

Severe hypertension, preeclampsia and small for gestational age in women with chronic hypertension diagnosed before and during pregnancy



Diane Nzelu^a, Dan Dumitrascu-Biris^a, Polly Kay^a, Kypros H. Nicolaides^b, Nikos A. Kametas^{a,b,*}

^a Antenatal Hypertension Clinic, Division of Women's Health, Kings College Hospital, Denmark Hill, London SE5 9RS, UK

^b Harris Birthright Research Centre for Fetal Medicine, Division of Women's Health, Kings College Hospital, Denmark Hill, London SE5 9RS, UK

ARTICLE INFO

Keywords:

Chronic hypertension
Pregnancy
Preeclampsia
Small for gestational age
Severe hypertension
Antihypertensive drugs

ABSTRACT

Objectives: To compare rates of severe hypertension (SH), preeclampsia (PE) birth of small for gestational age (SGA) neonates between women with chronic hypertension (CH) diagnosed during the first trimester of pregnancy and those with pre-pregnancy CH.

Study design: Prospective cohort study of women with CH and singleton pregnancies referred to an Antenatal Hypertension Clinic at 8–14 weeks' gestation. At presentation the patients were subdivided into four groups based on blood pressure (BP) control. Group 1 included women without a preceding history of CH presenting with BP of $\geq 140/90$ mmHg ($n = 86$). Groups 2–4 had pre-pregnancy CH; in group 2 the BP was $< 140/90$ mmHg without antihypertensive medication ($n = 200$), in group 3 the BP was $< 140/90$ mmHg with antihypertensive medication ($n = 231$) and in group 4 the BP was $\geq 140/90$ mmHg despite antihypertensive medication ($n = 173$).

Main outcome measures: PE, SH (BP $\geq 160/110$ mmHg), SGA (birthweight < 10 th percentile).

Results: In group 1, the rate of SH (15.1%), was similar to that in group 2 (10.5%) and group 3 (23.8%) but significantly lower than in group 4 (52.6%). In group 1, the rate of PE (12.8%) and SGA < 10 th centile (18.6%) were similar to those in group 2 (16.5% and 21.0%) and significantly lower than in group 3 (26.0 and 30.7%) and group 4 (26.6% and 31.8%).

Conclusion: In women diagnosed with CH in the first trimester of pregnancy, the rates of SH, PE and SGA are similar to those with pre-pregnancy CH who present with BP below 140/90 without the need for antihypertensive medication.

1. Introduction

Chronic hypertension (CH) is found in 1–5% of pregnancies and is associated with an increased risk of maternal and perinatal morbidity, including development of severe hypertension (SH) or preeclampsia (PE) and delivery of small for gestational age (SGA) neonates [1–7]. We have proposed that women with pre-pregnancy CH fall into three broad categories in relation to their blood pressure (BP) control when they present to hospital in the first trimester of pregnancy (those with BP $< 140/90$ mmHg without antihypertensive medication, those with BP $< 140/90$ mmHg with antihypertensive medication and those with persistent hypertension BP $\geq 140/90$ mmHg despite antihypertensive medication) with increasing incidence in development of severe hypertension (11%, 22% and 52%), preterm preeclampsia (7%, 16% and 20%), and birth of SGA neonates (9%, 12% and 15%) [8].

Professional bodies include in the definition of CH in pregnancy two groups of women; first those with hypertensive disease before the onset of pregnancy and those without such history that are diagnosed with hypertension during the first 20 weeks' gestation [9,10]. However, we could not identify any studies comparing pregnancy outcomes between those with pre-pregnancy CH and those with the diagnosis made during the course of pregnancy.

The objective of this study is to compare the rates of severe hypertension, PE and SGA between women with CH diagnosed during pregnancy and those in women with pre-pregnancy CH.

* Corresponding author at: Antenatal Hypertension Clinic, Fetal Medicine Research Institute, King's College Hospital, 16-20 Windsor Walk, Denmark Hill, London SE5 8BB, UK.

E-mail address: nick.kametas@kcl.ac.uk (N.A. Kametas).

