



Cerebroplacental ratio and neonatal outcome in low-risk pregnancies with reduced fetal movement: A prospective study

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ABSTRACT

Objective: To evaluate the effectiveness of the cerebroplacental ratio (CPR) in predicting poor outcomes in low-risk pregnancies with reduced fetal movements (RFMs).

Study Design: This prospective study included singleton pregnancies at 28–40 weeks, presenting with RFM but no additional risk factors. Sub analysis was performed for pregnancies between 36 and 40 weeks. Umbilical artery (UA) and middle cerebral artery (MCA) pulsatility indices (PIs) were measured, and the MCA-PI to UA-PI ratio (CPR) was calculated. Mode of delivery, gestational age, fetal monitoring category, Apgar score at 1 and 5 min, birth weight, presence of meconium, umbilical artery pH, and neonatal intensive care unit (NICU) admission were recorded. Women with good and poor outcomes were compared with doppler indices and pregnancy characteristics.

Results: Of 96 women, 86 had good outcomes. There was no significant difference in UA-PI (0.871 ± 0.171 vs. 0.815 ± 0.179 , $P = 0.446$), MCA-PI (1.778 ± 0.343 vs. 1.685 ± 0.373 , $P = 0.309$), or CPR (2.107 ± 0.635 vs. 2.09 ± 0.597 , $P = 0.993$) between the poor and good outcome groups. No difference was found in the location of the placenta, biophysical profile (BPP) score, fetal sex, or amniotic fluid index (AFI) at the time of presentation. The proportion of nulliparous patients in the poor outcome group was higher than that of multiparous patients. Sub analysis for 36–40 weeks revealed the same results; no significant difference in UA-PI (0.840 ± 0.184 vs. 0.815 ± 0.195 , $P = 0.599$), MCA-PI (1.724 ± 0.403 vs. 1.626 ± 0.382 , $P = 0.523$), or CPR (2.14 ± 0.762 vs. 2.08 ± 0.655 , $P = 0.931$) between poor and good outcome groups.

Conclusions: CPR is not predictive of neonatal outcome in low-risk pregnancies with RFM. However, a higher proportion of poor outcomes in nulliparous women warrants further investigation.

1. Introduction

Approximately 40% of pregnant women report at least one episode of reduced fetal movement (RFM) [1]. Out of these, while there is only one transient episode in most cases, approximately 4–15% of women are referred to prenatal clinics due to recurrence of reduction in fetal movement [2–4]. It has been reported in previous studies that pregnancies complicated with RFM are associated with higher rates of poor neonatal outcomes and increased prenatal morbidity and mortality [5–9]. In addition, other studies have shown that RFM combined with intrauterine growth restriction (IUGR) can predict abnormal pregnancy outcomes [10,11].

Owing to the association between RFM and hypoxemia, fetal

movement monitoring is a simple and widely used method for monitoring fetal status [12,13]. However, a Cochrane review in 2007 suggested that there was insufficient evidence to recommend routine fetal movement monitoring [14]. Therefore, it is still unclear whether there is a benefit to maternal monitoring fetal movements to assess this condition [15]. In addition, the effect of various factors such as placental location, amount of amniotic fluid, fetal size, and maternal factors such as activity, body mass index (BMI), and psychological state on the sensation of fetal movements remains unclear [16].

In this context, measuring the fetal cerebroplacental ratio (CPR) could be a potential method for predicting poor neonatal outcomes. CPR is the ratio of the middle cerebral artery pulsatility index (MCA-PI) to the umbilical artery pulsatility index (UA-PI) [17] and is an indicator of

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fetal blood redistribution [18]. This ultrasound-assisted index can predict adverse neonatal outcomes in small for gestational age (SGA) fetuses that show placental and brain vessel resistance.

To the best of our knowledge, no previous study has evaluated low-risk pregnancies with RFM for poor outcomes based on CPR. Therefore, this prospective study aimed to evaluate the effectiveness of CPR in predicting poor neonatal outcomes in low-risk pregnancies with RFM. Additionally, we examined the effect of various factors on the sensation of fetal movements and neonatal outcomes.

2. Materials and methods

This study was approved by The Institutional Review Board (Helsinki Committee) of the Galilee Medical Center approved this study. All the study participants provided written informed consent.

