Chronic hypertension and adverse pregnancy outcomes: a cohort study

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Short Title: Chronic hypertension and pregnancy complications

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ABSTRACT

Objective: To examine the association between chronic hypertension (CH) and a wide range of adverse pregnancy outcomes after adjustment for confounding factors in obstetric history and maternal characteristics.

Methods: This was a prospective screening study for adverse pregnancy outcomes in women with singleton pregnancies attending the first routine hospital visit at 11^{+0}-13^{+6} weeks' gestation. Data on maternal characteristics, medical and obstetric history and pregnancy outcomes were collected. Regression analysis was performed to examine the association between CH and adverse pregnancy outcomes including late miscarriage, stillbirth, pre-eclampsia (PE), gestational diabetes mellitus (GDM), spontaneous and iatrogenic preterm birth (PTB), small for gestational age (SGA) neonate, large for gestational age (LGA) neonate and elective and emergency cesarean section (CS).

Results: The study population of 109,932 pregnancies included 1,417 (1.3%) with CH. After adjusting for potential confounding variables from maternal characteristics, medical and obstetric history, CH was associated with increased risk of stillbirth OR 2.38, 95% CI 1.51-3.75), PE (OR 5.76, 95% CI 4.93-6.73), SGA (OR 2.06, 95% CI 1.79-2.39), GDM (OR 1.61, 95% CI 1.27-2.05), iatrogenic PTB <37 weeks (OR 3.73, 95% CI (3.07-4.53) and elective CS (OR 1.79, 95%CI 1.52-2.11), decreased risk of LGA (OR 0.65, 0.51-

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0.83), and had no significant effect on late miscarriage, spontaneous PTB or emergency CS.

Conclusion: CH should be combined with other maternal characteristics and medical and obstetric history when calculating an individualised adjusted risk for adverse pregnancy complications. CH increases the risk for stillbirth, PE, SGA, GDM, iatrogenic PTB and elective CS and reduces the risk for LGA.

Key Words: Chronic hypertension; preeclampsia; preterm birth; small for gestational age; large for gestational age; miscarriage, stillbirth, gestational diabetes; cesarean section

Introduction

Chronic hypertension (CH) is associated with increased risk for many pregnancy complications. A recent systematic review and meta-analysis of 55 studies encompassing 795,221 pregnancies reported that in women with CH the pooled incidences of superimposed preeclampsia (PE), preterm birth (PTB) at <37 weeks' gestation, birth weight <2500 g and cesarean section (CS) were 26%, 20%, 17% and 41%, respectively; compared to national averages the relative risks for CH were 7.7 for PE, 2.7 for PTB, 2.7 for birth weight <2500 g and 1.3 for CS.[1] However, there was large heterogeneity between the included studies in the incidence of all outcomes and this is not surprising. First, the meta-analysis included a mixture of prospective and retrospective cohort studies and even randomised controlled trials, excluding the treatment arm if a difference existed in outcomes and including both arms if no benefit of the intervention was seen. Second, most of the data (>94%) were derived from a USA database on patients after hospitalization for delivery where outcomes were largely dependent on codes collected for billing purposes, which are susceptible to under ascertainment and misclassification bias.[2] Third, the study period ranged between 1973 and 2010, the studies differed in the inclusion or exclusion of multiple gestations and congenital abnormalities, in the definition of CH and in the definition of outcome measures; for example, in the case of superimposed PE 16 studies did not report diagnostic criteria and the remaining 39 studies used 18 different definitions, and fourth, most papers did not report relevant maternal characteristics precluding assessment of confounders.

The aim of this prospective study of women recruited at the routine hospital visit at 11-13 weeks' gestation was to examine the association between CH and a wide range of well-defined adverse pregnancy outcomes after adjustment for confounding factors in maternal characteristics, medical history and obstetric history. The rationale for such objective is to estimate the patient-specific risk for pregnancy complications as the basis for assessment of the value of therapeutic interventions aiming at their prevention.

Methods

Study population

This was a prospective screening study for adverse obstetric outcomes in pregnant women attending for their first routine hospital visit at King's College Hospital, London, UK (between March 2006 and July 2015) and Medway Maritime Hospital, Kent, UK (between February 2007 and November 2015). This visit, which was held at 11^{+0}-13^{+6} weeks of gestation, included recording of maternal demographic characteristics and obstetric and medical history, measurement of maternal weight and height, ultrasound examination for the measurement of the fetal crown-rump length (CRL) to determine gestational age,[3] measurement of the fetal nuchal translucency thickness,[4] and examination of the fetal anatomy for the diagnosis of major fetal defects.[5]

Written informed consent was obtained from women who agreed to participate in the study, which was approved by the Ethics Committee of each participating Hospital. Data on pregnancy outcomes were collected from the hospital maternity records and the women's general medical practitioners.

We excluded pregnancies with fetal aneuploidies or major defects diagnosed either prenatally or in the neonatal period, pregnancies ending in miscarriage at <16 weeks' gestation and those ending in termination for psychosocial reasons.

Maternal characteristics and obstetric history

Participants completed a questionnaire on their age, racial origin (Caucasian, Afro-Caribbean, South Asian, East Asian or mixed), method of conception (spontaneous, *in vitro* fertilization or use of ovulation induction drugs), cigarette smoking during pregnancy, medical history of CH, diabetes mellitus (type 1 or 2), systemic lupus erythematosus (SLE) or antiphospholipid syndrome (APS), family history of PE (none or mother had PE), family history of diabetes mellitus (none or first or second degree relative) and obstetric history, including PE, GDM, stillbirth, spontaneous and iatrogenic PTB, CS, miscarriage at 16^{+0}- 23^{+6} weeks at any previous pregnancy and birth of small for gestational age (SGA) neonate with birth weight <10^{th} percentile or large for gestational age (LGA) neonate with birth weight >90^{th} percentile in the last pregnancy that delivered at ≥24 weeks' gestation. The questionnaire was then reviewed by a doctor together with the woman and their weight and height were measured.

Outcome measures

Outcome measures included late miscarriage, stillbirth, PE, GDM, spontaneous and iatrogenic PTB, birth of SGA or LGA neonate, and delivery by elective or emergency CS.

Late miscarriage included spontaneous delivery or fetal death at 16^{+0}-23^{+6} weeks' gestation. Stillbirths were fetal deaths at ≥24 weeks.

