

## Role of middle cerebral artery and umbilical artery Doppler velocimetry studies to compare the outcome in post-dated and normal dated pregnancies in a rural population of eastern India

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### Abstract

**Background:** Doppler ultrasound velocimetry of umbilical and foetal vessels has become established method of antenatal monitoring, allowing non-invasive assessment of foetal circulation.

**Aims:** To compare role of middle cerebral artery and umbilical artery Doppler velocimetry studies in normal uncomplicated pregnancies and post-dated pregnancies.

**Materials and Methods:** A comparative study was conducted on 130 pregnant women having gestational age of 36 weeks or more who came to the labor ward in reference study period of 1 year in Burdwan Medical College. Study group consists of 65 pregnant women with gestational age of 40-42 weeks while control groups with gestational age of 36-40 weeks. USG Doppler studies were done, APGAR score of neonates were calculated at 1min and 5 min. Comparison of all variables were done using by a software package SPSS 16.

**Results:** No statistically significant difference was noted in Doppler indices (except CPR) in pregnancy with normal and adverse perinatal outcome. 27.6% of mothers of 40-42 weeks had adverse perinatal outcome where as 100% mother of 36-40 weeks' had normal outcome. Among post-dated pregnancies 48% mothers of 41-42 weeks had adverse perinatal outcome in comparison to 15% at 36-40 weeks of gestation. Only CPR showed significant difference for predicting adverse perinatal outcome (p=0.001). Low CPR (1.34) has high sensitivity and positive predictive value but poor specificity and negative predictive value.

**Conclusion:** Doppler indices except CPR are not trustworthy. Although CPR cut-off value of 1.335 assures about fetal wellbeing, its low specificity can lead to undue concern and interference.

**Keywords:** Doppler Velocimetry, post-dated pregnancy, foetomaternal outcome.

### 1. Introduction

The prevalence of post term pregnancy is about 10% when dating is based on the first day of the last menstrual period, but this is only about 5% when dating is by an early ultrasound scan. In about 30% of post term pregnancies, the fetuses develop a post maturity syndrome.

Post term pregnancy is associated with increased risk of both intrauterine and postnatal death. When neonatal and post neonatal mortality rates are included, the overall risk of death increased from 0.7 per 1000 ongoing pregnancies at 37 weeks to 5.8 per 1000 pregnancies at 43 weeks [1]. Children born post term have more developmental abnormalities compared with those born before 42 weeks [2].

The amniotic fluid volume decreases from about 37 weeks, and, during the post-dated period, it is estimated that there is a decrease in amniotic fluid volume of about 33% per week [3,4]. This decrease in amniotic fluid volume, combined with the increased incidence of meconium staining of the amniotic fluid in post term pregnancies, results in an increased risk of meconium aspiration syndrome.

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For the first time Satomura demonstrated that the Doppler technique could evaluate blood flow [5]. Nowadays, Doppler ultrasound velocimetry of uteroplacental umbilical and fetal vessels has become established method of antenatal monitoring, allowing noninvasive assessment of fetal circulation<sup>6</sup>. Its indices provide important information on the hemodynamic of the vascular area under study [7]. Circulatory changes, reflected in certain fetal Doppler waveforms, predict adverse perinatal outcome [8]. Umbilical arteries are the common vessels assessed by Doppler ultrasound, but recent studies confirm the efficacy of middle cerebral artery (MCA) Doppler assessment for detecting fetal compromise.[9-11]

Fetal hypoxia is one of the major causes of high perinatal morbidity and mortality rate [12,13]. Fetal hypoxia activates a number of defence mechanisms, such as modification of fetal heart rate (FHR), increase in blood pressure and redistribution of blood to the heart, brain, and adrenal glands. Low oxygen partial pressure (pO<sub>2</sub>) leads to cerebral vasodilatation and a fall in vascular resistance, which results in a decrease in middle cerebral artery resistance index (MCA RI). Doppler ultrasound indices such as cerebroplacental ratio (CPR) evaluation are commonly used nowadays. It enables to assess the fetal response to hypoxia by detecting blood flow distribution pattern in placento-umbilical and feto-cerebral circulations [14]. With progression of gestational age, the resistance in fetal circulation gradually decreases. Nevertheless, the value of MCA RI should remain higher than umbilical artery resistance ratio (UA RI) value, which implicates that C/U, being the ratio of MCA RI to UA RI, should be higher than 1–1.1 in uncomplicated pregnancies [15]. Moreover, when fetal hypoxia occurred, CPR showed better correlation with pO<sub>2</sub> reduction than MCA RI.

