Prediction of adverse perinatal outcomes by the cerebroplacental ratio in women undergoing induction of labour

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Running Head: Preinduction CPR

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Abstract

Objective: To investigate the performance of screening for adverse perinatal outcome by the cerebroplacental ratio (CPR) measured within 24 hours of induction of labor.

Methods: This was a prospective observational study in 1,902 singleton pregnancies undergoing induction of labor at ≥ 37 weeks' gestation. Doppler ultrasound was used to measure the pulsatility index (PI) in the umbilical artery (UA) and fetal middle cerebral artery (MCA) before induction of labor. The measured UA PI and MCA PI and their ratio were converted to multiples of the median (MoM) after adjustment for gestational age. Univariate and multivariate logistic regression analysis was used to determine whether CPR improved the prediction of adverse perinatal outcome that was provided by maternal characteristics, medical history and obstetric factors. The detection rate (DR) and false-positive rate (FPR) of screening by CPR were estimated for cesarean section for presumed fetal distress and neonatal adverse outcome, which included umbilical arterial or venous cord blood pH ≤7 and ≤7.1, respectively, 5-minute Apgar score <7, admission to the neonatal intensive care unit (NICU) for >24 hours, or hypoxic ischemic encephalopathy.

Results: A combination of maternal and pregnancy characteristics, including age, weight, racial origin, previous obstetric history, preeclampsia, gestational age at delivery and amniotic fluid volume, identified 39% of pregnancies requiring cesarean section for fetal distress at FPR of 10%; addition of CPR did not improve the performance of screening. In screening for adverse neonatal outcome by a combination of parity and CPR the DR was 17% at FPR of 10%.

Conclusion: Low CPR, measured within 24 hours of induction of labor, is associated with increased risk of cesarean section for fetal distress and adverse neonatal outcome, but the performance of CPR for such surrogates of adverse perinatal outcome is poor.

Introduction

Doppler assessment of impedance to flow in the umbilical artery (UA), fetal middle cerebral artery (MCA) and the ratio of the pulsatility index (PI) in these vessels, or cerebroplacental ratio (CPR), are used for assessment of fetal oxygenation. In the 1980's studies of fetal blood obtained by cordocentesis from small for gestational age (SGA) fetuses demonstrated that increased impedance to flow in the UA and decreased impedance to flow in MCA are associated with fetal hypoxemia and acidemia.[1-4] Subsequent studies in SGA fetuses in the 1990's reported that low CPR was associated with adverse perinatal outcome, including higher rates of perinatal death, cesarean section for fetal distress in labor, neonatal acidosis, 5 minute Apgar scores <7, and neonatal intensive care unit (NICU) stay >24 hours.[5-7] Renewed interest in the CPR has be stimulated by the possibility that this index may be predictive of adverse perinatal outcome not only in SGA but also in appropriately grown for gestational age (AGA) fetuses. Prior *et al*, measured the CPR in 400 pregnancies with AGA fetuses immediately before established labor and reported that CPR <10th percentile, compared to those with CPR ≥10th percentile, was associated with a 6-fold increased risk for delivery by cesarean section for fetal distress and that in the group with CPR >90th percentile none had cesarean section for fetal distress.[8] Subsequent studies proposed that a low CPR can identify AGA fetuses that have not reached their growth potential as a consequence of suboptimal placental function,[9] and that low CPR, measured within two weeks of birth, is associated with the need for operative delivery for presumed fetal compromise and with neonatal unit admission at term regardless of the fetal size.[9-12] However, these studies examined high-risk pregnancies and did not report on the performance of CPR in the prediction of adverse outcome.

A screening study in 30,870 women with singleton pregnancies attending for a routine hospital visit at 30-34 weeks' gestation investigated the potential value of CPR in the prediction of adverse perinatal outcome and reported that although there was an association between CPR and birthweight Z-score, umbilical cord blood pH and admission to NICU, the performance of screening by CPR was poor with detection rates (DR) of 5-11% at a false positive rate (FPR) of 5%.[13] A possible explanation for such poor performance of screening was that the perinatal adverse events at term were too remote from the gestation at which CPR was assessed. However, another study of 6,178 singleton pregnancies routinely screened at 35-37 weeks' gestation, also reported significant associations between CPR and indicators of adverse perinatal outcome but again the performance of screening by CPR was poor with DR of 6-15%, at FPR of 6%.[14]

The objective of this study is to investigate whether the performance of screening by CPR for adverse perinatal outcome is improved by undertaking the assessment within 24 hours of induction of labor.