The diagnosis of PE was made according to the guidelines of the International Society for the Study of Hypertension in Pregnancy.[6] The systolic blood pressure should be ≥140 mm Hg and/or the diastolic blood pressure should be ≥90 mmHg on at least two occasions four hours apart developing after 20 weeks' gestation in a previously normotensive woman and in addition there should be significant proteinuria (≥300 mg in 24 hours, or two readings of at least ++ on dipstick analysis of midstream or catheter urine specimen, if no 24-hour collection is available). In CH diagnosis of superimposed PE requires the development of significant proteinuria after 20 weeks' gestation in a previously non proteinuric woman. In the investigation of the relationship between CH and PE we excluded pregnancies ending in miscarriage.

Screening for GDM was based on a two-step approach. In all women, random plasma glucose was measured at 24 - 28 weeks' gestation and, if the concentration was >6.7 mmol/L, an oral glucose tolerance test was carried out within two weeks. A diagnosis of GDM was made if the fasting plasma glucose level was ≥6 mmol/L or the plasma glucose level 2 hours after the oral administration of 75 g glucose was ≥7.8 mmol/L.[7] In women with normal random blood glucose, an oral glucose tolerance test was performed if they had persistent glycosuria, developed polyhydramnios or the fetus became macrosomic. In the investigation of the relationship between CH and GDM we excluded pregnancies with pre-pregnancy diabetes mellitus and those ending in miscarriage or delivery before 30 weeks because they might not have had screening and diagnosis of GDM.

Preterm birth was divided into spontaneous and iatrogenic. Spontaneous PTB included those with spontaneous onset of labor and those with preterm prelabor rupture of membranes (PPROM) occurring at <37 and <34 weeks' gestation. In the investigation of the relationship between CH and spontaneous PTB, we excluded pregnancies ending in miscarriage and those with iatrogenic PTB. In the investigation of the relationship between CH and iatrogenic PTB, we excluded pregnancies ending in miscarriage and those with spontaneous PTB.

SGA and LGA neonates were defined as those with birth weight <5th and <10th percentile or above the 95th and 90th percentile for gestational age, respectively, without adjustment for maternal characteristics.[8] In the investigation of the relationship between CH and SGA or LGA, we excluded pregnancies ending in miscarriage.

Emergency CS included all cases where such delivery was undertaken after the onset of labor, usually for failure to progress, fetal distress or intrapartum hemorrhage. This group also included cases of antepartum hemorrhage requiring CS. Elective CS was performed before the onset of labor for obstetric or medical indications or at the request of the mother. In the investigation of the relationship between CH and emergency CS, we excluded pregnancies ending in miscarriage and those with elective CS. In the investigation of the relationship between CH and elective CS, we excluded pregnancies ending in miscarriage and those with emergency CS.

Statistical Analysis

Comparison of the maternal characteristics and obstetric history between pregnancies with and without CH was by the χ2-square test or Fisher's exact test for categorical variables and Mann-Whitney U-test for continuous variables, respectively. Multivariable logistic regression analysis was performed to examine the effect of age, weight and racial origin on the incidence of CH in the study population.

Univariable logistic regression analysis was performed to examine the association between CH and each of the adverse pregnancy outcomes. The risk for each of the pregnancy outcomes was then calculated from the formula: odds/(1 + odds), where odds = e^{Y}, and Y was derived from the univariable logistic regression analysis. Multivariable logistic regression analysis was performed for the prediction of each pregnancy outcome from maternal age, weight, height, racial origin, mode of conception, smoking, medical history (CH, diabetes, SLE or APS), history of adverse outcome in a previous pregnancy (PE, GDM, late miscarriage, stillbirth, birth of SGA or LGA neonate, spontaneous or iatrogenic PTB and CS), and family history of PE or diabetes mellitus. Prior to performing the multivariable regression analysis, continuous variables were centered by subtracting the mean from each measured value (69 from maternal weight in kg, 164 from maternal height in centimeters and 30 from maternal age in years). In case of continuous variables, the association with each adverse outcome was assessed to determine whether the relationship was linear or non-linear by introducing linear, quadratic, and cubic terms in the regression model. If non-linear trends were significant they were introduced in the model as such, otherwise, linear terms were used.

The statistical software package SPSS Statistics 20.0 (SPSS Inc., Chicago, Ill., USA) was used for data analyses.

Results

Study population

A flow chart of study participants is shown in Figure 1. During the study period, first-trimester combined screening for aneuploidies was carried out in 116,441 singleton pregnancies. We excluded from further analysis 6,509 (5.6%) women because there were no or incomplete data on pregnancy outcome (n=4,248), prenatal or postnatal diagnosis of aneuploidy or major defect or pregnancy termination for psychosocial reasons (n=1,999) and miscarriage at <16 weeks' gestation (n=262).

In the 109,932 pregnancies included in the study there were 1,417 (1.3%) who reported a medical history of CH. Maternal characteristics, medical history and previous obstetric history in those with and without CH are compared in Table 1. In the CH group there was a significantly higher age and weight and higher incidence of Afro-Caribbean racial origin, medical history of SLE or APS and diabetes mellitus, family history of PE and diabetes mellitus and previous obstetric history of late miscarriage, stillbirth, PE, GDM, SGA, LGA, spontaneous and iatrogenic PTB and CS.

In the study population the incidence of CH increased exponentially with maternal age and weight (Figure 2) and compared to Caucasian women it was higher in those of Afro-Caribbean racial origin (OR 3.03, 95% CI 2.71-3.39) and South Asian origin (1.93, 95% CI 1.46-2.54).

Univariable logistic regression analysis demonstrated that CH was significantly associated with late miscarriage, stillbirth, PE, birth of SGA neonates, GDM, spontaneous and iatrogenic PTD and both elective and emergency CS, but not the birth of LGA neonates (Table 2). The overall incidence of SGA neonates in patients with CH was twice as high as that in the group without CH, but the incidence of SGA in patients that developed PE was similar in those with or without CH. In the group that did not develop PE, the incidence of SGA was higher in those with than without CH.

The results of multivariable logistic regression analysis for the prediction of pregnancy complications from maternal characteristics, medical history and previous obstetric history are summarized in Tables 3-11; CH provided significant independent contribution to stillbirth (OR 2.38, 95% CI 1.51-3.75), PE (OR 5.76, 95% CI 4.93-6.73), SGA <10^{th} percentile (OR 2.06, 95% CI 1.79-2.39), LGA >90^{th} percentile (OR 0.65, 0.51-0.83), GDM (OR 1.61, 95% CI 1.27-2.05), iatrogenic PTB <37 weeks (OR 3.73, 95% CI (3.07-4.53) and elective CS (OR 1.79, 95% CI 1.52-2.11), but not late miscarriage, spontaneous PTB or emergency CS.

