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Prediction of adverse perinatal outcome by cerebroplacental ratio in women undergoing induction of labor

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KEYWORDS: adverse neonatal outcome; cerebroplacental ratio; Cesarean section; Doppler ultrasound; fetal distress; induction of labor

ABSTRACT

Objective *To investigate the performance of screening for adverse perinatal outcome by the cerebroplacental ratio (CPR) measured within 24 h prior to induction of labor.*

Methods *This was a prospective observational study of 1902 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) within 24 h before induction of labor. The measured UA-PI and MCA-PI and their ratio were converted to multiples of the median after adjustment for gestational age. Univariable and multivariable logistic regression analysis was used to determine whether CPR improved the prediction of adverse perinatal outcome 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 adverse neonatal outcome, which included umbilical arterial or venous cord blood pH ≤ 7 and ≤ 7.1, respectively, 5-min Apgar score < 7, admission to the neonatal intensive care unit for > 24 h or hypoxic ischemic encephalopathy.*

Results *A combination of maternal and pregnancy characteristics, including age, weight, racial origin, previous obstetric history, pre-eclampsia, gestational age at delivery and amniotic fluid volume, identified 39% of pregnancies requiring Cesarean section for fetal distress at a 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 a FPR of 10%.*

Conclusion *Low CPR, measured within 24 h prior to 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 surrogate measures of fetal hypoxic morbidity 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), is used for assessment of fetal oxygenation. In the 1980s, studies of fetal blood obtained by cordocentesis in small-for-gestational-age (SGA) fetuses demonstrated that increased impedance to flow in the UA and decreased impedance to flow in the MCA are associated with fetal hypoxemia and acidemia[1–4]. Subsequent studies in SGA fetuses in the 1990s 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-min Apgar score < 7 and neonatal intensive care unit (NICU) stay > 24 h[5–7]. Renewed interest in the CPR has been stimulated by the possibility that this index may be predictive of adverse perinatal outcome not only in SGA but also in appropriate-for-gestational-age (AGA) fetuses. Prior *et al.* measured the CPR in 400 pregnancies with an AGA fetus immediately before established labor and reported that CPR < 10^{th} percentile, compared to CPR ≥ 10^{th} percentile, was associated with a six-fold increased risk for delivery by Cesarean section for fetal distress and that, in the group with CPR > 90^{th} percentile, none had Cesarean section for fetal distress[8]. Subsequent

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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 2 weeks prior to birth, is associated with the need for operative delivery for presumed fetal compromise and with neonatal unit admission at term, regardless of 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 a singleton pregnancy 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 birth-weight *Z*-score, umbilical cord blood pH and admission to NICU, the performance of screening by CPR was poor, with a detection rate (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 adverse perinatal events at term were too remote from the gestational age at which CPR was assessed. However, another study of 6178 singleton pregnancies screened routinely 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 was to investigate whether the performance of screening by CPR for adverse perinatal outcome is improved by undertaking the assessment within 24 h prior to induction of labor.

METHODS

Study population

The data for this study were derived from a prospective observational study for prediction of adverse pregnancy outcome following induction of labor during the period 1 May 2016 to 31 July 2018, at Medway Maritime Hospital, Gillingham, UK. At our hospital, women booked for induction of labor attend the preinduction clinic within 24 h prior to administration of the induction agent. At this appointment, we record maternal characteristics and medical and obstetric histories, and perform an ultrasound scan to, first, determine presentation, second, estimate fetal weight from measurements of fetal head circumference, abdominal circumference and femur length[15], third, assess amniotic fluid volume by measurement of the deepest pool of fluid without any fetal parts, classifying oligohydramnios and polyhydramnios by a deepest pool of < 2 cm and > 8 cm, respectively, and, fourth, carry out transabdominal color Doppler for measurement of PI in the UA and MCA[16]. Gestational age was determined by the measurement of fetal crown–rump length at 11–13 weeks or 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 delivered a phenotypically normal neonate. Written informed consent was obtained from the women agreeing to participate in the study, which was approved by the London-Dulwich Research Ethics Committee (REC reference 16/LO/0367).