Methods

Study population

This data for this study were derived from a prospective observational study for prediction of adverse pregnancy outcomes following induction of labor during the period 1st May 2016 to 31st July 2018, at Medway Maritime Hospital, England. At our hospital, women booked for induction of labor attend the Pre-Induction Clinic within 24 hours prior to the administration of the induction agent. At this appointment, we recorded maternal characteristics, medical and obstetric history, and performed an ultrasound scan to first, determine presentation, second, estimate the fetal weight from measurements of fetal head circumference, abdominal circumference, and femur length,[15] third, assess amniotic fluid volume by measurement of deepest pool of fluid without any fetal parts and classifying oligohydramnios and polyhydramnios by a deepest pool of < 2 cm and > 8 cm, respectively, and fourth, to carry out transabdominal color Doppler for measurement of the PI in the UA and MCA.[16] Gestational age was determined by the measurement of fetal crown-rump length at 11-13 weeks or the fetal head circumference at 19-24 weeks.[17,18]

We included singleton pregnancies that were booked for induction of labor at ≥ 37 weeks' gestation and delivering phenotypically normal neonates. Written informed consent was obtained from the women agreeing to participate in the study, which was approved by London-Dulwich Research Ethics Committee (REC reference 16/LO/0367).

Patient characteristics

Patient characteristics recorded included maternal age, racial origin (White, Black, South Asian, East Asian and mixed), method of conception (spontaneous or assisted by use of ovulation induction drugs or *in vitro* fertilization), cigarette smoking during pregnancy, medical history of chronic hypertension or diabetes mellitus, obstetric complications such as obstetric cholestasis, gestational diabetes mellitus, gestational hypertension, or preeclampsia, and obstetric history (nulliparous if no previous pregnancies at ≥ 24 weeks and parous, with or without history of previous cesarean section). Maternal weight and height were measured.

The indications for induction of labor were postdates (n=710), maternal request (n=278), diabetes mellitus or gestational diabetes (n=150), obstetric cholestasis (n=86), chronic hypertension, preeclampsia or gestational hypertension (n=84), suspected SGA fetus (n=197), reduced fetal movements (n=180), suspected large for gestational age fetus (n=72), spontaneous prelabor amniorrhexis (n=98), polyhydramnios (n=31), maternal medical condition such cardiac disease (n=12), or antepartum haemorrhage (n=4).

Outcome measures

Data on pregnancy outcome were collected from the hospital maternity records. We obtained data for gestational age at delivery, mode of delivery (vaginal delivery or cesarean section), indication for cesarean section, birth weight, 5-minute Apgar score, umbilical arterial or venous pH and details of admission to neonatal intensive care unit (NICU). Adverse outcome was defined as first, cesarean section for presumed fetal distress in labor and second, adverse neonatal outcome (umbilical arterial or venous cord blood pH ≤7 and ≤7.1, respectively, 5-minute Apgar score <7, admission to the NICU for >24 hours and hypoxic ischemic encephalopathy). Cesarean section for presumed fetal distress in labor was carried out if there was evidence of a pathological electronic fetal heart rate pattern, a STAN event on fetal electrocardiogram analysis or fetal scalp pH < 7.1. In-utero interventions were attempted based on standard local guidelines and depending on the urgency for delivery. Hypoxic-ischemic encephalopathy was diagnosed when there was 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.

Statistical analysis

Data were expressed as median (interquartile range [IQR]) for continuous variables and n (%) for categorical variables. Mann-Whitney U-test and χ^2-square test or Fisher's exact test, were used for comparing outcome groups for continuous and categorical data, respectively. Significance was assumed at 5%.