2.1. Study design and population

This prospective cohort study was performed between January 2018 and January 2020. A total of 110 women with singleton low-risk pregnancies in the gestational age range of 28–40 weeks (based on a reliable last menstrual period [LMP] date and ultrasound confirmation in the first trimester of pregnancy), who were referred to our prenatal clinic because of RFM, as perceived by them, were included. Women with multiple pregnancies, congenital fetal anomalies, IUGR, oligohydramnios, polyhydramnios, gestational diabetes, or hypertension were excluded from the study.

All the participants underwent a non-stress test (NST) and BPP. In addition, estimated fetal weight and CPR were measured. Initially, the NST was performed for 20–30 min, and the participants were classified as category 1, 2, or 3 [19]. The estimated fetal weight (EFW) was calculated using the Hadlock 4 formula. In addition, the placental location and BPP were determined. Subsequently, UA and MCA PI were measured, and the MCA PI-to-UA PI ratio (CPR) was calculated. CPR and Doppler results were not used in patient management since we did not encounter any absent or reversed diastolic flow cases. Per the conventional procedure, the UA Doppler waveform was recorded in a free loop, while the MCA Doppler waveform was recorded as close as possible to the vessel origin from the circle of Willis.

All eligible women were followed up until spontaneous or induced labor and delivery. Neither the pregnant women nor the health care providers who carried out prenatal and intrapartum care were aware of the CPR values.

Cases with Apgar score < 7 at 5 min, cord blood pH < 7.16, monitoring category three during labor, presence of meconium, NICU admission, and fetal death were classified as those with poor outcomes.

2.2. Data collection

Various parameters include maternal age, BMI, gravidity, parity, history of abortions, gestational age, duration and characteristics of RFM (reduced or absent), NST, BPP, CPR results, amniotic fluid index (AFI), and placental location were recorded for all the participants. Further, the mode of delivery, gestational age, fetal monitor category, fetal sex, Apgar score at 1 and 5 min, birth weight, presence of meconium, umbilical artery pH, and NICU admission were recorded.

2.3. Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows, version 25 (IBM Corp., Armonk, NY, USA). After checking the normality of the continuous data, the characteristics of the groups with good and poor outcomes were compared using an independent t-test and/or Mann–Whitney U test, as needed. Categorical variables were compared using the chi-square test or Fisher's exact test. A P-value < 0.05 was considered statistically significant. While qualitative data were

described in terms of frequencies and percentages, quantitative data were expressed as mean, standard deviation, median, and range. The receiver operator curve was utilized to predict poor pregnancy outcomes.

Sub analysis was performed for women with gestational age 36–40 weeks and an interval below 15 days between examination and delivery.

The sample size is calculated based on the expected difference between patients with poor and good outcomes. According to the researchers' opinion, a difference higher than 0.5 of CPR would be considered significant.

Assuming that the percentage of patients with poor birth outcomes is estimated at 25% out of our study population and based on the independent sample t-test, a two-sided hypothesis, a significance level of 5%, to achieve a power of 80% it is required to collect a total of 90 patients.

3. Theory

Abnormal CPR indicates the redistribution of blood circulation from the heart to the brain and is associated with emergency cesarean section due to fetal distress, neonatal intensive care unit (NICU) admission, and poor neonatal neurological outcome [20]. In addition, low CPR is associated with an increased risk of stillbirth, regardless of gestational age or fetal weight [21]. Furthermore, CPR predicts abnormal pregnancy outcomes better than biophysical profile (BPP), UA flow, or MCA alone [22]. Therefore, CPR assessment should be considered an essential tool for predicting adverse neonatal outcomes [23].

Given the association between RFM and adverse perinatal outcomes, we hypothesize that CPR may be altered in patients presenting with RFM.

4. Results

We initially included 110 singleton pregnant women referred to the prenatal clinic on account of RFM. 14 women were eventually excluded because of complications such as polyhydramnios diagnosed during ultrasound assessment (n = 5) and delivery at a different hospital and inability to follow up (n = 9). Finally, 96 women were included in the study, all with the available data on perinatal and neonatal outcomes without any risk factors for poor outcomes. Of the 96 study subjects, 86 had good perinatal and neonatal outcomes, while ten were associated with poor outcomes.

A comparison of the maternal and obstetric characteristics of women with poor and good outcomes is presented in Table 1. There were no significant differences in age, BMI, occupational status, or gestational week between the groups at the time of inclusion in the study. In addition, there were no significant differences between the groups in terms of decreased fetal movement (i.e., decrease in the intensity or number of movements) or the recurrence or duration of RFM. Further, there were no significant differences in placental location, BPP score, AFI at the time of presentation, or fetal sex. The only significant differences between the two groups were gravidity and parity, with more nulliparity observed in the group with poor outcomes.