In the stillbirths from the group with CH, compared to those without CH, the median gestational age at birth was lower [28.2, interquartile range (IQR) 26.1-32.7 weeks vs median 35.4, IQR 28.1-39.3 weeks; p=0.002] and there was a higher proportion with PE (59.1% vs 9.1%, p<0.0001), SGA <10^{th} percentile (81.8% vs 39.1%, p<0.0001) and PE or SGA (90.9% vs 41.5%, p<0.001) (Figure 3).

In the group without CH the mean birth weight z-score was 0.0 and one standard deviation was 1.1; the distribution of birth weight in the group with CH was shifted to the left with mean z-score of -0.22 and standard deviation of 1.2 (p<0.0001; Figure 4).

The incidence of iatrogenic PTB at <37 weeks was 12% in those with CH and 2% in those without CH. In the CH group the indications for iatrogenic delivery were fetal growth restriction, PE or fetal death in 79% (126/160) of cases and CH *per se* in 19 (12%). In pregnancies without CH the indications for iatrogenic delivery were fetal growth restriction, PE or fetal death in 61% (1,236/2,033).

Odds ratios, for the risk of pregnancy complications from CH, after adjustment for maternal characteristics, medical history and previous obstetric history, are shown in Figure 5.

Discussion

The incidence of CH increases with maternal age and weight and is three-times higher in women of Afro-Caribbean racial origin and twice as high in those of South Asian origin, compared to Caucasian women. In our multiracial inner city population the incidence of CH was 1.3%, but inevitably this rate will vary with the demographic characteristics of different study populations. Previous studies in non-pregnant populations have also documented that the incidence of CH increases with age and weight and is higher in Black than in White individuals.[9,10]

Pregnancy in women with CH, after adjustment for other maternal characteristics, medical history and obstetric history, is associated with increased risk for a wide range of adverse pregnancy outcomes, including stillbirth, PE, SGA, GDM, iatrogenic PTB and elective CS, decreased risk for LGA, and does not have a significant effect on the incidence of late miscarriage, spontaneous PTB or emergency CS.

In this study the patients were recruited at 11-13 weeks' gestation when the fetuses were demonstrated to be alive and we therefore examined the rate of late rather than total miscarriage. Early miscarriages are often the consequence of severe chromosomal abnormalities, whereas the two most likely causes of late miscarriage are extreme placental impairment or extreme early spontaneous delivery of a fetus that dies during labor and / or delivery. We found that the incidence of late miscarriage was not significantly increased in pregnancies with CH.

The risk of stillbirth in patients with CH, after adjustment for confounding factors, was 2.4 times higher than in those without CH. This finding is compatible with the adjusted odds ratio of 2.6 observed in a systematic review and meta-analysis of 96 population-based studies in developed countries.[11] The increased risk of stillbirth in patients with CH is likely to be the consequence of severe early onset impaired placental perfusion and function; in the CH group, compared to those without CH, the gestational age at stillbirth was substantially lower (28 vs 35 weeks) and the proportion with PE or SGA was much higher (91% vs 42%). In the group without CH many of the stillbirths in the UK are potentially avoidable if the current policy of antenatal monitoring by abdominal palpation or measurement of the symphysis-fundal height is replaced by routine ultrasound examination in the third trimester; most stillbirths in SGA fetuses occur after 32 weeks' gestation and could be avoided by timely delivery. In contrast, stillbirths in the group of CH may be unavoidable because they occur early and the fetuses may be too small to be viable; 68% (15/22) of stillbirths in this study occurred at <29 weeks' gestation and 93% (14/15) of these were SGA. Strategies for prevention of stillbirth in pregnancies with

CH should focus on pharmacological interventions in early pregnancy to improve placentation.

Superimposed PE complicated 23% of pregnancies with CH. The incidence of preterm PE was 8.5% and term PE 14.3% which could lead to the erroneous conclusion that CH is more closely associated with term rather than preterm PE. However, a higher incidence of term than preterm PE was also observed in pregnancies without PE (1.5% vs. 0.6%). After adjustment for confounding factors the risk of both preterm and term PE was 5-6 times higher in women with CH than in those without CH. We have previously reported the use of multivariate analysis to estimate the risk for PE from maternal characteristics and medical history and demonstrated that the strongest risk factor is CH.[12] In our survival model for prediction of PE we proposed that all women will develop PE if pregnancy continued indefinitely and in a low-risk population the mean gestational age at delivery with PE is 55 weeks; in CH the distribution of delivery with PE is shifted to the left by eight weeks with a consequent increase in the incidence of both preterm and term PE.[12]

In pregnancies with CH the incidence of SGA neonates was twice as high as in pregnancies without CH. It was previously suggested that such an association is the mere consequence of PE and that CH in the absence of PE does not increase the risk of SGA.[13] We found that the incidence of SGA in patients that develop PE is considerably higher than in those without PE both in the CH group and in those without CH. However, even in the group of patients with CH that did not develop PE there was a 1.8-fold increase in the risk for SGA. Furthermore, in the CH group the distribution of birth weight adjusted for the gestational age at birth was Gaussian, rather than bimodal, and this was shifted to the left of the distribution of pregnancies without CH, suggesting that CH *per se* is associated with impaired placental perfusion and function.

In the univariate analysis the incidence of LGA neonates was similar in those with and without CH. However, in the multivariate analysis, after adjustment for other factors in maternal characteristics, medical history and obstetric history, CH was associated with a highly significant reduction in the risk of LGA neonates reflecting the overall effect on shifting the distribution in birth weight to the left.

In women with CH the incidence of GDM was substantially higher than in those without CH (8.1% vs. 2.3%). After adjusting for maternal age and weight, Afro-Caribbean, South Asian and East Asian racial origin, conception by the use of ovulation induction drugs, family history of diabetes mellitus and history of previous pregnancies affected by GDM and birth of LGA neonates, factors that are known to increase the risk of GDM,[14] the odds ratio for GDM in pregnancies with CH was 1.6. The association between CH and GDM may be explained by the increased insulin resistance, chronic inflammation and endothelial dysfunction observed in both conditions.[15,16]

Previous studies have documented an association between CH and increased rates of PTB and CS.[1] Our study has clarified that after adjustment for confounding factors, CH was associated with a 3.7-fold increase in risk for iatrogenic PTB and 1.8-fold increase in risk for elective CS, without a significant effect on spontaneous PTB or emergency CS. Consequently, the association of CH with PTB is the result of medical intervention due to fetal growth restriction, PE or fetal death, which accounted for about 80% of iatrogenic PTBs, rather than CH *per se* being implicated in the pathogenesis of spontaneous onset of labor or PPROM. Similarly, the association with increased rate of CS is the

consequence of elective surgery rather than emergency CS for failure to progress or intrapartum fetal distress.