Univariable and multivariable logistic regression analysis was carried out to determine which of the factors from maternal or pregnancy characteristics and measurements of fetal-placental Dopplers, provided a significant contribution in the prediction of cesarean section for fetal distress and adverse neonatal outcome. Prior to the regression analysis, the continuous variables, such as age, weight and height were centred by subtracting the arithmetic mean from each value to avoid effects of multicollinearity. Multiple categorical variables were dummy coded as binary variables to estimate the independent effect of each category. The measured UA PI and MCA PI and their ratio were converted to multiples of the median (MoM) after adjustment for gestational age.[16] The birth weight Z-score was derived from the normal range for gestational age.[15] We estimated cut-offs for 5th, 10th, 90th and 95th percentiles for UA PI, MCA PI, and CPR and determined the prevalence of abnormal Doppler values in each of the outcome groups. We examined the performance of CPR MoM in the sub-groups of SGA fetuses (birthweight <10th percentile) and non-SGA fetuses (birthweight ≥10th percentile). Predicted probabilities from logistic regression analysis were used to construct receiver operating characteristic (ROC) curves to assess performance of screening for these adverse outcomes. The area under ROC (AUROC) curves for fetal Doppler alone was compared to that obtained from all factors.[19]

The statistical package SPSS 24.0 (IBM SPSS Statistics for Windows, Version 24.0, Armonk, NY: IBM Corp; 2016) was used for data analyses.

Results

Study population

During the study period, there were 1,902 women who underwent an induction of labor and met the inclusion criteria. There were 1,408 (74.0%) vaginal deliveries and 494 (26.0%) that needed cesarean section, including 47 (9.5%) for failed induction, 181 (36.6%) for failure to progress, 258 (52.2%) for fetal distress and 8 (1.6%) for other indications.

Cesarean section for fetal distress

The maternal and pregnancy characteristics of those delivering by cesarean section for fetal distress are compared to those with vaginal delivery in Table 1. In pregnancies that required cesarean section for fetal distress, compared to those delivering vaginally, the median maternal age and weight were higher, there was a higher incidence of women of Black and South Asian racial origin, parous women with a previous cesarean section, PE, oligohydramnios and polyhydramnios and, higher median gestational age at delivery and UA PI MoM and lower CPR MoM, higher prevalence of UA PI MoM >90th percentile and CPR MoM <10th percentile.

Univariable regression analysis demonstrated that in prediction of cesarean section for fetal distress, there was a statistically significant contribution from maternal age and weight, Black and South Asian racial origin, parous women with previous vaginal delivery, PE, gestational age at delivery, amniotic fluid volume, UA PI MoM and CPR MoM (Table 2). Multivariable regression analysis demonstrated that in prediction of cesarean section for fetal distress, there was a statistically significant contribution from all above factors except UA PI MoM ($p=0.264$) ($R^2=0.209$; $p<0.0001$) (Table 2).

In screening for cesarean section for fetal distress by maternal factors, obstetric and medical history the DR was 39.1% at FPR of 10%; addition of CPR did not improve the performance of screening (AUROC: 0.767, 95% CI 0.733, 0.800 vs. 0.763, 95% CI 0.730, 0.796; p=0.271) (Figure 1). In SGA neonates, the performance of screening by maternal factors, obstetric and medical history (DR 30.9%, FPR 10%) was improved by the addition of CPR (DR 34.5%, FPR 10%; AUROC: 0.658, 95% CI 0.604, 0.710 vs. 0.672, 95% CI 0.617, 0.723; p=0.048).

The CPR was <10th percentile in 50.9% (28 of 55) of SGA neonates that were delivered by cesarean section for fetal distress and in 29.9% (79 of 264) of SGA neonates that were born vaginally (p=0.003). In the non-SGA neonates, the CPR was <10th percentile in 23.6% (48 of 203) of those delivered by cesarean section for fetal distress and in 20.2% (231 of 1,144) of those that were born vaginally (p=0.263).

Adverse neonatal outcome

The maternal and pregnancy characteristics of those with adverse neonatal outcome are compared to those without such outcome in Table 3. In pregnancies with adverse neonatal outcome, compared to those without, there was a lower incidence of parous women with previous vaginal birth, lower median MCA PI MoM and CPR MoM, and higher prevalence of CPR MoM <10th percentile.

Univariable regression analysis demonstrated that in prediction of adverse neonatal outcome, there was a statistically significant contribution from parity, MCA PI MoM and CPR MoM (Table 4). Multivariable regression analysis demonstrated that in prediction of adverse neonatal outcome there was a statistically significant contribution from parous women with a previous vaginal birth and CPR MoM but not MCA PI MoM (p=0.522) (R^2=0.025; p=0.001) (Table 4). The performance of screening by history alone in prediction of adverse neonatal outcome (DR 12.8% at FPR of 10%) was significantly improved by the addition of CPR (DR 16.9% at FPR of 10%; AUROC: 0.581, 95% CI 0.514, 0.647 vs. 0.632, 95% CI 0.573, 0.692; p=0.028) (Figure 1).