<https://doi.org/10.1016/j.preghy.2018.10.006>

Received 22 December 2017; Received in revised form 27 September 2018; Accepted 13 October 2018

Available online 15 October 2018

2210-7789/© 2018 International Society for the Study of Hypertension in Pregnancy. Published by Elsevier B.V. All rights reserved.

2. Methods

2.1. Study population

This was an analysis of prospectively collected data in the Antenatal Hypertension Clinic at King's College Hospital, London, between January 2011 and September 2017. According to local protocols, pregnant women with pre-pregnancy hypertension and those presenting for the first time as hypertensive at their booking visit with their midwife are referred to this clinic for the management of their pregnancy. In the latter group, the diagnosis of CH was made if the BP was $\geq 140/90$ mmHg on two consecutive clinical visits; the BP was measured using a validated automated device [11]. The first visit at the Antenatal Hypertension Clinic was at < 14 weeks' gestation and included recording of maternal demographic characteristics and obstetric, medical and drug history, measurement of maternal weight, height and BP and assessment of renal and liver function.

In the management of patients with CH our policy has been to maintain the BP at 130–140/80–90 mmHg throughout pregnancy with the use of antihypertensive medication; these medications were stopped or reduced if the BP fell $< 130/80$ mmHg on two consecutive visits. Following their initial visit, women were reviewed at 20–24 weeks and, at a minimum of every four weeks thereafter until delivery. At each visit, an assessment of BP, renal and liver function tests were carried out along with urinalysis for proteinuria and ultrasound examination for fetal anatomy and growth. All data were collected by two trained research doctors under the supervision of a senior specialist in Maternal-Fetal Medicine. Data on pregnancy outcomes were collected from the hospital maternity records and the women's general medical practitioners.

The inclusion criteria for this study were singleton pregnancies with pre-pregnancy or newly-diagnosed CH in the absence of renal or liver disease, presenting to the Antenatal Hypertension Clinic at < 14 weeks' gestation and resulting in the live birth or stillbirth of non-malformed babies at ≥ 24 weeks' gestation. We excluded pregnancies with fetal aneuploidies or major defects diagnosed antenatally or in the neonatal period and pregnancies ending in miscarriage at < 24 weeks' gestation.

The study is part of our routine clinical management and 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.

2.2. Outcome measures

The cohort was divided into four groups. Group 1 consisted of women without a pre-pregnancy diagnosis of CH, presenting in the first trimester of pregnancy with BP $\geq 140/90$ mmHg and not taking antihypertensive medication at the time of diagnosis. Groups 2–4 consisted of women with pre-pregnancy CH according to their blood pressure control and need for antihypertensive medications at the first visit to the Antenatal Hypertension Clinic; in group 2, the BP was $\leq 140/90$ mmHg without antihypertensive medication, in group 3, the BP was $\leq 140/90$ mmHg with antihypertensive medication and, in group 4 the BP was $\geq 140/90$ mmHg despite antihypertensive medication.

The outcome measures were severe hypertension, PE and birth of SGA neonates. Severe hypertension was defined by the presence of systolic BP ≥ 160 mmHg and/or diastolic BP ≥ 110 mmHg on two consecutive measurements taken at least five minutes apart. Preeclampsia was defined according to the International Society for the Study of Hypertension in Pregnancy (ISSHP) [9] as the presence of hypertension along with at least one of the following: renal involvement (proteinuria ≥ 300 mg/24 h and/or creatinine ≥ 90 μ mol/L or 1 mg/dL), liver impairment (transaminases > 70 IU/L), neurological complications (e.g. eclampsia), thrombocytopenia (platelet count $< 150,000/\mu$ L) [9]. In addition, PE was subdivided according to gestational age at diagnosis into preterm PE with onset at < 37 weeks'

gestation and term PE with onset at ≥ 37 weeks. Small for gestational age (SGA) was defined as birth weight < 10 th percentile without adjustment for maternal characteristics [12]. As the ISSHP [9] guidelines recognise that the inclusion of fetal growth restriction in the definition of PE is controversial, we present the data on prevalence of SGA separately to those of the maternal features of the disease.