No significant differences between poor and good outcomes in the UA-PI (0.871 ± 0.171 vs. 0.815 ± 0.179, P = 0.446), MCA-PI (1.778 ± 0.343 vs. 1.685 ± 0.373, P = 0.309), or CPR (2.107 ± 0.635 vs. 2.09 ± 0.597, P = 0.993) (Table 2).

While the gestational age at the time of inclusion in the study ranged from 28 to 40 weeks, approximately 69% of the women in both groups were between 36 and 40 weeks of gestation and delivered within 15 days. Comparison of the maternal and obstetric characteristics of women with poor and good outcomes of 36–40 weeks of gestation at inclusion are presented in Table 3. There were no significant differences in age, BMI, or occupational status. Furthermore, there were no significant differences between the groups regarding decreased fetal movement or the recurrence or duration of RFM. Further, there were no significant differences in placental location, BPP score, AFI at the time of

Table 1
Demographics and obstetric data of the study population Gestational week 28–40.

(N = 96)	Good outcome (86)	Poor outcome (10)	P-value 2-sided
Maternal age mean (std. Deviation)	28 ± (5.6)	26.8 (2.1)	0.349 +
BMI mean (std. Deviation)	28.5 ± (4.9)	28 ± (3.2)	0.818 +
Working (N)%	(58) 68.6%	(8) 80%	0.718 ^a
Smoking (N)%	(5) 5.8%	(0) 0%	1.000 ^a
Gravidity - Median(range)	2 (0–7)	1 (1–4)	0.027 +
Parity - Median(range)	1 (0–4)	0 (0–2)	0.019 +
Nullipara (N) %	(35) 40.7%	(8) 80%	0.039 **
Multipara (N)%	(51) 59.3%	(2) 20%	
Gestational age at enrollment and doppler examination (standard deviation)	37.3 ± (3.3)	37.7 ± (4.2)	0.955 +
Gestational week 28–31.6 (N)%	(13) 15.1%	(2) 20%	0.767 +
Gestational week 32–35.6 (N)%	(14) 16.2%	(1) 10%	
Gestational week 36–40 (N)%	(59) 68.6%	(7) 70%	
Recurrence of reduce fetal movements (N)%	(6) 7%	(1) 10%	0.549 ^a
Decrease in intensity of fetal movement (N)%	(37) 46.3%	50% (5)	1.000 ^a
Decrease in the number of fetal movements (N)%	36.1% (25)	(1) 10%	0.270 ^a
Absence of fetal movements (N)%	(33) 38%	(5) 50%	0.510 ^a
Decrease in the intensity and number of fetal movements (N)%	(18) 20.9%	(1) 10%	0.681 ^a
Duration of the compliance (hours) mean (std. Deviation)	33.8 ± (45.5)	46 ± (65.8)	0.487 +
Anterior placenta (N)%	(56) 65.1%	(8) 80%	0.873 ^a
Posterior placenta (N)%	(23) 26.7%	(2) 20%	
Fundal placenta (N)%	(7) 8.1%	(0)	
BPP Score at compliance < 8/8	(2) 2.4%	(0)	1.000 ^a
Male infant (N)%	(43) 50%	(4) 40%	0.741 ^a
Female infant (N)%	50% (43)	(6) 60%	
Gestational age at delivery, mean (std. Deviation)	39 ± (1.0)	38.7 ± (2.1)	0.555 ++
Fetal wight (gram) mean (std. Deviation)	3344 ± (427)	3069 ± (537)	0.226 ++

BMI, Body mass index; BPP, biophysical profile
^a Fisher's Exact Test, + Mann-Whitney Test, ** Chi-Square Tests, Wilcoxon Rank-Sum ++

Table 2
Results of Doppler studies in both groups Gestational week 28–40.

	Good outcome	Poor outcome	P-value 2-sided Mann-Whitney Test
UA-PI Mean(Standard deviation)	0.815 ± (0.179)	0.871 ± (0.171)	0.446
MCA-PI Mean(Standard deviation)	1.685 ± (0.373)	1.778 ± (0.343)	0.309
CPR Mean(Standard deviation)	2.09 ± (0.597)	2.107 ± (0.635)	0.993

UA, Umbilical artery; PI, pulsatility index; MCA, middle cerebral artery; CPR, cerebroplacental ratio (MCA-PI to UA-PI ratio)

presentation, or fetal sex. The only significant differences between the two groups were the parity median (1 vs. 0 P = 0.047). In this subgroup of women, there were no significant differences between poor or good outcomes in the UA-PI (0.840 ± 0.184 vs. 0.815 ± 0.195, P = 0.599), MCA-PI (1.724 ± 0.403 vs. 1.626 ± 0.382, P = 0.523), or CPR (2.14 ± 0.762 vs. 2.08 ± 0.655, P = 0.931) respectively (Table 4).