Patient characteristics

Recorded patient characteristics included maternal age, racial origin (white, black, South Asian, East Asian or 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 pre-eclampsia, and obstetric history (nulliparous if no previous pregnancy ≥ 24 weeks or parous, with or without history of 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, pre-eclampsia 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 as cardiac disease ($n = 12$) or antepartum hemorrhage ($n = 4$).

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-min Apgar score, umbilical arterial or venous pH and details of admission to 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-min Apgar score < 7, admission to the NICU for > 24 h or 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-min Apgar score < 5 or UA cord pH < 7.0 or base deficit > 12 mmol/L, supported by neuroimaging evidence of acute brain injury.

Statistical analysis

Data are expressed as median (interquartile range (IQR)) for continuous variables and *n* (%) for categorical variables. Mann–Whitney *U*-test and χ^2 test or Fisher's exact test were used for comparison of 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 fetoplacental 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 centered 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 subgroups of SGA fetuses (birth weight < 10th percentile) and non-SGA fetuses (birth weight ≥ 10th percentile). Predicted probabilities from logistic regression analysis were used to construct receiver–operating characteristics (ROC) curves to assess performance of screening for these adverse outcomes. The area under the ROC curve (AUC) for fetal Doppler alone was compared to that obtained using all factors[19].

The statistical package SPSS 24.0 (IBM Corp., Armonk, NY, USA) was used for data analyses.

RESULTS

Study population

During the study period, there were 1902 women who underwent induction of labor and met the inclusion criteria. There were 1408 (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 eight (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 were higher incidences of women of black and South Asian racial origin, parous women with a previous Cesarean section, pre-eclampsia, oligohydramnios and polyhydramnios, and median gestational age at delivery and UA-PI MoM were higher, CPR MoM was lower,

Table 1 Maternal and pregnancy characteristics in pregnancies with vaginal delivery compared to those that had Cesarean section (CS) for fetal distress

Characteristic	*Vaginal delivery (n = 1408)*	*CS for fetal distress (n = 258)*
Maternal age (years)	28.7 (24.8–33.1)	29.8 (25.8–33.6)†
Maternal weight (kg)	83.8 (73.0–96.4)	88.2 (77.0–102.3)‡
Maternal height (m)	1.65 (1.61–1.70)	1.65 (1.60–1.68)
Cigarette smoker	200 (14.2)	27 (10.5)
Racial origin		
White	1283 (91.1)	217 (84.1)
Black	41 (2.9)	14 (5.4)†
South Asian	61 (4.3)	20 (7.8)†
East Asian	7 (0.5)	1 (0.4)
Mixed	16 (1.1)	6 (2.3)
Conception		
Spontaneous	1361 (96.7)	243 (94.2)
Assisted	47 (3.3)	15 (5.8)
Obstetric history		
Nulliparous	545 (38.7)	175 (67.8)
Parous, previous CS	61 (4.3)	27 (10.5)‡
Parous, no previous CS	802 (57.0)	56 (21.7)‡
Medical disorder		
Chronic hypertension	7 (0.5)	1 (0.4)
Diabetes mellitus	15 (1.1)	3 (1.2)
Pregnancy complication		
Gestational diabetes	87 (6.2)	21 (8.1)
Obstetric cholestasis	69 (4.9)	9 (3.5)
GH	33 (2.3)	5 (1.9)
Pre-eclampsia	17 (1.2)	10 (3.9)‡
Amniotic fluid volume		
Normal	1320 (93.8)	221 (85.7)
Oligohydramnios	47 (3.3)	22 (8.5)‡
Polyhydramnios	41 (2.9)	15 (5.8)†
Fetoplacental Doppler		
UA-PI MoM	1.03 (0.91–1.16)	1.06 (0.92–1.20)†
UA-PI > 90th percentile	269 (19.1)	64 (24.8)†
MCA-PI MoM	0.98 (0.85–1.14)	0.97 (0.82–1.09)
MCA-PI <10th percentile	274 (19.5)	64 (24.8)†
CPR MoM	0.95 (0.80–1.13)	0.90 (0.74–1.10)‡
CPR < 10th percentile	310 (22.0)	76 (29.5)‡
GA at delivery (weeks)	40.1 (39.0–41.5)	40.5 (39.4–41.6)‡
Birth weight (g)	3460 (3087–3800)	3530 (3100–3873)
Birth weight < 10th percentile	264 (18.8)	55 (21.3)
Neonatal morbidity		
5-min Apgar score < 7	6 (0.4)	10 (3.9)‡
Low cord blood pH*	30 (2.1)	9 (3.5)
Admission to NICU > 24 h	20 (1.4)	18 (7.0)‡
Hypoxic ischemic encephalopathy	0 (0)	1 (0.4)