2.3. Statistical analysis

Normality of continuous variables was assessed by the Kolmogorov-Smirnov test. Numerical data were expressed as median and inter-quartile range (IQR). Maternal and pregnancy characteristics at the first hospital visit and pregnancy outcomes were compared between group 1 and each of groups 2–4; the Kruskal-Wallis test with Bonferroni correction for post-hoc analysis was used for numerical variables and the Chi-square test was used for categorical variables.

Statistical analysis was performed using SPSS (Version 22; SPSS Inc, Chicago, IL).

3. Results

3.1. Population characteristics

The inclusion criteria were met by 690 of the 800 pregnancies examined in the Antenatal Hypertension Clinic; 110 (13.7%) women were excluded because they presented beyond ≥ 14 weeks' gestation ($n = 33$), had pre-existing renal disease ($n = 35$), were multiple pregnancies ($n = 24$), had major fetal anomalies ($n = 7$), had suffered a miscarriage ($n = 37$) or had incomplete data on pregnancy outcome ($n = 15$). The 690 women included in the study were classified as group 1 ($n = 86$), group 2 ($n = 200$), group 3 ($n = 231$) and group 4 ($n = 173$).

Maternal characteristics, previous obstetric history and results of investigations at the first visit to the Antenatal Hypertension clinic are compared between the four groups of CH in Table 1. The median gestational age at presentation was 10 weeks and this was similar in the four groups. Weight and body mass index were higher in group 1 than in group 2, but not significantly different from groups 3 and 4. The incidence of women of black racial origin was lower in group 1 compared to groups 3 and 4. Systolic and diastolic BP were both higher in group 1 than in groups 2 and 3. There were no significant differences between group 1 and groups 2–4 in age, height and family history of PE.

Data from 586 of the 604 pregnancies in groups 2–4 were reported previously [8].

3.2. Pregnancy outcomes

Pregnancy outcome measures in the four groups of women with CH are compared in Table 2 and Fig. 1. In group 1, the rate of SH (15.1%), was similar to that in group 2 (10.5%) and group 3 (23.8%) but significantly lower than in group 4 (52.6%). In group 1, at presentation all patients were hypertensive and were treated with antihypertensive drugs; however, during the course of pregnancy there was a decrease in BP and by the time of delivery 51.2% of cases had BP $< 140/90$ mmHg without the need for medication. This proportion was similar to that in group 2 but significantly higher than in groups 3 and 4. In patients requiring antihypertensive drugs during the course of pregnancy the rate was similar in groups 1 and 2 and significantly lower than in groups 3 and 4; in group 1 the rate of multiple anti-hypertensive medication use was approximately twice as high than in group 2 (11.6% vs 5.0%), but substantially lower than in group 3 (24.7%) or group 4 (41.0%). At the time of delivery, group 1 compared to group 2 had significantly lower use of Nifedipine but no difference in the use of Labetalol or Methyldopa (Table 2). Compared to groups 3 and 4, group 1 had significantly lower use of Nifedipine and Labetalol but no difference in the use of Methyldopa (Table 2).

Table 1

Comparison of maternal characteristics and results of investigations at the booking visit between women with pre-pregnancy chronic hypertension stratified according to blood pressure control at first hospital visit and those with newly diagnosed hypertension in pregnancy.