The CPR was <10th percentile in 31.3% (5 of 16) of SGA neonates with adverse neonatal outcome and in 34.2% (111 of 325) of SGA neonates without such adverse outcome (p=0.811). In the non-SGA neonates, the CPR was <10th percentile in 34.5% (19 of 55) of those with adverse neonatal outcome and in 19.8% (296 of 1,494) of those without adverse outcome (p=0.008).

Discussion

Principal findings of the study

The findings of this study of induction of labor demonstrate that about 80% of pregnancies requiring cesarean section for fetal distress in labor and those with adverse neonatal outcome deliver AGA neonates. Consequently, if a major contributor to these adverse events is impaired placentation the vast majority of such impairment is observed in association with AGA fetuses.

The study has also shown that there is a significant association between adverse perinatal outcome and CPR. This is not surprising because redistribution in the fetal circulation, with preferential blood flow to the brain at the expense of the viscera, has been demonstrated by cordocentesis to be associated with fetal hypoxemia and acidemia in both SGA and AGA fetuses.[1-4,20] However, the performance of CPR in screening for adverse perinatal outcome is poor even when the assessment is carried out within 24 hours of delivery.

A combination of maternal and pregnancy characteristics, including age, weight, racial origin, previous obstetric history, PE, gestational age at delivery and amniotic fluid volume, identified about 40% of the pregnancies requiring cesarean section for fetal distress, at FPR of 10%, and this performance of screening was not improved by addition of CPR. In screening by CPR $<10^{th}$ percentile the DR of cesarean section for fetal distress was 51% at FPR of 30% in SGA neonates and the respective values for non-SGA neonates were 24% and 20%. In the case of adverse neonatal outcome, the CPR was $<10^{th}$ percentile in 31% of SGA neonates at FPR of 34% and the respective values for non-SGA neonates were 35% and 20%.

Strengths and limitations of the study

The strengths of our study are first, examination of a large number of pregnancies within 24 hours of induction of labor, second, inclusion of a consecutive series of pregnancies undergoing induction of labor at term without exclusions according to fetal size or pregnancy complication so that the results can be generalizable, third, measurement of MCA-PI and UA-PI by appropriately-trained doctors, and fourth, use of a wide range of well accepted indicators for adverse perinatal outcome.

The main limitation of this and previous studies is the use of cesarean section for fetal distress and adverse neonatal outcome as surrogate markers of prelabor fetal hypoxia. It is therefore uncertain whether the low performance of CPR in the prediction of these adverse outcomes is a reflection that CPR provides poor assessment of fetal oxygenation or that the contribution of maternal and pregnancy characteristics as well as events in labor play a much greater role than prelabor fetal oxygentation in the development of fetal distress in labor or adverse neonatal outcome.

Another limitation of the study is that pregnancies undergoing induction of labor at term are preselected, because in some cases of SGA fetuses with abnormal Doppler results elective delivery by cesarean section would have been carried out; had induction of labor been undertaken is such cases it is likely that some would have ended up with cesarean section for fetal distress and asphyxia at birth reflected in low Apgar score, low cord blood pH and admission to NICU. Consequently, the performance of screening by CPR for adverse perinatal outcome in SGA fetuses would have been negatively biased.

Comparison with findings from previous studies

The results of our study are similar to our previous studies reporting on clinical utility of CPR measured at 32 and 36 weeks' gestation, which demonstrate that the performance of screening of CPR in prediction of adverse perinatal outcomes is poor with DR ranging from about 5 to 15%, at FPR of about 5%.[13,14]

Two previous studies examined the value of CPR in predicting adverse outcome in pregnancies undergoing induction of labor at ≥ 37 weeks' gestation. One study examined 164 women with SGA fetuses and reported that the DR and FPR of pre-induction CPR <5th percentile were 70% and 46%, respectively, for cesarean section for fetal distress and 66% and 40% for adverse neonatal outcome.[21] Another study in 151 AGA fetuses reported that the pre-induction CPR was not significantly different between those with operative delivery for intrapartum fetal compromise or umbilical arterial blood pH <7.0 and those with normal outcome; moreover, there was no significant association between CPR and cord blood pH.[22]