The strengths of this study include first, prospective collection of data from a large inner city multiracial population, second, accurate assessment of gestational age and use of a wide range of well-defined adverse pregnancy outcomes, and third, application of multivariable logistic regression analysis to control for risk factors associated with each adverse outcome. The diagnosis of CH was based on the medical history obtained from women at the time of their hospital visit at 11-13 weeks and the incidence may therefore be underestimated, because we did not include cases where the diagnosis was made during the current pregnancy. A limitation of the study is that we did not examine the effect of baseline blood pressure or antihypertensive treatments on outcome but these are beyond the scope of the current investigation.

In the proposed new pyramid of pregnancy care estimation of patient and disease specific risk for pregnancy complications and any possible therapeutic interventions should be undertaken at the 11-13 weeks hospital visit.[17] The importance of screening for CH at the booking visit in pregnancy with subsequent increased antenatal surveillance is supported by the National Institute for Health and Clinical Excellence (NICE) in the UK.[18] However, there is lack of national and/or international guidance on the management of CH in pregnancy. Future studies will determine whether the incidence of pregnancy complications in women with CH can be reduced by such measures as strict control of blood pressure or the use of aspirin or pravastatin soon after the 11-13 weeks visit.

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Figure legends

Figure 1. Flow chart of study participants.

Figure 2. Relationship between maternal age and weight with the incidence of chronic hypertension.

Figure 3. Birth weight and gestational age at birth of stillbirths from the chronic hypertension (CH) group (left) and those without CH (right). Closed circles are the cases with preeclampsia.

Figure 4. Distribution of birth weight z-scores in pregnancies with chronic hypertension (red curve) and without chronic hypertension (blue curve).

Figure 5. Forrest plot of odds ratios with 95% confidence intervals, for the risk of pregnancy complications from chronic hypertension, after adjustment for maternal characteristics, medical history and previous obstetric history.

Table 1. Maternal characteristics, medical and obstetric history in pregnancies with and without chronic hypertension.

Maternal characteristics	**Chronic hypertension (n=1,417)**	**No chronic hypertension (n=108,515)**
GA at recruitment (weeks), median (IQR)	12.7 (12.3-13.1)	12.7 (12.3-13.1)
Age (years), median (IQR)	34.6 (30.7-38.4) **	30.9 (26.3-34.9)
Weight (kg), median (IQR)	81.5 (69.0-95.3) **	66.5 (59.0-77.0)
Height (cm), median (IQR)	164.4 (160.0-169.0)	164.3 (160.0-168.8)
Racial origin		
Caucasian, n (%)	731 (51.6)	82,066 (75.6)
Afro-Caribbean, n (%)	599 (42.3) **	17,289 (15.9)
South Asian, n (%)	55 (3.9)	4,480 (4.1)
East Asian, n (%)	14 (1.0) *	2,080 (1.9)
Mixed, n (%)	18 (1.3) **	2,600 (2.4)
Method of conception		
Spontaneous, n (%)	1,362 (96.1)	105,011 (96.8)
Ovulation drugs, n (%)	21 (1.5)	1,382 (1.3)
In vitro fertilization, n (%)	34 (2.4)	2,122 (2.0)
Cigarette smoking, n (%)	101 (7.1) **	11,551 (10.6)
History of SLE / APS, n (%)	16 (1.1) **	189 (0.2)
History of diabetes mellitus		
Type I, n (%)	20 (1.4) **	450 (0.4)
Type II, n (%)	65 (4.6) **	448 (0.4)
Family history of PE	144 (10.2) **	4,397 (4.1)
Family history of diabetes mellitus		
First degree, n (%)	267 (18.8) **	12,958 (11.9)
Second degree, n (%)	95 (6.7)	8,535 (7.9)
Obstetric history		
Nulliparous, n (%)	454 (32.0) **	50,969 (47.0)
Previous late miscarriage, n (%)	67 (4.7) **	1,308 (1.2)
Previous stillbirth, n (%)	49 (3.5) **	856 (0.8)
Previous PE, n (%)	312 (22.0) **	3,318 (3.1)
Previous GDM, n (%)	50 (3.5) **	1,534 (1.4)
Previous SGA <10th, n (%)	176 (12.4) **	6,700 (6.2)
Previous LGA >90th, n (%)	134 (9.5) **	6,193 (5.7)
Previous spontaneous PTB <37 w, n (%)	85 (6.0) **	3,414 (3.1)
Previous iatrogenic PTB <37 w, n (%)	134 (9.5) **	1,852 (1.7)
Previous CS, n (%)	343 (24.2) **	13,499 (12.4)

IQR = interquartile range; SLE = systemic lupus erythematosus; APS = antiphospholipid syndrome; PE = preeclampsia; GDM = gestational diabetes mellitus; SGA = birth weight <10th percentile; LGA = birth weight >10th percentile; PTB = preterm birth <37 weeks; CS = cesarean section

*p<0.05
**p<0.01

Table 2. Univariate logistic regression analysis demonstrating the association of chronic hypertension with pregnancy complications