Clinical feature	Group 1 (n = 86)	Group 2 (n = 200)	Group 3 (n = 231)	Group 4 (n = 173)
Antihypertensive medications				
One drug, n (%)	–	–	217 (93.9)	161 (93.1)
Two or more drugs, n (%)	–	–	14 (6.1)	12 (6.9)
Gestational age in weeks, median (IQR)	10.3 (9.4–11.3)	10.0 (9.3–11.0)	10.0 (9.1–10.9)	10.0 (9.0–11.0)
Age in years, median (IQR)	34.0 (32.0–37.0)	34.0 (30.0–37.7)	35.0 (32.0–38.0)	35.0 (31.0–39.0)
Body mass index in kg/m ² , median (IQR)	31.5 (27.0–37.0)	28.0 (25.0–33.2)**	31.0 (27.0–35.0)	32.0 (28.0–37.0)
Weight in kg, median (IQR)	89.9 (72.8–102.3)	79.4 (67.0–91.6)**	84.0 (72.0–95.2)	88.7 (74.1–103.4)
Height in meters, median (IQR)	166.0 (162.0–169.3)	165.0 (161.0–169.8)	165.0 (160.0–168.0)	165.0 (160.0–170.0)
Family history of preeclampsia, n (%)	12 (14.0)	25 (12.5)	26 (11.3)	24 (13.9)
Multiparous, n (%)	57 (66.3)	112 (56)	181 (78.4) [†]	122 (70.5)
Preeclampsia in previous pregnancy, n (%)	33 (38.4)	51 (25.5) [†]	114 (49.4)	76 (43.9)
Racial origin				
Black, n (%)	47 (54.7)	100 (50.0)	156 (67.5) [†]	117 (67.6) [†]
White, n (%)	32 (37.2)	81 (40.5)	54 (23.4) [†]	45 (26.0)
South-East Asian, n (%)	4 (4.7)	9 (4.5)	13 (5.6)	1 (0.6) [†]
Other, n (%)	3 (3.5)	10 (5.0)	8 (3.5)	10 (5.8)
Systolic BP in mmHg, median (IQR)	140.0 (140.0–147.0)	120.0 (111.0–133.0)	124.0 (120.0–130.0)	146.0 (140.0–154.0)
Diastolic BP in mmHg, median (IQR)	90.0 (82.0–93.0)	76.0 (70.0–80.0)	79.0 (70.0–80.0)	90.0 (85.0–98.0)
Serum creatinine in µmol/L, median (IQR)	51.0 (43.0–58.0)	49.0 (42.0–56.0)	51.0 (46.0–58.0)	52.0 (45.0–62.0)
Aspartate transaminase in IU/L, median (IQR)	18.0 (16.0–22.0)	19.0 (16.0–22.0)	19.0 (16.0–22.0)	18.0 (16.0–21.0)
24 h urine protein > 300 mg, n (%)	0 (0)	0 (0)	0 (0)	0 (0)

IQR = interquartile range.

* Statistically significant difference between group 1 and the current group at < 0.05 level.

** Statistically significant difference between group 1 and the current group at < 0.01 level.

In group 1, the rate of PE (12.8%) and SGA < 10th centile (18.6%) were similar to those in group 2 (16.5% and 21.0%, respectively) and significantly lower than in group 3 (26.0 and 30.7%, respectively) and group 4 (26.6% and 31.8, respectively).

4. Discussion

4.1. Principal findings of the study

Women newly diagnosed with CH in the first trimester of pregnancy, a previously poorly defined group, have a high risk of development of SH (15%) and PE (12%), delivering SGA neonates < 10th centile (19%). Consequently, these women require close antenatal surveillance similar to that in women with pre-pregnancy CH.

Table 2

Pregnancy outcome in women with pre-pregnancy chronic hypertension stratified according to blood pressure control at first hospital visit and those with newly diagnosed chronic hypertension.