Data are given as median (interquartile range) or *n* (%). *Umbilical arterial or venous cord blood pH ≤ 7 and ≤ 7.1, respectively. †$P < 0.05$. ‡$P < 0.01$. CPR, cerebroplacental ratio; GA, gestational age; GH, gestational hypertension; MCA, middle cerebral artery; MoM, multiples of the median; NICU, neonatal intensive care unit; PI, pulsatility index; UA, umbilical artery.

and there was a 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, being parous with no previous Cesarean section, pre-eclampsia, 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 of the 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 and obstetric and medical history, the DR was 39.1% at FPR of 10%; addition of CPR did not improve the performance of screening (AUC, 0.767 (95% CI, 0.733–0.800) *vs* 0.763 (95% CI, 0.730–0.796); $P = 0.271$) (Figure 1). In prediction of SGA neonates, the performance of screening by maternal factors and obstetric and medical history (DR of 30.9% at FPR of 10%) was improved by the addition of CPR (DR of 34.5% at FPR of 10%; AUC, 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 1144) 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

Table 2 Univariable and multivariable logistic regression analysis in prediction of Cesarean section (CS) for fetal distress using maternal and pregnancy characteristics

	Univariable analysis		*Multivariable analysis*	
Characteristic	*OR (95% CI)*	P	*OR (95% CI)*	P
Maternal age – 30 (in years)	1.026 (1.004–1.050)	0.023	1.065 (1.038–1.093)	< 0.0001
Maternal weight – 88 (in kg)	1.014 (1.007–1.021)	< 0.0001	1.022 (1.013–1.031)	< 0.0001
Maternal height – 1.64 (in 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	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, no previous CS	0.217 (0.158–0.299)	< 0.0001	0.167 (0.118–0.236)	< 0.0001
Medical disorder				
Chronic hypertension	0.779 (0.095–6.356)	0.815		
Pre-existing diabetes mellitus	1.093 (0.314–3.801)	0.889		
Pregnancy complication				
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		
Pre-eclampsia	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
Fetoplacental 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 (in weeks)	1.179 (1.071–1.298)	0.001	1.166 (1.046–1.300)	0.006

GA, gestational age; MoM, multiples of the median; OR, odds ratio; PI, pulsatility index.

adverse neonatal outcome, compared to those without, there was a lower incidence of parous women with no previous Cesarean section, 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 no previous Cesarean section 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 of 12.8% at FPR of 10%) was significantly improved by the addition of CPR (DR of 16.9% at FPR of 10%; AUC, 0.581 (95% CI, 0.514–0.647) *vs* 0.632 (95% CI, 0.573–0.692); $P = 0.028$) (Figure 1).