Implications for clinical practice

There are two potential benefits of measuring fetal CPR in a preinduction of labor clinic. First, identify pregnancies that are at such high risk of developing fetal distress in labor or an adverse neonatal outcome as a result of being subjected to labor, that are better managed by elective cesarean section. Second, stratify the intensity of monitoring during labor with high intensity for those with low CPR and low intensity for those with normal CPR. However, the poor performance of screening by CPR precludes any useful role in achieving either of these objectives.

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Figure legend

Figure 1. Receiver operating characteristic curves for prediction of cesarean section for fetal distress (left) and adverse neonatal outcome (right) by maternal factors (black), cerebroplacental ratio (blue) and combination of the two (red).

Table 1. Maternal and pregnancy characteristics in pregnancies with vaginal delivery compared to those that had cesarean section for fetal distress

Maternal and pregnancy characteristics	Vaginal delivery (n=1,408)	CS for fetal distress (n=258)
Maternal age in years, median (IQR)	28.7 (24.8-33.1)	29.8 (25.8-33.6)*
Maternal weight in kg, median (IQR)	83.8 (73.0-96.4)	88.2 (77.0-102.3)**
Maternal height in meters, median (IQR)	1.65 (1.61-1.70)	1.65 (1.60-1.68)
Cigarette smoker, n (%)	200 (14.2)	27 (10.5)
Racial origin		
White, n (%)	1283 (91.1)	217 (84.1)
Black, n (%)	41 (2.9)	14 (5.4)*
South Asian, n (%)	61 (4.3)	20 (7.8)*
East Asian, n (%)	7 (0.5)	1 (0.4)
Mixed, n (%)	16 (1.1)	6 (2.3)
Conception		
Spontaneous, n (%)	1361 (96.7)	243 (94.2)
Assisted conception, n (%)	47 (3.3)	15 (5.8)
Obstetric history		
Nulliparous, n (%)	545 (38.7)	175 (67.8)
Parous, previous CS, n (%)	61 (4.3)	27 (10.5)**
Parous, previous vaginal birth, n (%)	802 (57.0)	56 (21.7)**
Medical disorders		
Chronic hypertension, n (%)	7 (0.5)	1 (0.4)
Diabetes mellitus, n (%)	15 (1.1)	3 (1.2)
Pregnancy complications		
Gestational diabetes, n (%)	87 (6.2)	21 (8.1)
Obstetric cholestasis, n (%)	69 (4.9)	9 (3.5)
Gestational hypertension, n (%)	33 (2.3)	5 (1.9)
Preeclampsia, n (%)	17 (1.2)	10 (3.9)**
Amniotic fluid volume		
Normal, n (%)	1320 (93.8)	221 (85.7)
Oligohydramnios, n (%)	47 (3.3)	22 (8.5)**
Polyhydramnios, n (%)	41 (2.9)	15 (5.8)*
Fetal-placental Doppler		
Umbilical artery PI in MoM, median (IQR)	1.03 (0.91-1.16)	1.06 (0.92-1.20) *
Umbilical artery PI >90th percentile, n (%)	269 (19.1)	64 (24.8) *
Middle cerebral artery PI in MoM, median (IQR)	0.98 (0.85-1.14)	0.97 (0.82-1.09)
Middle cerebral artery PI <10th percentile, n (%)	274 (19.5)	64 (24.8) *
Cerebroplacental ratio in MoM, median (IQR)	0.95 (0.80-1.13)	0.90 (0.74-1.10) **
Cerebroplacental ratio <10th percentile, n (%)	310 (22.0)	76 (29.5) **
GA at delivery in weeks, median (IQR)	40.1 (39.0-41.5)	40.5 (39.4-41.6)**
Birth weight in g, median (IQR)	3460 (3087-3800)	3530 (3100-3873)
Birth weight <10th percentile, n (%)	264 (18.8)	55 (21.3)
Neonatal morbidity		
5 minute Apgar score <7, n (%)	6 (0.4)	10 (3.9)**
Low cord blood pH [a], n (%)	30 (2.1)	9 (3.5)
Admission to NICU for >24 hours, n (%)	20 (1.4)	18 (7.0)**
Hypoxic ischemic encephalopathy, n (%)	0	1 (0.4)