Clinical feature	Group 1 (n = 86)	Group 2 (n = 200)	Group 3 (n = 231)	Group 4 (n = 173)
Severe hypertension, n (%)	13 (15.1)	21 (10.5)	55 (23.8)	91 (52.6) ^{***}
Antihypertensive medications at delivery				
No drugs, n (%)	44 (51.2)	126 (63.0)	56 (24.2) ^{***}	11 (6.4) ^{***}
One drug, n (%)	32 (37.2)	64 (32.0)	118 (51.1) [*]	91 (52.6) [*]
Two or more drugs, n (%)	10 (11.6)	10 (5.0) [†]	57 (24.7) [†]	71 (41.0) ^{***}
Labetalol, n (%)	19 (22.1)	35 (17.5)	105 (38.7) ^{**}	99 (51.6) ^{***}
Nifedipine, n (%)	24 (27.9)	116 (42.8) ^{**}	28 (14.0) [†]	99 (51.6) ^{***}
Methyldopa, n (%)	4 (4.7)	6 (3.0)	26 (9.6)	13 (6.8)
Preeclampsia, n (%)				
Total, n (%)	11 (12.8)	33 (16.5)	60 (26.0) [†]	46 (26.6) [†]
Onset < 37 weeks, n (%)	9 (10.5)	14 (7.0)	36 (15.6)	35 (20.2) [*]
Onset ≥ 37 weeks, n (%)	2 (2.3)	19 (9.5) [†]	24 (10.4) [†]	11 (6.4)
Gestation at onset, median (IQR)	34.9 (30.9–36.0)	37.1 (33.4–38.7)	35.6 (32.7–37.7)	34.0 (28.6–37.1)
Birthweight < 10th centile, n (%)	16 (18.6)	42 (21.0)	71 (30.7) [†]	55 (31.8) ^{***}
Birthweight < 5th centile, n (%)	8 (9.3)	26 (13.0)	41 (17.7)	35 (20.2) [*]
Birth weight percentile, median (IQR)	38.3 (16.2–59.7)	31.4 (11.5–56.9)	27.8 (7.2–52.4) [*]	22.4 (7.6–48.3) [*]
Gestation at delivery, median (IQR)	38.3 (37.1–38.7)	37.8 (37.3–39.3)	38.0 (36.3–39.0)	38.1 (35.7–39.0) [†]

IQR = interquartile range.

* Statistically significant difference between group 1 and the current group at < 0.05 level.

** Statistically significant difference between group 1 and the current group at < 0.01 level.

*** Statistically significant difference between group 1 and the current group at < 0.001 level.

4.2. Comparison with findings of previous studies

There are no previous studies specifically reporting on complications of pregnancies with newly diagnosed CH. We have previously reported that in women with pre-pregnancy CH, the rates of development of SH, PE and SGA are related to use of antihypertensive medications and level of BP control at the first hospital visit during the first-trimester of pregnancy [8]. The rates of pregnancy complications in women with newly diagnosed CH are in general similar to those in women with pre-pregnancy CH that present with BP < 140/90 mmHg without antihypertensive medication and lower than in those with BP < 140/90 mmHg with antihypertensive medication and those with persistent hypertension BP ≥ 140/90 mmHg despite antihypertensive medication.