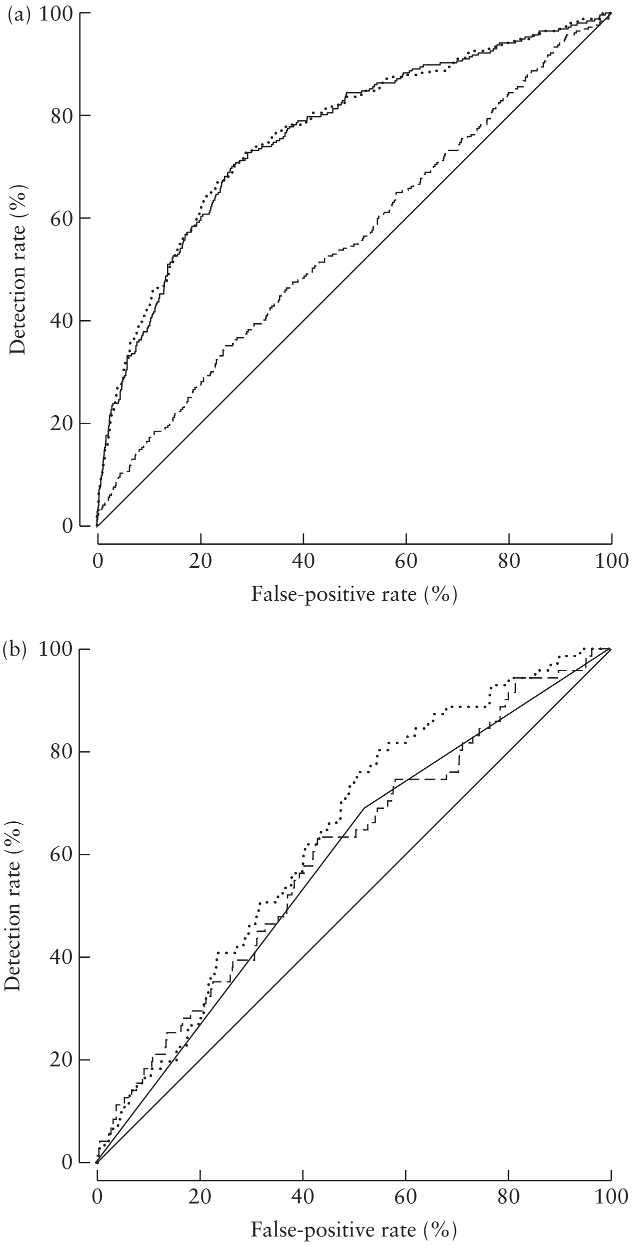

Figure 1 Receiver–operating characteristics curves for prediction of Cesarean section for fetal distress (a) and adverse neonatal outcome (b) by maternal factors (——), cerebroplacental ratio (– – –) and combination of the two (·····).

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

Characteristic	*No adverse neonatal outcome (n = 1819)*	*Adverse neonatal outcome (n = 71)*
Maternal age (years)	29.1 (25.0–33.3)	28.7 (25.2–32.8)
Maternal weight (kg)	85.0 (74.2–98.2)	86.0 (72.3–98.0)
Maternal height (m)	1.65 (1.61–1.69)	1.65 (1.61–1.69)
Cigarette smoker	243 (13.4)	9 (12.7)
Racial origin		
Caucasian	1640 (90.2)	63 (88.7)
Afro-Caribbean	60 (3.3)	3 (4.2)
South Asian	88 (4.8)	5 (7.0)
East Asian	9 (0.5)	0 (0)
Mixed	22 (1.2)	0 (0)
Conception		
Spontaneous	1745 (95.9)	67 (94.4)
Assisted	74 (4.1)	4 (5.6)
Obstetric history		
Nulliparous	834 (45.8)	44 (62.0)
Parous, previous CS	117 (6.4)	5 (7.0)
Parous, no previous CS	868 (47.7)	22 (31.0)‡
Medical disorder		
Chronic hypertension	8 (0.4)	0 (0)
Diabetes mellitus	21 (1.2)	1 (1.4)
Pregnancy complication		
Gestational diabetes	123 (6.8)	4 (5.6)
Obstetric cholestasis	84 (4.6)	3 (4.2)
GH	39 (2.1)	3 (4.2)
Pre-eclampsia	35 (1.9)	1 (1.4)
Amniotic fluid volume		
Normal	1673 (92.0)	63 (88.7)
Oligohydramnios	74 (4.1)	5 (7.0)
Polyhydramnios	72 (4.0)	3 (4.2)
Fetoplacental Doppler		
UA-PI MoM	1.03 (0.91–1.16)	1.07 (0.93–1.19)
UA-PI > 90th percentile	354 (19.5)	15 (21.1)
MCA-PI MoM	0.98 (0.84–1.12)	0.92 (0.80–1.04)†
MCA-PI < 10th percentile	362 (19.9)	20 (28.2)
CPR MoM	0.95 (0.79–1.13)	0.87 (0.71–1.07)‡
CPR ratio < 10th percentile	407 (22.4)	24 (33.8)†
GA at delivery (weeks)	40.2 (39.0–41.5)	40.3 (39.2–41.5)
Birth weight (g)	3490 (3120–3850)	3390 (3010–3775)
Birth weight < 10th percentile	325 (17.9)	16 (22.5)
Neonatal morbidity		
5-min Apgar score < 7	—	19 (26.8)
Low cord blood pH*	—	42 (59.2)
Admission to NICU > 24 h	—	28 (39.4)
Hypoxic ischemic encephalopathy	—	1 (1.4)

