflecting the higher rates of severe disease and the need for preterm delivery in groups 3 and 4. It is likely that four subgroups of women with CH represent distinct profiles at different stages of their cardiovascular disease. In nonpregnant women, the progression from normotension to mild and then severe hypertension is initially characterized by a hyperdynamic circulation, leading to increased sheer stress and impairment of the

TABLE 4 Results of the multivariate regression analysis for the pertinent maternal and neonatal outcomes, controlling for significant maternal demographic characteristics

	Severe hypertension	Superimposed PE	Fetal growth restriction	Delivery <37 weeks	Cesarean section	Composite morbidity
Variable	Odds ratio (95% CI)	Odds ratio (95% CI)	Odds ratio (95% CI)	Odds ratio (95% CI)	Odds ratio (95% CI)	Odds ratio (95% CI)
Age	1.03 (0.99-1.06)	1.00 (0.98-1.04)	0.98 (0.94-1.01)	0.99 (0.95-1.03)	1.05 (1.02-1.08)***	1.01 (0.98-1.05)
BMI	1.02 (0.99-1.05)	0.99 (0.97-1.01)	0.98 (0.95-1.00)	1.00 (0.98-1.03)	1.03 (1.01-1.05)**	1.03 (1.00-1.05)
Nulliparous	0.69 (0.44-1.08)	0.56 (0.37-0.84)**	0.61 (0.38-1.01)	0.56 (0.35-0.97)*	0.47 (0.32-0.69)***	0.43 (0.25-0.69)**
Previous PE	1.03 (0.69-1.55)	0.76 (0.53-1.1)	1.06 (0.67-1.68)	0.81 (0.50-1.29)	0.78 (0.55-1.10)	0.54 (0.34-0.87)*
Race						
White	reference	reference	reference	reference	reference	reference
Black	0.68 (0.44-1.05)	1.44 (0.99-2.07)	2.03 (1.23-3.34) **	1.63 (0.99-2.66)	1.36 (0.96-1.93)	0.97 (0.62-1.50)
SE Asian	0.61 (0.22-1.68)	1.31 (0.54-3.16)	4.79 (1.90-12.04) **	3.01 (1.13-9.03) *	1.99 (0.85-4.69)	1.71 (0.66-4.46)
Mixed	0.84 (0.36-1.95)	0.87 (0.40-1.85)	1,88 (0.78-4.56)	1.28 (0.49-3.34)	1.16 (0.59-2.32)	0.87 (0.39-2.38)
CH groups						
Group 1	1.45 (0.72-2.90)	1.27 (0.74-2.18)	1.08 (0.52-2.23)	1.84 (0.89-3.77)	1.04 (0.63-1.71)	1.53 (0.79-2.99)
Group 2	reference	reference	reference	reference	reference	reference
Group 3	2.56 (1.53-4.29)***	2.15 (1.43-3.25)***	2.12 (1.27-3.54)**	2.18 (1.24-3.84)**	2.12 (1.45-3.10)***	2.20 (1.35-3.69)**
Group 4	9.03 (5.39-15.12)***	2.47 (1.59-3.80)***	2.05 (1.18-3.56)*	3.16 (1.78-5.64)***	1.68 (1.12-2.53)*	2.00 (1.16-3.47)*

Abbreviations: BMI, body mass index at booking; CH, chronic hypertension; PE, preeclampsia; SE Asian, South East Asian.
Group 1: new onset, Group 2: not treated and controlled, Group 3: treated and controlled, Group 4: treated not controlled
Results are presented as adjusted odds ratios (95% CI) and significance levels are demonstrated by asterisks: *$P < .05$, ** $P < .01$, *** $P < .0001$.

endothelial function, which results in structural remodeling of small arterial resistance vessels with relative thickening of the muscular media, vasoconstriction, and decreased capacity for vasodilatation.[7,8] We hypothesize that groups 1 and 2 represent women in the early stages of disease with, to a degree, preserved endothelial function who are likely to respond to antihypertensives (group 1) or to the early pregnancy stimulus for vasodilatation (group 2) and therefore manage to compensate for the cardiovascular stress of pregnancy.[7,9] In contrast, groups 3 and 4 probably contain women with severe endothelial damage and an inability to vasodilate in early pregnancy with subsequent high rates of severe hypertension, preterm PE, FGR, and the need for preterm delivery.

Compared with the general obstetric population, pregnancies in women with CH in our study were shown to be at much higher risk of adverse perinatal outcomes. Babies of mothers with CH had a three-fold higher rate of death in the antenatal and neonatal period,[10] two-fold higher rate of preterm delivery[11] and birthweight below the 10th centile, a 40% increase in admission to the NNU,[12] and an eight-fold increase in rate of respiratory distress syndrome.[13] Similarly, women with CH had a 12-fold higher prevalence of PE compared with the general obstetric population in the UK,[14] a three-fold higher rate of induction of labor,[15] a 28% lower rate of vaginal delivery,[15] and a 44% higher rate of cesarean section.[15]

Previous studies on perinatal outcomes in women with CH are heterogeneous, using different definitions of PE throughout four decades and providing birthweight below the 10th centile as a proxy for FGR, without any ultrasound evidence of placental insufficiency. Furthermore, only a handful of studies provided data on placental abruptions or neonatal outcomes. Population studies lack sensitivity because they report on data spanning more than a decade, from many centers, using different definitions and suboptimal case ascertainment.[2] It is not a surprise therefore, that the rates of superimposed PE ranged between 6% and 34%[16] and the rates of small for gestational age and pregnancy loss ranged between 5% and 28% and between 1% and 6%, respectively. Consequently, there was a lack of contemporaneous reports on perinatal outcomes in women with CH from single-center large prospective cohorts.