The present study was conducted to compare role of middle cerebral artery and umbilical artery Doppler velocimetry studies in normal uncomplicated pregnancies (36-40 weeks' gestational age) and post-dated pregnancies in a rural population of eastern India so that foetomaternal complications can be minimized.

## 2. Materials and methods

The Study was conducted in the Department of Obstetrics & Gynaecology, Burdwan Medical College and Hospital, Burdwan after taking Institutional ethical clearance and informed consent of the subjects in a time span of one year.

Study group consists of 65 pregnant women with gestational age of 40-42 weeks and control groups include the same number of pregnant women with gestational age of 36-40 weeks.

### 2.1 Inclusion Criteria

- Singleton, viable fetus in the cephalic presentation.
- History of regular menstrual cycles.
- Gestational age was calculated from the first day of last normal menstrual period or by first-trimester or second-trimester (before 20 weeks) ultrasound examination.

### 2.2 Exclusion Criteria:

- Gestational age uncertain.
- Medical disorders in pregnancy as hypertension, diabetes mellitus, chronic renal failure, SLE, antiphospholipid antibody (APLA) syndrome etc.
- Prelabour rupture of membranes.
- Polyhydramnios.
- Women with multiple pregnancies.
- Congenital foetal anomalies.
- Antepartum haemorrhage.
- Previous caesarean section.
- Fetal malpresentation.

### 2.3 Parameters studied:

Ultrasonography (USG): Routine ultrasonography for fetal biometry which includes biparietal diameter(BPD), Femur-length(FL), Abdominal circumference(AC), Head-circumference(AC), AC/HC, FL/AC, Liquor pocket and AFI, and Placental grading.

#### ➤ USG Doppler studies:

- Umbilical artery S/D ratio, pulsatility index (PI =S-D/A) and resistance index (RI) =S-D/S.
- Middle cerebral artery S/D ratio, pulsatility index (S-D/A) and resistance index(S-D/S).
- To calculates the CPR (MCA PI/ UA PI) for evaluation of foetal status in utero in both the groups.

#### ➤ APGAR score:

The neonates were subjected to APGAR scoring at 1 and 5 minutes. Adverse Neonatal outcome was considered by any of the following criteria:

- APGAR score is less than 3 at 1 minute
- APGAR score is less than 6 at 5 minutes.
- Neonatal admission to neonatal intensive care unit.
- Intrauterine fetal death or early neonatal death.

### 2.4 Methodology

After proper counselling and obtaining informed consent from each antenatal mother selected in the study population, detailed history taking and clinical examinations were performed. All the antenatal women in the subject & control groups were examined by routine ultrasound scan and Doppler subsequently. Doppler indices are calculated by the dedicated software supplied within the Doppler equipment. The average values of at least four consecutive waveforms were calculated. All participants were sure of their date of the last menstrual period and had regular menstrual cycles previously.

Their gestational age was further corroborated by first trimester ultrasound. When a discrepancy more than seven days was detected, first trimester ultrasound was used to calculate gestational age. Women selected for the study were subjected to complete general, physical, obstetric and pelvic examinations. Routine baseline investigations, NST, AFI and BPS were carried out on admission and repeated biweekly till onset of labor or termination of pregnancy. Blood flow velocity waveforms of UA and MCA were obtained with pulsed Doppler ultrasound equipment. The peak systolic, end diastolic, and mean velocity were recorded from these vessels, and Umbilical artery S/D ratio, PI and Middle Cerebral Artery PI and CPR were calculated. Pregnancy was terminated if NST was nonreactive, AFI <5 cm, BPS < 8/10 or if the period of gestation extended beyond 42 weeks. Adverse perinatal outcome was defined as presence of one or more of the following conditions – fetal distress as evidenced by fetal bradycardia or persistent tachycardia requiring caesarean section or instrumental delivery, meconium stained liquor, APGAR score of < 6 at 5 minutes, neonatal complications like meconium aspiration syndrome or respiratory distress syndrome, admission to neonatal intensive care unit (NICU), and perinatal mortality. Perinatal outcomes were analyzed in both the groups.

**2.5 Statistics**

Comparison of all variables were done using by a software package SPSS 16. Sensitivity, Specificity, Positive predictive value, Negative predictive value of different arterial Doppler indices and cerebroplacental ratio (CPR) were evaluated. A receiver operator characteristic curve (ROC) was plotted to ascertain the best cut-off value of CPR for predicting adverse perinatal outcome in post-dated pregnancy. P-value of <0.05 was considered as significant.