Pregnancy complication	Chronic hypertension	No chronic hypertension	OR (95% CI)	P value
Fetal loss				
Late miscarriage, n/N (%)	29/1,417 (2.0)	776/108,515 (0.7)	2.56 (1.81 - 3.61)	<0.0001
Stillbirth, n/N (%)	22/1,388 (1.6)	427/107,739 (0.4)	4.05 (2.63 - 6.23)	<0.0001
Preeclampsia				
All, n/N (%)	286/1,388 (20.6)	2,274/107,739 (2.1)	12.0 (10.5 - 13.8)	<0.0001
< 37 weeks, n/N (%)	102/1,204 (8.5)	614/106,079 (0.6)	15.9 (12.8 - 19.8)	<0.0001
≥ 37 weeks, n/N (%)	184/1,286 (14.3)	1660/107,125 (1.5)	10.6 (9.0 - 12.5)	<0.0001
Small for gestational age				
Birth weight <5th percentile, n/N (%)	159/1,388 (11.5)	5,945/107,739 (5.5)	2.22 (1.87 - 2.62)	<0.0001
With preeclampsia, n/N (%)	62/286 (21.7)	434/2,274 (19.1)	1.17 (0.87 - 1.58)	0.296
Without preeclampsia, n/N (%)	97/1,102 (8.8)	5,511/105,465 (5.2)	1.75 (1.42 - 2.16)	<0.0001
Birth weight <10th percentile, n/N (%)	267/1,388 (19.2)	11,768/107,739 (10.9)	1.94 (1.70 - 2.22)	<0.0001
With preeclampsia, n/N (%)	87/286 (30.4)	648/2,274 (28.5)	1.10 (0.84 - 1.43)	0.498
Without preeclampsia, n/N (%)	180/1,102 (16.3)	11,120/105,465 (10.5)	1.66 (1.41 - 1.95)	<0.0001
Large for gestational age				
Birth weight >90th percentile, n/N (%)	135/1,388 (9.7)	10,823/107,739 (10.0)	0.97 (0.81 - 1.15)	0.694
Birth weight >95th percentile, n/N (%)	82/1,388 (5.9)	6113/107,739 (5.7)	1.04 (0.83 - 1.31)	0.708
Gestational diabetes mellitus, n/N (%)	104/1,284 (8.1)	2,438/106,504 (2.3)	3.50 (2.85-4.29)	<0.0001
Spontaneous preterm birth				
< 34 weeks, n/N (%)	24/1,317 (1.8)	1,017/107,007 (1.0)	1.93 (1.29 - 2.91)	0.002
< 37 weeks, n/N (%)	54/1,224 (4.4)	3,882/105,579 (3.7)	1.21 (0.92 - 1.59)	0.175
Iatrogenic preterm birth				
< 34 weeks, n/N (%)	69/1,362 (5.1)	661/106,651 (0.6)	8.56 (6.64 - 11.03)	<0.0001
< 37 weeks, n/N (%)	160/1,330 (12.0)	2,033/101,697 (2.0)	6.84 (5.77 - 8.12)	<0.0001
Cesarean section				
Elective, n/N (%)	354/1,127 (31.4)	12,034/92,365 (13.0)	3.06 (2.69 - 3.47)	<0.0001
Emergency, n/N (%)	261/1,034 (25.2)	15,374/95,705 (16.1)	1.76 (1.53-2.03)	<0.0001

OR = odds ratio; CI = confidence interval

Table 3. Logistic regression analysis for the prediction of late miscarriage by maternal factors, medical history and obstetric history.

Independent variable	**Miscarriage**	
	OR (95% CI)	**p**
(Maternal age in years – 30)	1.03 (1.01-1.04)	<0.0001
(Maternal weight in kg – 69)	1.01 (1.01-1.02)	<0.0001
(Maternal height in meters – 1.64)	0.98 (0.97-0.99)	0.004
Racial origin		
Caucasian (Reference)	1.00	
Afro-Caribbean	3.34 (2.85-3.90)	<0.0001
South Asian	1.67 (1.18-2.37)	0.004
East Asian	1.46 (0.85-2.51)	0.169
Mixed	2.39 (1.65-3.48)	<0.0001
Conception		
Spontaneous (Reference)	1.00	
Ovulation drugs	3.55 (2.47-5.10)	<0.0001
In vitro fertilization	1.79 (1.19-2.69)	0.005
Cigarette smoking	1.23 (0.97-1.57)	0.092
History of chronic hypertension	**1.33 (0.90-1.97)**	**0.158**
History of SLE / APS	0.76 (0.19-3.14)	0.706
History of diabetes mellitus		
None (Reference)	1.00	
Type I	1.76 (1.78-3.99)	0.177
Type II	1.22 (0.64-2.35)	0.547
Obstetric history		
No previous pregnancy $\geq$16 weeks (Reference)	1.00	
Pregnancies with late miscarriage	4.41 (3.34-5.82)	<0.0001
Pregnancies without late miscarriage	0.86 (0.74-1.00)	0.053

OR=odds ratio; CI=confidence interval; SLE = systemic lupus erythematosus; APS = antiphospholipid syndrome.

Table 4. Logistic regression analysis for the prediction of stillbirth by maternal factors, medical history and obstetric history.

Independent variable	Stillbirth	
	OR (95% CI)	**p**
(Maternal age in years – 30)	1.00 (0.99-1.02)	0.736
(Maternal weight in kg – 69)	1.01 (1.01-1.02)	<0.0001
(Maternal height in meters – 1.64)	0.98 (0.96-0.99)	0.006
Racial origin		
Caucasian (Reference)	1.00	
Afro-Caribbean	2.14 (1.72-2.66)	<0.0001
South Asian	1.23 (0.76-2.01)	0.404
East Asian	0.96 (0.42-2.17)	0.920
Mixed	1.26 (0.69-2.30)	0.459
Conception		
Spontaneous (Reference)	1.00	
Ovulation drugs	2.02 (1.10-3.70)	0.023
In vitro fertilization	1.67 (0.94-2.95)	0.080
Cigarette smoking	1.70 (1.29-2.23)	<0.0001
History of chronic hypertension	**2.38 (1.51-3.75)**	**<0.0001**
History of SLE / APS	0.78 (0.11-5.66)	0.806
History of diabetes mellitus		
None (Reference)	1.00	
Type I	4.51 (2.30-8.85)	<0.0001
Type II	1.84 (0.85-4.01)	0.123
Obstetric history		
Nulliparous (Reference)	1.00	
Parous with previous stillbirth	3.94 (2.49-6.23)	<0.000.1
Parous without previous stillbirth	0.74 (0.61-0.91)	0.003

OR=odds ratio; CI=confidence interval; SLE = systemic lupus erythematosus; APS = antiphospholipid syndrome.

Table 5. Logistic regression analysis for the prediction of all preeclampsia and preeclampsia with delivery at <37 and ≥37 weeks' gestation by maternal factors, medical history and obstetric history.