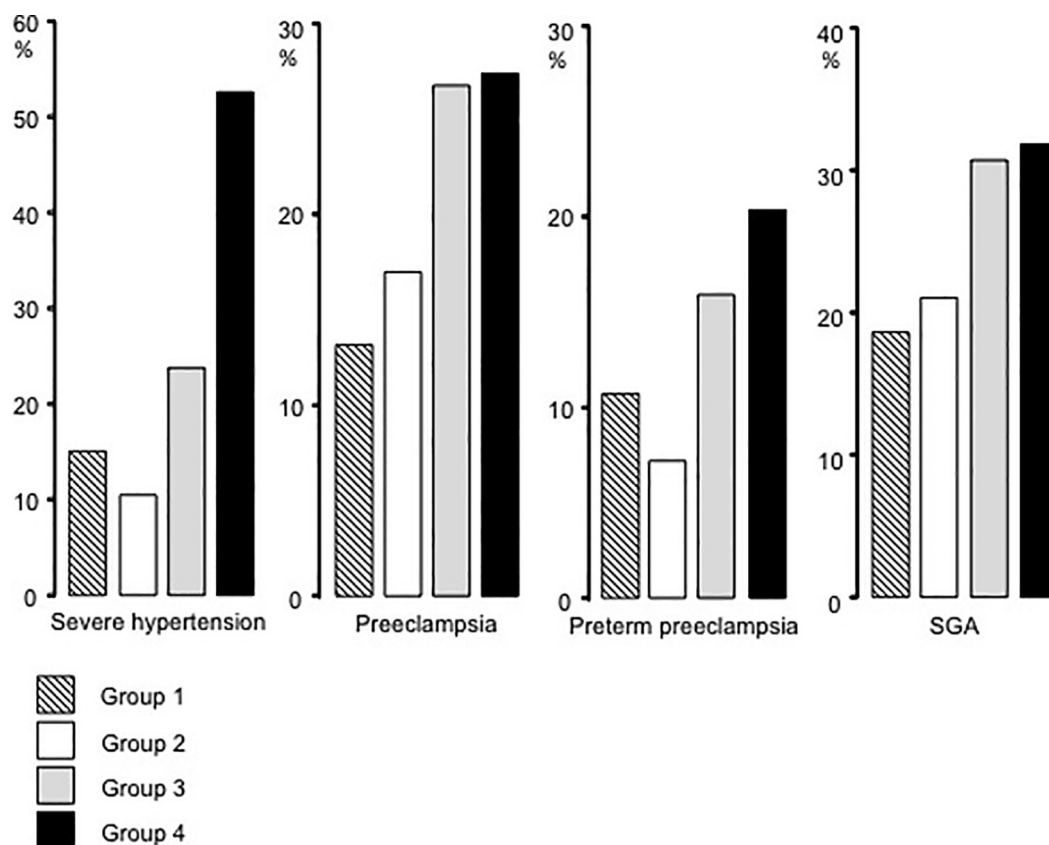


Fig. 1. Pregnancy complications in women diagnosed with chronic hypertension in early pregnancy.

4.3. Implications for practice and future research

The results of this study have implications for the management of women with CH both during and after pregnancy. The high rates of pregnancy complications, in both those with pre-pregnancy CH and those with newly diagnosed CH, were observed despite our policy of aiming to maintain the BP at 130–140/80–90 mmHg throughout pregnancy. It is uncertain if the incidence of these complications would have been different if the control of BP was less tight, aiming for BP at < 160/105 mmHg, as recommended by the American College of Obstetricians and Gynecologists (ACOG) [13]. However, a recent trial of women with CH or gestational hypertension and diastolic BP of 90–105 mm Hg, reported that a policy of tight control in BP with a target diastolic BP of 85 mm Hg, compared to a policy of less-tight control with target diastolic BP of 100 mm Hg, was associated with a lower incidence of SH (28% vs. 41%) but no significant difference in incidence of PE or SGA [14]. Therefore, a less-tight BP control would have resulted in even higher rates of SH without any improvement in the rates of SGA.

The next question that needs to be addressed is whether an even tighter BP control early in pregnancy would have led to improved outcomes. Outside pregnancy there is an inverse relationship between BP levels and risk of cardiovascular disease (CVD) [15] and recent studies suggest that tight BP control with systolic BP < 120 mmHg is associated with improved outcomes [16]. Additional strategies that target the vasculature, such as metformin [17] or statins [18], to slow or reverse end organ damage may be more effective in those with already significant cardiovascular disease, such as the groups 3–4 in our study. In any case, we would recommend that future studies investigating these interventions in pregnancies with CH should stratify the population according to our approach because, as we demonstrated, the effect of the drugs is likely to vary according to the severity of the underlying disease.

Outside of pregnancy, epidemiological studies have shown an increasing incidence of hypertension amongst young adults, estimated at almost 20% in women aged < 45 years [19]. However, despite these trends, the awareness and management of hypertension amongst young adults and primary care physicians remains significantly lower when compared to the older population with only half receiving the appropriate treatment [20]. Hypertension contributes to more CVD events in women relative to men (32 vs. 19%) [21] and the accumulation of even modestly elevated BP pressure over young adulthood is linked to atherosclerosis, coronary calcification, and greater left ventricular mass [22,23]. The implications of this are not just for pregnancy where it is well established that CH is an independent risk factor for the development of PE [6] but also, later in life, for CVD, the leading cause of death in women [24]. Increasingly, therefore, pregnancy will present a unique opportunity to identify women requiring follow up and management of their CVD risk factors for several decades beyond pregnancy.

A study reporting on non-pregnant population demonstrated that in patients with BP < 120/80 the lowest rate of cardiovascular morbidity was observed in those without the need of anti-hypertensive medication to achieve ideal BP control [22]. This study therefore highlights that BP control to normal levels with antihypertensive medications, does not completely abolish the risks of CVD [22] and all efforts should be made to remove risk factors such as obesity and hyperlipidaemia, before endothelial dysfunction and end-organ damage occurs. Therefore, our aims in this group of women with newly diagnosed CH in pregnancy should be to organise postnatal follow-up for monitoring and controlling their risk factors in order to minimise their long-term risk of CVD before they transition to the severity of groups 3 and 4.