CS = cesarean section; IQR = interquartile range; GA = gestational age; UA = umbilical artery; MCA = middle cerebral artery; Low cord blood pH [a] = umbilical arterial or venous cord blood pH ≤7 and ≤7.1, respectively; Significance value * p<0.05; ** p<0.01

Table 2. Univariate and multivariate logistic regression analysis in prediction of cesarean section for fetal distress from maternal and pregnancy characteristics

Maternal and pregnancy characteristics	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P value	OR (95% CI)	P value
Maternal age – 30 (years)	1.026 (1.004-1.050)	0.023	1.065 (1.038-1.093)	<0.0001
Maternal weight – 88 (kg)	1.014 (1.007-1.021)	<0.0001	1.022 (1.013-1.031)	<0.0001
Maternal height – 1.64 (m)	0.986 (0.965-1.007)	0.202	0.956 (0.932-0.981)	0.001
Cigarette smoker	0.706 (0.461-1.081)	0.109		
Racial origin		0.014		
White	1.000 (Reference)			
Black	2.019 (1.082-3.766)	0.027	2.444 (1.212-4.929)	0.013
South Asian	1.939 (1.147-3.277)	0.013	1.970 (1.092-3.552)	0.024
East Asian	0.845 (0.103-6.899)	0.875		
Mixed	2.217 (0.858-5.729)	0.100		
Conception				
Spontaneous	1.000 (Reference)			
Assisted conception	1.787 (0.984-3.247)	0.057		
Obstetric history				
Nulliparous	1.000 (Reference)			
Parous, previous CS	1.378 (0.850-2.237)	0.194		
Parous, previous vaginal birth	0.217 (0.158-0.299)	<0.0001	0.167 (0.118-0.236)	<0.0001
Medical disorders				
Chronic hypertension	0.779 (0.095-6.356)	0.815		
Pre-existing diabetes mellitus	1.093 (0.314-3.801)	0.889		
Pregnancy complications				
Gestational diabetes	1.345 (0.819-2.210)	0.241		
Obstetric cholestasis	0.701 (0.346-1.423)	0.326		
Gestational hypertension	0.823 (0.318-2.219)	0.689		
Preeclampsia	3.299 (1.493-7.289)	0.003	3.102 (1.288-7.467)	0.006
Amniotic fluid volume		<0.0001		<0.0001
Normal	1.000 (Reference)			
Oligohydramnios	2.796 (1.652-4.731)	<0.0001	2.476 (1.381-4.441)	0.002
Polyhydramnios	2.185 (1.189-4.015)	0.012	3.443 (1.753-6.762)	<0.0001
Fetal-placental Doppler				
Umbilical artery PI MoM	2.664 (1.386-5.122)	0.003		
Middle cerebral artery PI MoM	0.569 (0.288-1.125)	0.105		
Cerebroplacental ratio MoM	0.453 (0.262-0.781)	0.004	0.454 (0.249-0.828)	0.010
Birth weight z-score	0.987 (0.897-1.085)	0.782		
GA at delivery – 40 (weeks)	1.179 (1.071-1.298)	0.001	1.166 (1.046-1.300)	0.006

CS = cesarean section; OR = odds ratio; CI = confidence interval; GA = gestational age; PI = pulsatility index

Table 3. Maternal and pregnancy characteristics in pregnancies with adverse neonatal outcome compared to those without