Independent variable	All pre-eclampsia		Pre-eclampsia at <37 w		Pre-eclampsia at ≥37 w	
	OR (95% CI)	p	OR (95% CI)	p	OR (95% CI)	p
(Maternal age in years - 30)	1.01 (1.00-1.02)	0.031	1.02 (1.00-1.03)	0.018	1.01 (1.00-1.02)	0.117
(Maternal age in years - 30)^2	1.00 (1.00-1.00)	0.001	-	-	-	-
(Maternal weight in kg - 69)	1.02 (1.01-1.02)	<0.0001	1.02 (1.01-1.02)	<0.0001	1.03 (1.02-1.04)	<0.0001
(Maternal weight in kg - 69)^2	1.00 (1.00-1.00)	<0.0001	-	-	1.00 (1.00-1.00)	<0.0001
(Maternal height in cm - 164)	0.96 (0.96-0.97)	<0.0001	0.96 (0.95-0.97)	<0.0001	0.97 (0.96-0.98)	<0.0001
Racial origin						
Caucasian (Reference)	1.00		1.00		1.00	
Afro-Caribbean	2.16 (1.97-2.37)	<0.0001	2.85 (2.41-3.37)	<0.0001	1.95 (1.75-2.17)	<0.0001
South Asian	1.39 (1.14-1.70)	0.001	1.68 (1.20-2.36)	0.003	1.24 (0.98-1.59)	0.078
East Asian	1.12 (0.81-1.56)	0.489	0.79 (0.39-1.60)	0.503	1.23 (0.85-1.78)	0.266
Mixed	1.07 (0.80-1.42)	0.668	1.38 (0.83-2.28)	0.213	0.97 (0.68-1.37)	0.849
Conception						
Spontaneous (Reference)	1.00		1.00		1.00	
Ovulation drugs	1.03 (0.73-1.47)	0.851	1.71 (1.01-2.90)	0.047	0.81 (0.51-1.28)	0.370
In vitro fertilization	1.69 (1.35-2.11)	<0.0001	2.35 (1.63-3.39)	<0.0001	1.53 (1.17-2.00)	0.002
Cigarette smoking	0.82 (0.70-0.95)	0.010	1.03 (0.78-1.36)	0.853	0.77 (0.64-0.93)	0.006
History of chronic hypertension	**5.76 (4.93-6.73)**	**<0.0001**	**6.23 (4.83-8.04)**	**<0.0001**	**5.41 (4.50-6.51)**	**<0.0001**
History of SLE / APS	1.77 (0.96-3.24)	0.067	3.58 (1.61-7.94)	0.002	1.11 (0.47-2.61)	0.808
History of diabetes mellitus						
None (Reference)	1.00		1.00		1.00	
Type I	1.62 (1.04-2.52)	0.033	3.51 (1.96-6.28)	<0.0001	0.95 (0.50-1.82)	0.885
Type II	1.01 (0.67-1.52)	0.966	1.81 (1.04-3.13)	0.035	0.67 (0.39-1.17)	0.159
Family history of preeclampsia	1.57 (1.34-1.83)	<0.0001	1.77 (1.35-2.32)	<0.0001	1.46 (1.21-1.75)	<0.0001
Obstetric history						
Nulliparous (Reference)	1.00		1.00		1.00	
Parous with previous preeclampsia	1.77 (1.54-2.03)	<0.0001	2.11 (1.67-2.68)	<0.0001	1.59 (1.35-1.87)	<0.0001
Parous without previous preeclampsia	0.32 (0.29-0.36)	<0.0001	0.34 (0.29-0.41)	<0.0001	0.32 (0.28-0.36)	<0.0001

OR=odds ratio; CI=confidence interval; SLE = systemic lupus erythematosus; APS = antiphospholipid syndrome; SGA = small for gestational age.

Table 6. Logistic regression analysis for the prediction of small for gestational age neonates by maternal factors, medical history and obstetric history.

Independent variable	SGA <5th percentile		SGA <10th percentile	
	OR (95% CI)	p	OR (95% CI)	p
(Maternal age in years - 30)	1.01 (1.00-1.02)	<0.0001	1.01 (1.00-1.01)	<0.0001
(Maternal age in years - 30)^2	1.00 (1.00-1.00)	<0.0001	1.00 (1.00-1.00)	<0.0001
(Maternal weight in kg – 69)	0.98 (0.98-0.98)	<0.0001	0.99 (0.98-0.99)	<0.0001
(Maternal weight in kg – 69)^2	1.00 (1.00-1.00)	<0.0001	1.00 (1.00-1.00)	<0.0001
(Maternal height in cm – 164)	0.96 (0.95-0.96)	<0.0001	0.96 (0.95-0.96)	<0.0001
Racial origin				
Caucasian (Reference)	1.00		1.00	
Afro-Caribbean	2.27 (2.13-2.43)	<0.0001	2.13 (2.02-2.24)	<0.0001
South Asian	2.10 (1.89-2.33)	<0.0001	1.91 (1.76-2.07)	<0.0001
East Asian	1.24 (1.04-1.47)	0.015	1.07 (0.94-1.23)	0.307
Mixed	1.52 (1.30-1.78)	<0.0001	1.46 (1.30-1.65)	<0.0001
Conception				
Spontaneous (Reference)	1.00		1.00	
Ovulation drugs	1.42 (1.15-1.76)	0.001	1.41 (1.20-1.65)	<0.0001
In vitro fertilization	1.00 (0.83-1.22)	0.976	1.02 (0.89-1.17)	0.776
Cigarette smoking	2.77 (2.58-2.98)	<0.0001	2.46 (2.32-2.60)	<0.0001
History of chronic hypertension*	**2.23 (1.87-2.67)**	**<0.0001**	**2.06 (1.79-2.39)**	**<0.0001**
History of SLE / APS	1.59 (0.95-2.67)	0.080	1.42 (0.94-2.15)	0.095
History of diabetes mellitus				
None (Reference)	1.00		1.00	
Type I	0.37 (0.19-0.72)	0.003	0.39 (0.25-0.62)	<0.0001
Type II	1.40 (1.00-1.96)	0.054	1.10 (0.83-1.46)	0.513
Obstetric history				
Nulliparous (Reference)	1.00		1.00	
Parous with previous SGA <10th	1.34 (1.23-1.46)	<0.0001	1.42 (1.33-1.52)	<0.0001
Parous without previous SGA <10th	0.39 (0.37-0.42)	<0.0001	0.41 (0.39-0.43)	<0.0001

OR=odds ratio; CI=confidence interval; SLE = systemic lupus erythematosus; APS = antiphospholipid syndrome; SGA = small for gestational age.

* Logistic regression analysis after exclusion of cases of cases of SGA associated with preeclampsia demonstrated that there was still a significant contribution of chronic hypertension for prediction of both SGA <5th percentile (OR 1.82, 95% CI 1.46-2.28) and SGA <10th percentile (OR 1.81, 95% CI 1.53-2.15).

Table 7. Logistic regression analysis for the prediction of large for gestational age neonates by maternal factors, medical history and obstetric history.