4.4. Strengths and limitations of the study

This is the first study to our knowledge that has reported on the

rates of SH, PE and SGA in women newly diagnosed with CH in pregnancy. Other strengths of this study include prospective collection of data from the first trimester through to delivery from a large population of pregnancies complicated with CH and use of the same protocol for the management of hypertension in pregnancy implemented throughout the study period.

Limitations of this study are the small sample size of women with newly diagnosed CH and lack of pre-conceptual and postnatal data in this group. The incidence of newly diagnosed CH is likely to be underestimated because we included only those cases presenting at < 14 weeks' gestation when blood pressure is already declining as a normal feature of pregnancy.

5. Conclusion

National guidelines for the management of hypertension in pregnancy include in the definition of CH both women with pre-pregnancy diagnosis but also those newly diagnosed in early pregnancy. However, the latter group have never been evaluated separately. Our study has demonstrated that women newly diagnosed with CH in pregnancy have high rates of SH, PE and SGA necessitating close antenatal surveillance similar to that in women with pre-pregnancy CH.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial or not-for-profit sectors.

Conflict of interest statement

The authors report no conflict of interest.

Sources of funding

No funding was received for this study.

References

- [1] E. Lecarpentier, G. Kayem, V. Tsatsaris, F. Goffinet, B. Sibai, B. Haddad, 750: adverse maternal and perinatal outcomes in women with chronic hypertension: a retrospective study of 362 patients, *Am. J. Obstet. Gynecol.* 204 (1) (2011) S294.
- [2] B.T. Bateman, P. Bansil, S. Hernandez-Diaz, J.M. Mhyre, W.M. Callaghan, E.V. Kuklina, Prevalence, trends and outcomes of chronic hypertension: a nationwide sample of delivery admissions, *Am. J. Obstet. Gynecol.* 134 (e1–134) (2012) e8.
- [3] C.V. Ananth, M.R. Peltier, W.L. Kinzler, J.C. Smulian, A.M. Vintzileos, Chronic hypertension and risk of placental abruption: is the association modified by is-chemic placental disease? *Am. J. Obstet. Gynecol.* 273 (e1–273) (197(3) 2007,) e7.
- [4] B.M. Sibai, Chronic hypertension in pregnancy, *Obstet. Gynecol.* 100 (2) (2002) 369–377.
- [5] A.E. Czeizel, F. Bánhidly, Chronic hypertension in pregnancy, *Curr. Opin. Obstet. Gynecol.* 23 (2) (2011) 76–81.
- [6] A.M. Panaitescu, A. Syngelaki, N. Prodan, R. Akolekar, K.H. Nicolaides, Chronic hypertension and adverse pregnancy outcomes: a cohort study, *Ultrasound Obstet. Gynecol.* (2017).
- [7] K. Broekhuijsen, A.C. Ravelli, J. Langenveld, M.G. Pampus, P.P. Berg, B.W. Mol, M. Franssen, Maternal and neonatal outcomes of pregnancy in women with chronic hypertension: a retrospective analysis of a national register, *Acta Obstet. Gynecol. Scand.* 94 (12) (2015) 1337–1345.
- [8] D. Nzelu, D. Dumitrascu, K. Nicolaides, N. Kametas, Chronic hypertension: first-trimester blood pressure control and likelihood of severe hypertension, pre-eclampsia and small for gestational age, *Am. J. Obstet. Gynecol.* (2017) (in press).
- [9] A. Tranquilli, G. Dekker, L. Magee, J. Roberts, B. Sibai, W. Steyn, G. Zeeman, M. Brown, The classification, diagnosis and management of the hypertensive disorders of pregnancy: a revised statement from the ISSHP, *Pregnancy Hypertens. Int. J. Women's Cardiovasc. Health* 4 (2) (2014) 97–104.