Prospective studies often provide better-quality evidence as they have strict criteria and more robust outcome reporting. The largest prospective reports on the rate of superimposed PE and fetal outcomes originated from the USA[17] and the UK[18] and examined prospectively 763 and 822 women, respectively. They were not single-center reports but subgroup analyses from randomized control trials. They reported superimposed PE rates of 25%[17] and 22%,[18] birthweight below the 10th centile 10.7%[17] and 19.9%,[18] stillbirth rate of 4.6%[17] and perinatal death 2.9%[18], and placental abruption rate of 1.5%.[17] In

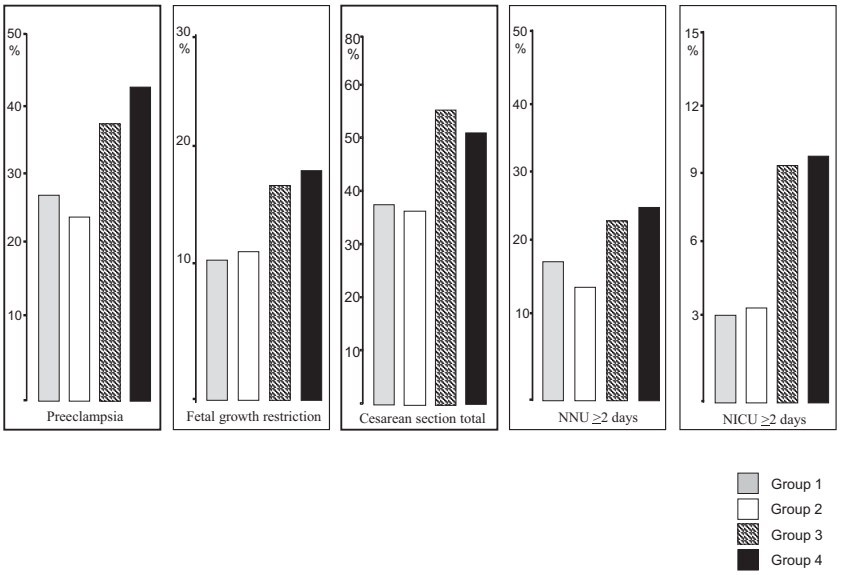

FIGURE 1 Difference in prevalence of adverse pregnancy outcomes in the four groups of women with chronic hypertension (CH) according to their blood pressure (BP) control at their booking visit in the first trimester: Group 1: women without history of CH, presenting with BP >140/90 mmHg (grey boxes). Group 2: women with BP <140/90 mmHg without antihypertensives (white boxes), Group 3: women with BP <140/90 mmHg with antihypertensives (boxes with diagonal stripes) and Group 4: women with BP ≥140/90 mmHg despite antihypertensives (black boxes). Data presented for preeclampsia, fetal growth restriction, delivery by cesarean section, and admission to Neonatal Unit (NNU) or Neonatal Intensive Care Unit (NICU) for 2 or more days

our study the rate of superimposed PE was higher than these two studies because we were using the more inclusive definition for PE from the International Society for the Study of Hypertension in Pregnancy, which incorporates not only proteinuria but also liver enzyme derangement, reduction in platelets, rise in creatinine, and FGR.[5] Similarly, the prevalence of placental insufficiency was higher in our population as 23.4% of babies had birthweight below the 10th centile and 14.9% had ultrasound evidence of FGR. However, despite the higher rates of PE and FGR and the fact that this is the first study reporting death rates up to 28 days after delivery, the stillbirth and neonatal death rates are lower than the two previously mentioned studies, possibly because of advances in neonatal care over the last two decades or because outcomes in such a high-risk population are better when these women are managed consistently in a specialist unit.

Our results agree with population studies[2] and two other large observational studies reporting an incidence of placental abruption in women with CH of 1.5%.[17,19] The fact that 75% of the placental abruptions were not lethal is positive and agrees with previous reports.[20] Unlike the stillbirths and neonatal deaths, where more than half of cases had evidence of FGR, placental abruptions have no discernible pattern in terms of the presence of placental insufficiency or uncontrolled BP.

The main strength of this study is the prospective examination of pregnancy outcomes in a large cohort of women with CH managed in a single center and a standardized protocol. It is the only study to demonstrate that perinatal outcomes are not uniform in this group of women, but are dependent on their cardiovascular adaptation in early pregnancy, possibly as a proxy of their cardiovascular reserve. Limitations of the study are the sample size in group 1, which probably reflects the low prevalence of CH in young women of reproductive age and the lack of postnatal long-term data of cardiovascular changes in the infants of these women.

5 | CONCLUSION

This study has demonstrated that in women with CH, worse perinatal outcomes occur in those who fail to adapt optimally in early pregnancy. These populations should be candidates for intensive monitoring during pregnancy and they should also be targets for further research to delineate the underlying pathophysiology mechanisms necessary to construct prevention and treatment strategies.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

How to cite this article: Dumitrascu-Biris D, Nzelu D, Dassios T, Nicolaides K, Kametas NA. Chronic hypertension in pregnancy stratified by first-trimester blood pressure control and adverse perinatal outcomes: A prospective observational study. *Acta Obstet Gynecol Scand*. 2021;100:1297–1304. https://doi.org/10.1111/aogs.14132