Independent variable	LGA >90th percentile		LGA >95th percentile	
	OR (95% CI)	p	OR (95% CI)	p
(Maternal age in years - 30)	1.00 (0.99-1.00)	0.428	1.00 (0.99-1.00)	0.526
(Maternal weight in kg – 69)	1.04 (1.03-1.04)	<0.0001	1.04 (1.04-1.04)	<0.0001
(Maternal weight in kg – 69)^2	1.00 (1.00-1.00)	<0.0001	1.00 (1.00-1.00)	<0.0001
(Maternal height in cm – 164)	1.03 (1.03-1.04)	<0.0001	1.03 (1.03-1.04)	<0.0001
Racial origin				
Caucasian (Reference)	1.00		1.00	
Afro-Caribbean	0.48 (0.45-0.52)	<0.0001	0.52 (0.48-0.57)	<0.0001
South Asian	0.62 (0.54-0.72)	<0.0001	0.64 (0.53-0.77)	<0.0001
East Asian	0.92 (0.77-1.11)	0.390	0.93 (0.73-1.20)	0.581
Mixed	0.73 (0.63-0.85)	<0.0001	0.74 (0.61-0.90)	0.003
Conception				
Spontaneous (Reference)	1.00		1.00	
Ovulation drugs	1.04 (0.87-1.24)	0.684	1.06 (0.84-1.33)	0.613
In vitro fertilization	1.06 (0.91-1.23)	0.475	1.17 (0.96-1.41)	0.115
Cigarette smoking	0.46 (0.43-0.50)	<0.0001	0.48 (0.43-0.54)	<0.0001
History of chronic hypertension	**0.65 (0.53-0.78)**	**<0.0001**	**0.65 (0.51-0.83)**	**<0.0001**
History of SLE / APS	1.04 (0.67-1.62)	0.855	0.67 (0.34-1.29)	0.231
History of diabetes mellitus				
None (Reference)	1.00		1.00	
Type I	4.03 (3.27-4.97)	<0.0001	4.99 (3.98-6.26)	<0.0001
Type II	1.61 (1.27-2.03)	<0.0001	1.66 (1.26-2.18)	<0.0001
Obstetric history				
Nulliparous (Reference)	1.00		1.00	
Parous with previous LGA >90th	5.65 (5.30-6.03)	<0.0001	5.94 (5.50-6.42)	<0.0001
Parous without previous LGA >90th	1.38 (1.31-1.44)	<0.0001	1.31 (1.23-1.40)	<0.0001

OR=odds ratio; CI=confidence interval; SLE = systemic lupus erythematosus; APS = antiphospholipid syndrome; LGA = large for gestational age.

Table 8. Logistic regression analysis for the prediction of gestational diabetes mellitus by maternal factors, medical history and obstetric history.

Independent variable	Gestational diabetes mellitus	
	OR (95% CI)	p
(Maternal age in years - 30)	1.07 (1.06-1.08)	<0.0001
(Maternal age in years - 30)^2	1.00 (0.99-1.00)	0.009
(Maternal weight in kg – 69)	1.05 (1.04-1.05)	<0.0001
(Maternal weight in kg – 69)^2	1.00 (1.00-1.00)	<0.0001
(Maternal height in cm – 164)	0.95 (0.94-0.95)	<0.0001
Racial origin		
Caucasian (Reference)	1.00	
Afro-Caribbean	1.56 (1.40-1.74)	<0.0001
South Asian	2.60 (2.21-3.07)	<0.0001
East Asian	2.79 (2.20-3.54)	<0.0001
Mixed	1.15 (0.86-1.54)	0.355
Conception		
Spontaneous (Reference)	1.00	
Ovulation drugs	1.40 (1.02-1.92)	0.040
In vitro fertilization	1.23 (0.95-1.59)	0.122
Cigarette smoking	0.87 (0.74-1.03)	0.113
History of chronic hypertension	**1.61 (1.27-2.05)**	**<0.0001**
History of SLE / APS	0.26 (0.06-1.12)	0.071
Family history of diabetes		
First degree relative	2.48 (2.24-2.75)	<0.0001
Second degree relative	1.89 (1.63-2.18)	<0.0001
Obstetric history		
Nulliparous (Reference)	1.00	
Parous with previous GDM	20.11 (17.57-23.02)	<0.0001
Parous without previous GDM	0.45 (0.41-0.50)	<0.0001
Parous with previous LGA >90th	1.80 (1.55-2.09)	<0.0001

OR=odds ratio; CI=confidence interval; SLE = systemic lupus erythematosus; APS = antiphospholipid syndrome; LGA = large for gestational age; GDM = gestational diabetes mellitus.

Table 9. Logistic regression analysis for the prediction of spontaneous preterm birth at <34 and <37 weeks' gestation by maternal factors, medical history and obstetric history.

Independent variable	Spontaneous preterm birth			
	<34 w		<37 w	
	OR (95% CI)	p	OR (95% CI)	p
(Maternal age in years - 30)	1.01 (0.99-1.02)	0.108	1.00 (0.99-1.00)	0.471
(Maternal weight in kg – 69)	1.00 (1.00-1.01)	0.180	1.00 (0.99-1.00)	0.008
(Maternal weight in kg – 69)^2	-	-	1.00 (1.00-1.00)	<0.0001
(Maternal height in cm –164)	0.98 (0.97-0.99)	<0.0001	0.99 (0.98-0.99)	<0.0001
Racial origin				
Caucasian (Reference)	1.00		1.00	
Afro-Caribbean	1.91 (1.65-2.23)	<0.0001	1.23 (1.13-1.34)	<0.0001
South Asian	1.41 (1.06-1.89)	0.019	1.18 (1.01-1.38)	0.040
East Asian	1.00 (0.62-1.64)	0.990	0.94 (0.74-1.20)	0.627
Mixed	1.49 (1.04-2.13)	0.031	1.11 (0.90-1.36)	0.324
Conception				
Spontaneous (Reference)	1.00		1.00	
Ovulation drugs	2.07 (1.37-3.12)	0.001	1.16 (0.88-1.53)	0.306
In vitro fertilization	1.87 (1.32-2.65)	<0.0001	1.53 (1.25-1.87)	<0.0001
Cigarette smoking	1.85 (1.56-2.20)	<0.0001	1.53 (1.39-1.68)	<0.0001
History of chronic hypertension	**1.35 (0.88-2.07)**	**0.166**	**1.03 (0.78-1.37)**	**0.832**
History of SLE / APS	3.31 (1.53-7.18)	0.002	2.46 (1.47-4.11)	0.001
History of diabetes mellitus				
None (Reference)	1.00		1.00	
Type I	4.36 (2.76-6.87)	<0.0001	4.42 (3.30-5.92)	<0.0001
Type II	1.46 (0.76-2.80)	0.251	1.61 (1.10-2.38)	0.015
Obstetric history				
Nulliparous (Reference)	1.00		1.00	
Parous with previous spontaneous birth <37 w	4.23 (3.52-5.08)	<0.0001	4.47 (4.03-4.97)	<0.0001
Parous without previous spontaneous birth <37 w	0.55 (0.48-0.64)	<0.0001	0.63 (0.58-0.68)	<0.0001

OR=odds ratio; CI=confidence interval; SLE = systemic lupus erythematosus; APS = antiphospholipid syndrome; PTB = preterm birth.