Maternal and pregnancy characteristics	No Adverse neonatal outcome (n=1,819)	Adverse neonatal outcome (n=71)
Maternal age in years, median (IQR)	29.1 (25.0-33.3)	28.7 (25.2-32.8)
Maternal weight in kg, median (IQR)	85.0 (74.2-98.2)	86.0 (72.3-98.0)
Maternal height meters, median (IQR)	1.65 (1.61-1.69)	1.65 (1.61-1.69)
Cigarette smoker, n (%)	243 (13.4)	9 (12.7)
Racial origin		
Caucasian, n (%)	1,640 (90.2)	63 (88.7)
Afro-Caribbean, n (%)	60 (3.3)	3 (4.2)
South Asian, n (%)	88 (4.8)	5 (7.0)
East Asian, n (%)	9 (0.5)	0
Mixed, n (%)	22 (1.2)	0
Conception		
Spontaneous, n (%)	1,745 (95.9)	67 (94.4)
Assisted conception, n (%)	74 (4.1)	4 (5.6)
Obstetric history		
Nulliparous, n (%)	834 (45.8)	44 (62.0)
Parous, previous CS, n (%)	117 (6.4)	5 (7.0)
Parous, previous vaginal birth, n (%)	868 (47.7)	22 (31.0)**
Medical disorders		
Chronic hypertension, n (%)	8 (0.4)	0
Diabetes mellitus, n (%)	21 (1.2)	1 (1.4)
Pregnancy complications		
Gestational diabetes, n (%)	123 (6.8)	4 (5.6)
Obstetric cholestasis, n (%)	84 (4.6)	3 (4.2)
Gestational hypertension, n (%)	39 (2.1)	3 (4.2)
Preeclampsia, n (%)	35 (1.9)	1 (1.4)
Amniotic fluid volume		
Normal, n (%)	1,673 (92.0)	63 (88.7)
Oligohydramnios, n (%)	74 (4.1)	5 (7.0)
Polyhydramnios, n (%)	72 (4.0)	3 (4.2)
Fetal-placental Doppler		
Umbilical artery PI in MoM, median (IQR)	1.03 (0.91-1.16)	1.07 (0.93-1.19)
Umbilical artery PI >90th percentile, n (%)	354 (19.5)	15 (21.1)
Middle cerebral artery PI in MoM, median (IQR)	0.98 (0.84-1.12)	0.92 (0.80-1.04)*
Middle cerebral artery PI <10th percentile, n (%)	362 (19.9)	20 (28.2)
Cerebroplacental ratio in MoM, median (IQR)	0.95 (0.79-1.13)	0.87 (0.71-1.07)**
Cerebroplacental ratio <10th percentile, n (%)	407 (22.4)	24 (33.8)*
GA at delivery in weeks, median (IQR)	40.2 (39.0-41.5)	40.3 (39.2-41.5)
Birth weight in g, median (IQR)	3490 (3120-3850)	3390 (3010-3775)
Birth weight <10th percentile, n (%)	325 (17.9)	16 (22.5)
Neonatal morbidity		
5 minute Apgar score <7, n (%)	-	19 (26.8)
Low cord blood pH [a], n (%)	-	42 (59.2)
Admission to NICU for >24 hours, n (%)	-	28 (39.4)
Hypoxic ischemic encephalopathy, n (%)	-	1 (1.4)

CS = cesarean section; IQR = interquartile range; GA = gestational age; Significance value * p<0.05; ** p<0.01

Table 4. Univariate and multivariate logistic regression analysis in prediction of adverse neonatal outcome from maternal and pregnancy characteristics

Maternal and pregnancy characteristics	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P value	OR (95% CI)	P value
Maternal age – 30 (years)	0.996 (0.956-1.036)	0.830		
Maternal weight – 88 (kg)	1.000 (0.988-1.013)	0.965		
Maternal height – 1.64 (m)	0.985 (0.949-1.023)	0.439		
Cigarette smoker	0.941 (0.462-1.919)	0.868		
Racial origin				
Caucasian	1.000 (Reference)			
Afro-Caribbean	1.302 (0.397-4.264)	0.663		
South Asian	1.479 (0.580-3.770)	0.412		
East Asian	-	-		
Mixed	-	-		
Conception				
Spontaneous	1.000 (Reference)			
Assisted conception	1.408 (0.500-3.964)	0.517		
Parity		0.022		
Nulliparous	1.000 (Reference)			
Parous, previous CS	0.810 (0.315-2.084)	0.662		
Parous, previous vaginal	0.480 (0.285-0.808)	0.006	0.550 (0.344-0.880)	0.013
Medical disorders				
Chronic hypertension	-	-		
Pre-existing diabetes mellitus	1.223 (0.162-9.223)	0.845		
Pregnancy complications				
Gestational diabetes	0.823 (0.295-2.295)	0.710		
Obstetric cholestasis	0.911 (0.281-2.956)	0.877		
Gestational hypertension	2.014 (0.607-6.679)	0.253		
Preeclampsia	0.728 (0.098-5.392)	0.756		
Amniotic fluid volume				
Normal	1.000 (Reference)			
Oligohydramnios	1.794 (0.701-4.593)	0.223		
Polyhydramnios	1.106 (0.339-3.608)	0.867		
Fetal-placental Doppler				
Umbilical artery PI MoM	2.831 (0.909-8.816)	0.073		
Middle cerebral artery PI MoM	0.250 (0.077-0.813)	0.021		
Cerebroplacental ratio MoM	0.278 (0.108-0.714)	0.008	0.301 (0.117-0.773)	0.008
Birth weight z-score	0.869 (0.738-1.024)	0.094		
GA at delivery – 40 (weeks)	0.967 (0.822-1.137)	0.686		