Data are given as median (interquartile range) or *n* (%). *Umbilical arterial or venous cord blood pH ≤ 7 and ≤ 7.1, respectively. †$P < 0.05$. ‡$P < 0.01$. CPR, cerebroplacental ratio; CS, Cesarean section; GA, gestational age; GH, gestational hypertension; MCA, middle cerebral artery; MoM, multiples of the median; NICU, neonatal intensive care unit; PI, pulsatility index; UA, umbilical artery.

Table 4 Univariable and multivariable logistic regression analysis in prediction of adverse neonatal outcome using maternal and pregnancy characteristics

	Univariable analysis		*Multivariable analysis*	
Characteristic	*OR (95% CI)*	P	*OR (95% CI)*	P
Maternal age − 30 (in years)	0.996 (0.956–1.036)	0.830		
Maternal weight − 88 (in kg)	1.000 (0.988–1.013)	0.965		
Maternal height − 1.64 (in 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	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, no previous CS	0.480 (0.285–0.808)	0.006	0.550 (0.344–0.880)	0.013
Medical disorder				
Chronic hypertension	—	—		
Pre-existing diabetes mellitus	1.223 (0.162–9.223)	0.845		
Pregnancy complication				
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		
Pre-eclampsia	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		
Fetoplacental 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 (in weeks)	0.967 (0.822–1.137)	0.686		

CS, Cesarean section; GA, gestational age; MoM, multiples of the median; OR, odds ratio; PI, pulsatility index.

The CPR was $< 10^{th}$ percentile in 31.3% (5 of 16) of SGA neonates with adverse neonatal outcome and in 34.2% (111 of 325) of those without ($P = 0.811$). In the non-SGA neonates, the CPR was $< 10^{th}$ percentile in 34.5% (19 of 55) of those with adverse neonatal outcome and in 19.8% (296 of 1494) of those without ($P = 0.008$).

DISCUSSION

Principal findings

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 an AGA neonate. 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.

This 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 h prior to delivery.

A combination of maternal and pregnancy characteristics, including age, weight, racial origin, obstetric history, pre-eclampsia, gestational age at delivery and amniotic fluid volume, identified about 40% of 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

The strengths of our study are, first, examination of a large number of pregnancies within 24 h prior to 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 poor 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 oxygenation 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 were 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 this study are similar to those of our previous studies reporting on clinical utility of CPR measured at 32 and 36 weeks' gestation, which demonstrate that the performance of screening by CPR in prediction of adverse perinatal outcome 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 a SGA fetus and reported that the DR and FPR of preinduction CPR $< 5^{th}$ percentile were, respectively, 70% and 46% for Cesarean section for fetal distress and 66% and 40% for adverse neonatal outcome[21]. Another study in 151 AGA fetuses reported that the preinduction CPR was not significantly different between those with operative delivery for intrapartum fetal compromise or UA 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, to identify pregnancies that are at high risk of developing fetal distress in labor or an adverse neonatal outcome as a result of labor induction, that are better managed by elective Cesarean section. Second, to 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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