Table 10. Logistic regression analysis for the prediction of iatrogenic preterm birth at <34 and <37 weeks' gestation by maternal factors, medical history and obstetric history.

Independent variable	Iatrogenic preterm birth			
	<34 w		<37 w	
	OR (95% CI)	p	OR (95% CI)	p
(Maternal age in years - 30)	1.00 (0.99-1.02)	0.210	1.00 (0.99-1.01)	0.099
(Maternal weight in kg – 69)	1.01 (1.00-1.02)	<0.0001	1.01 (1.00-1.01)	<0.0001
(Maternal height in meters –1.64)	0.96 (0.95-0.97)	<0.0001	0.97 (0.96-0.98)	<0.0001
Racial origin				
Caucasian (Reference)	1.00		1.00	
Afro-Caribbean	1.89 (1.58-2.25)	<0.0001	1.45 (1.30-1.62)	<0.0001
South Asian	1.23 (0.86-1.77)	0.267	1.14 (0.92-1.41)	0.248
East Asian	1.32 (0.77-2.26)	0.320	0.81 (0.56-1.19)	0.288
Mixed	1.60 (1.05-2.45)	0.029	1.16 (0.88-1.54)	0.283
Conception				
Spontaneous (Reference)	1.00		1.00	
Ovulation drugs	1.44 (0.82-2.53)	0.200	1.45 (1.04-2.02)	0.029
In vitro fertilization	2.53 (1.76-3.65)	<0.0001	2.17 (1.71-2.75)	<0.0001
Cigarette smoking	1.70 (1.36-2.11)	<0.0001	1.81 (1.60-2.05)	<0.0001
History of chronic hypertension	**4.30 (3.23-5.72)**	**<0.0001**	**3.73 (3.07-4.53)**	**<0.0001**
History of SLE / APS	2.06 (0.81-5.27)	0.130	2.89 (1.66-5.04)	<0.0001
History of diabetes mellitus				
None (Reference)	1.00		1.00	
Type I	4.32 (2.65-7.04)	<0.0001	10.21 (7.85-13.26)	<0.0001
Type II	2.18 (1.21-3.72)	0.009	4.92 (3.69-6.56)	<0.0001
Parity				
Nulliparous (Reference)	1.00		1.00	
Parous with previous iatrogenic birth <37 w	5.18 (4.09-6.54)	<0.0001	6.35 (5.48-7.35)	<0.0001
Parous without previous iatrogenic birth <37 w	0.53 (0.44-0.62)	<0.0001	0.67 (0.61-0.74)	<0.0001

OR=odds ratio; CI=confidence interval; SLE = systemic lupus erythematosus; APS = antiphospholipid syndrome; PTB = preterm birth.

Table 11. Logistic regression analysis for the prediction of elective and emergency cesarean section by maternal factors, medical history and obstetric history.

Independent variable	Emergency cesarean section		Elective cesarean section	
	OR (95% CI)	p	OR (95% CI)	p
(Maternal age in years - 30)	1.05 (1.05-1.06)	<0.0001	1.06 (1.06-1.07)	<0.0001
(Maternal age in years - 30)^2	1.00 (0.99-1.00)	<0.0001	-	-
(Maternal weight in kg - 69)	1.02 (1.02-1.03)	<0.0001	1.02 (1.01-1.02)	<0.0001
(Maternal weight in kg - 69)^2	1.00 (1.00-1.00)	<0.0001	-	-
(Maternal height in cm - 164)	0.94 (0.94-0.95)	<0.0001	0.97 (0.96-0.97)	<0.0001
Racial origin				
Caucasian (Reference)	1.00		1.00	
Afro-Caribbean	1.37 (1.31-1.44)	<0.0001	0.84 (0.79-0.90)	<0.0001
South Asian	1.02 (0.93-1.11)	0.739	0.99 (0.89-1.11)	0.916
East Asian	1.01 (0.88-1.15)	0.915	0.89 (0.75-1.05)	0.175
Mixed	0.94 (0.83-1.07)	0.345	0.78 (0.66-0.91)	0.001
Conception				
Spontaneous (Reference)	1.00		1.00	
Ovulation drugs	0.98 (0.84-1.16)	0.836	1.18 (0.98-1.42)	0.081
In vitro fertilization	1.24 (1.11-1.39)	<0.0001	1.93 (1.69-2.20)	<0.0001
Cigarette smoking	1.10 (1.03-1.18)	0.004	1.05 (0.97-1.13)	0.236
History of chronic hypertension	**0.99 (0.85-1.17)**	**0.944**	**1.79 (1.52-2.11)**	**<0.0001**
History of SLE / APS	1.07 (0.71-1.62)	0.744	1.57 (1.02-2.40)	0.039
History of diabetes mellitus				
None (Reference)	1.00		1.00	
Type I	2.35 (1.84-3.01)	<0.0001	4.35 (3.33-5.68)	<0.0001
Type II	1.09 (0.84-1.43)	0.517	2.00 (1.54-2.60)	<0.0001
Obstetric history				
Nulliparous (Reference)	1.00		1.00	
Parous with previous CS	2.06 (1.95-2.18)	<0.0001	12.80 (12.11-13.52)	<0.0001
Parous without previous CS	0.19 (0.18-0.20)	<0.0001	0.53 (0.50-2.56)	<0.0001
Onset of labor				
Spontaneous (Reference)	1.00		-	-
Induced	2.42 (2.32-2.52)	<0.0001	-	-

OR=odds ratio; CI=confidence interval; SLE = systemic lupus erythematosus; APS = antiphospholipid syndrome; CS = cesarean section.