The poor outcome characteristics of the study population are presented in Table 5. A significant difference was in the Apgar score after 1 and 5 min and meconium presentation in the study population week 28–40 (9 (7–9) vs 9(6–9) P = 0.011), (10 (8–10) vs 9 (8–10) P = 0.011) and (0 vs (5)50%, P < 0.001) respectively, as well as in the group of gestational age 36–40 (9(7–9) vs 9(6–9) p = 0.012), (9(8–9) vs 9

Table 3
Demographics and obstetric data of the Gestational week 36–40.

	Good outcome	Poor outcome	P 2-sided
(N = 66)	(59) 89.4%	(7)10.6%	
Maternal age mean (std. Deviation)	28.8 ± (5.6)	26.4 ± (2.5)	0.316 +
BMI mean (std. Deviation)	29 ± (5.3)	29.1 ± (2.4)	0.832 +
Working (N)%	(39) 66.1%	(6)85.7%	0.416 ^a
Smoking (N)%	(4) 6.8%	(0) 0%	1.000 ^a
Gravidity- Median(rang)	2 (0–7)	1 (1–4)	0.122 +
Parity- Median(rang)	1 (0–4)	0 (0–2)	0.047 +
Nullipara (N) %	(21) 35.6%	(5)71.4%	0.102 ^a
Multipara (N)%	(38) 64.4%	(2)28.6%	0.102 ^a
Recurrence of RFM (N)%	(6) 10.2%	(1)14.3%	0.562 ^a
Decrease in intensity of fetal movements (N)%	(32) 58.2%	(4) 57.1%	1.000 ^a
Decrease in the number of fetal movements (N)%	(18) 32.7%	(1) 14.3%	0.422 ^a
Absent of fetal movements (N)%	(20) 33.9%	(3) 42.9%	0.687 ^a
Decrease in intensity and number of fetal movements (N)%	(12) 20.3%	(1) 14.3%	1.000 ^a
Duration of the compliance (hours) mean (std. Deviation)	31.6 ± 46.9	36.8 ± 59.7	0.764 +
Anterior placenta (N)%	(43) 72.9%	(5) 71.4%	0.795 ^a
Posterior placenta (N)%	(11) 18.6%	(2) 28.6%	0.687 ^a
Fundal placenta (N)%	(5) 8.5%	(0)	1.000 ^a
BPP Score at the compliance < 8/8	(2) 3.4%	0.0% (0)	1.000 ^a
Male (N)%	(30)50.8%	(3) 42.9%	1.000 ^a
Female (N)%	(29)49.2%	(4)57.1%	1.000 ^a
Gestational age at delivery, mean (std. Deviation)	39.3 ± (0.9)	39.4 ± (0.9)	0.826 ++
Fetal wight (Gram) mean (std. Deviation)	3357 ± 436	3238 ± 308	0.557 ++

BMI, Body mass index; BPP, biophysical profile; RFM, Reduce fetal movements.
^a Fisher's Exact Test, + Mann-Whitney Test, ** Chi-Square Tests, Wilcoxon Rank-sum ++

Table 4
Results of Doppler studies in both groups of 36–40 weeks gestational age.

	Good outcome	Poor outcome	P 2-sided Wilcoxon Rank
UA-PI Mean (std. Deviation)	0.815 ± (0.195)	0.840 ± (0.184)	0.599
MCA-PI Mean (std. Deviation)	1.626 ± (0.382)	1.724 ± (0.403)	0.523
CPR Mean (std. Deviation)	2.08 ± (0.655)	2.14 ± (0.762)	0.931

UA, Umbilical artery; PI, pulsatility index; MCA, middle cerebral artery; CPR, cerebroplacental ratio (MCA-PI to UA-PI ratio)

(8–9) P = 0.031 and (0 vs 57, P < 0.001) respectively. No significant differences observed between poor and good outcomes in fetal PH.