- [10] National Institute for Health and Clinical Excellence, Hypertension in pregnancy: the management of hypertensive disorders during pregnancy, NICE guideline (CG107), 2010.
- [11] Y. Chung, A. de Greeff, A. Shennan, Validation and compliance of a home monitoring device in pregnancy: microlife WatchBP home, *Hypertens. Pregnancy* 28 (3) (2009) 348–359.
- [12] K. Maršál, P.H. Persson, T. Larsen, H. Lilja, A. Selbing, B. Sultan, Intrauterine growth curves based on ultrasonically estimated foetal weights, *Acta Paediatr.* 85 (7) (1996) 843–848.
- [13] ACOG Committee on Obstetric Practice, ACOG practice bulletin. Diagnosis and management of preeclampsia and eclampsia. Number 33, January 2002. American College of Obstetricians and Gynecologists, *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics*, 77(1) (2002) 67.
- [14] L.A. Magee, P. von Dadelszen, E. Rey, S. Ross, E. Asztalos, K.E. Murphy, J. Menzies, J. Sanchez, J. Singer, A. Gafni, A. Gruslin, M. Helewa, E. Hutton, S.K. Lee, T. Lee, A.G. Logan, W. Ganzevoort, R. Welch, J.G. Thornton, J.M. Moutquin, Less-tight versus tight control of hypertension in pregnancy, *N. Engl. J. Med.* 372 (5) (2015) 407–417.
- [15] Prospective Studies Collaboration, Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies, *Lancet* 360 (9349) (2002) 1903–1913.
- [16] SPRINT Research Group, A randomized trial of intensive versus standard blood-pressure control, *N. Engl. J. Med.* 2015 (373) (2015) 2103–2116.
- [17] F.C. Brownfoot, R. Hastie, N.J. Hannan, P. Cannon, L. Tuohey, L.J. Parry, S. Senadheera, S.E. Illanes, J. Tu'uhevaha, S. Tong, Metformin as a prevention and treatment for preeclampsia: effects on soluble fms-like tyrosine kinase 1 and soluble endoglin secretion and endothelial dysfunction, *Am. J. Obstet. Gynecol.* 356214 (e1–3563) (2016) e15.
- [18] M.M. Costantine, E. Tamayo, F. Lu, E. Bytautiene, M. Longo, G.D. Hankins, G.R. Saade, Using pravastatin to improve the vascular reactivity in a mouse model of soluble Fms-like tyrosine kinase-1-induced preeclampsia, *Obstet. Gynecol.* 116 (1) (2010) 114–120.
- [19] T. De Venecia, M. Lu, V.M. Figueredo, Hypertension in young adults, *Postgrad. Med.* 128 (2) (2016) 201–207.
- [20] Y. Zhang, A.E. Moran, Trends in the prevalence, awareness, treatment, and control of hypertension among young adults in the United States, 1999 to 2014 novelty and significance, *Hypertension* 70 (4) (2017) 736–742.
- [21] S. Cheng, B. Claggett, A.W. Correia, A.M. Shah, D. Gupta, H. Skali, H. Ni, W.D. Rosamond, G. Heiss, A.R. Folsom, Temporal trends in the population attributable risk for cardiovascular disease: the atherosclerosis risk in communities study, *Circulation (CIRCULATIONAHA)* (2014) 113.008506.
- [22] K. Liu, L.A. Colangelo, M.L. Daviglius, D.C. Goff, M. Pletcher, P.J. Schreiner, C.T. Sibley, G.L. Burke, W.S. Post, E.D. Michos, Can antihypertensive treatment restore the risk of cardiovascular disease to ideal levels?: The Coronary Artery Risk Development in Young Adults (CARDIA) Study and the Multi-Ethnic Study of Atherosclerosis (MESA), *J. Am. Heart Assoc.* 4 (9) (2015) e002275.
- [23] M.J. Pletcher, K. Bibbins-Domingo, C.E. Lewis, G.S. Wei, S. Sidney, J.J. Carr, E. Vittinghoff, C.E. McCulloch, S.B. Hulley, Prehypertension during young adulthood and coronary calcium later in life: prehypertension and coronary calcium, *Ann. Intern. Med.* 149 (2) (2008) 91–99.
- [24] World Health Organization, World Health Organization statistical information system, Website accessed July, 2009.