CS = cesarean section; OR = odds ratio; CI = confidence interval; GA = gestational age; PI = pulsatility index

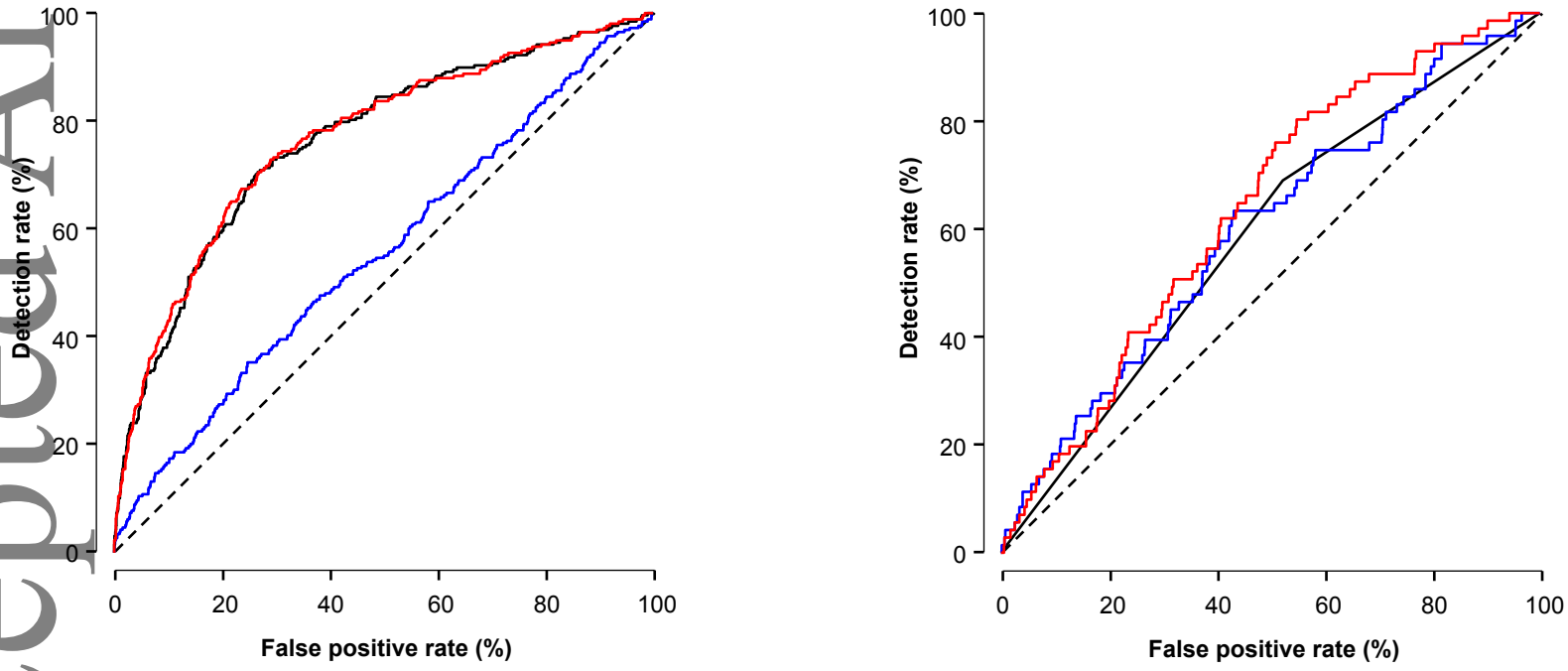

Figure 1.