5. Discussion

This study was designed to determine the relationship between CPR and neonatal outcomes in low-risk pregnancies with RFM. To the best of our knowledge, no previous study has assessed women who presented with no risk factors for poor outcomes. Abnormal CPR represents the redistribution of blood to the brain and is associated with emergency cesarean section due to fetal distress, NICU admission, and poor neonatal neurologic outcome [20]. In addition, low CPR in high-risk pregnancies is associated with an increased risk of stillbirth regardless of gestational age or fetal weight [21]. Nevertheless, no data is available regarding the association between CPR and low-risk pregnancies.

In a study by Binder et al. [24] CPR values measured in terms of multiples of the median (MoM) were found to be significantly lower in

Table 5
The poor outcome characteristics of the study population.

	Good outcome	Poor outcome	P-value 2-sided
(N = 96) Gestational week 28–40	(86)	(10)	
Fetal PH median (Range)	7.31 (2.24–7.37)	7.31 (7.10–7.35)	0.282 ++
Apgar score - 1 min, median (Range)	9 (7–10)	9 (6–9)	0.011 ++
Apgar score - 5 min, median (Range)	10 (8–10)	9(8–10)	0.011 ++
Meconium(N)%	0	(5) 50%	P < 0.001 a
(N = 66) Gestational week 36–40	(59) 89.4%	(7)10.6%	
Fetal PH median (range)	7.31 (2.24–7.37)	7.31 (7.10–7.35)	0.284 ++
Apgar score – 1 min, median (range)	9(7–9)	9 (6–9)	0.012 ++
Apgar score – 5 min, median (range)	9(8–9)	9 (8–9)	0.031 ++
Meconium (N)%	(0)	(4)57.1%	P < 0.001 a

^a Fisher's Exact Test, Wilcoxon Rank-sum ++

the cases where women presented with RFM compared with the control cases (women at a similar gestational age, but no RFM) [24]. However, unlike our study, they did not consider risk factors. The present study revealed that it was impossible to predict poor outcomes such as low Apgar score at 1 min, higher rate of NICU admission, meconium presence, or cesarean section due to suspected fetal distress in low-risk cases of RFM based on CPR values. In other words, we were unable to observe a correlation between the CPR index and pregnancy outcomes in this study group. Further, there was no association between the characteristics of the complaint, such as reduced or absent movements, and pregnancy outcome.

In contrast, other studies that have evaluated the CPR index as a predictor of adverse perinatal outcomes have concluded that low CPR is associated with abnormal fetal heart rate, reduced Apgar score, and acidosis in neonates [24]. This difference may be attributed to the fact that our patients were all considered low-risk pregnancies, with high-risk factors serving as reasons for exclusion from our study. On the contrary, the study by Binder et al. [24] considered all pregnant women, including those with high-risk features such as hypertension and SGA fetuses, in addition to low-risk pregnancies.

An attempt was made to examine the relationship between the demographic and obstetric characteristics of the participants and their pregnancy outcomes. We found that nulliparous women complaining of RFM were more likely to have a poor outcome than multiparous women (80% vs. 20%, Table 1), which was unanticipated because nulliparous women are expected to be less aware of RFM than multiparous women. However, our results indicated that we should be more attentive to RFM in nulliparous women. While placental location did not predict abnormal pregnancy outcomes, a higher proportion of women presented with anterior placenta; this is consistent with the results from previous studies.

We know that gestational age (GA) at examination (28–40 weeks) mixes two different physiopathological scenarios. It is well known that CPR is a marker of adverse pregnancy outcomes [22] regardless of fetal weight at the end of pregnancy. This characteristic does not apply at the beginning of the third trimester when CPR is affected only in the case of hemodynamic progression and in the context of early-growth restriction. For this reason, we have added another comparison of women with GA of 36–40 weeks that were delivered within 15 days of the CPR. Nevertheless, we could not observe a correlation between the CPR index and pregnancy outcomes in this sub-group of women. It is important to note that there was no difference in the rate of poor outcomes between

gestational age groups, which was 10.4%, 10.6% and 10% in the 28–40, 36–40, 28–36 gestational week, respectively.

5.1. Strengths and limitation

This study was prospective, and the participants had no additional risk factors other than RFM for a poor outcome; these facts represent the key strengths of this study. Further, a comprehensive Doppler assessment was performed, and fetal Doppler, EFW, BPP, and NST measurements were taken. The possible limitations of the study are the relatively small number of participants.

5.2. Conclusions

The study results show that CPR cannot be used as an indicator for predicting neonatal outcomes in low-risk pregnancies with RFM. However, our observation of the increased rate of poor outcomes in nulliparous women than among multiparous women deserves further investigation.

Conflicts of interest

The authors declare no conflicts of interest related to this work.

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