**3. Results**

Most of the pregnant mothers (71.54%) are between 20-50 years of age, 70.77% in post-dated pregnancy and 72.31% are in dated pregnancy (36-40

weeks of gestation). Majority of the pregnant women are primi-gravida in both the groups (57.77%). Majority of women are of Muslim in both case and control groups (56.92% and 53.38%). Most of mothers of post-dated pregnancy belong to upper lower class (49.23%). The mean value of UA S/D, UAPI, UARI, MCA S/D, MCAPI, MCARI and CPR showed no statistically significant difference between case and control groups. It suggests impedance to flow to the umbilical artery and middle cerebral artery is not altered and not significantly different beyond term pregnancy. No significant difference was found in mean UA S/D, UAPI, UARI, MCA S/D, MCAPI, MCARI and CPR value between 40-41 and 41-42 weeks of gestation (Table 1-4).

27.6% of pregnant mothers at gestational age of 40-42 weeks had adverse perinatal outcome where as 100% mother in 36-40 weeks’ gestational age had normal outcome. Among post-dated pregnancies 48% mothers having gestational age of 41-42 weeks had adverse perinatal outcome in comparison to 15% at 36-40 weeks of gestation. APGAR score in 1 and 5 minutes was low in post-dated pregnancy compared to term pregnancy. No statistical significant difference was noted in UA S/D, UAPI, UARI, MCA S/D, MCAPI, and MCARI in pregnancy with normal and adverse perinatal outcome. Only CPR showed significant difference for predicting adverse perinatal outcome (p=0.001). Mean CPR value was low (1.34) in case of adverse perinatal outcome.

The sensitivity of UA S/D, MCAPI, and UARI for predicting adverse outcome was nil. UAPI sensitivity was very low (5.56%). MCARI sensitivity and specificity is 60% and 75% respectively. The sensitivity and positive predictive value of CPR screening efficiency for prediction of adverse perinatal outcome in post-dated pregnancy were same (85.11%). It assures the obstetrician of the fetal wellbeing. The specificity and negative predictive values of CPR however were very low (61.11%). Its false positive rate was very high (38.88%).

**Table 1: Comparison of different Doppler indices between case and control group**

	Group		p Value	Significance
	Case	Control		
	Mean ± Std. Deviation	Mean ± Std. Deviation		
UA S/D	1.99 ± 0.08	1.98 ± 0.1	0.386	Not Significant
UAPI	0.86 ± 0.05	0.88 ± 0.05	0.117	
UARI	0.53 ± 0.04	0.54 ± 0.04	0.151	
MCA S/D	2.12 ± 0.12	2.13 ± 0.17	0.633	
MCAPI	1.19 ± 0.09	1.21 ± 0.08	0.112	
MCARI	0.71 ± 0.03	0.72 ± 0.05	0.095	
CPR	1.38 ± 0.07	1.39 ± 0.04	0.699	

Table 1 shows distribution of different Doppler indices i.e. UA S/D, UA PI, UA RI, MCA S/D, MCA PI, MCA RI and CPR in case and control. The mean value of

the Doppler indices shows no statically significant difference between case and control.

**Table 2: Comparison of different Doppler indices in post-dated pregnancy between (40 to 41) and (41 to 42) weeks.**

	Gestational Age		p Value	Significance
	40-41 weeks	41-42 weeks		
	Mean ± Std. Deviation	Mean ± Std. Deviation		
UA S/D	1.98 ± 0.08	2.01 ± 0.08	0.296	Not Significant
UAPI	0.85 ± 0.06	0.87 ± 0.05	0.279	
UARI	0.53 ± 0.04	0.52 ± 0.04	0.620	
MCA S/D	2.12 ± 0.12	2.13 ± 0.13	0.537	
MCAPI	1.19 ± 0.09	1.19 ± 0.09	0.824	
MCARI	0.7 ± 0.02	0.71 ± 0.03	0.413	
CPR	1.39 ± 0.07	1.37 ± 0.07	0.243	

Table 2 shows Comparison of different Doppler indices i.e. UA S/D, UA PI, UA RI, MCA S/D, MCA PI, MCA RI and CPR in post-dated pregnancy between (40 to 41) and (41 to 42) weeks. No statistical significant difference is found in this Doppler parameter between 40-41 and 41-42 weeks of gestation.

**Table 3: Comparison of perinatal outcome between case and control**

		Group		Total	p Value	Significance
		Case	Control			
Perinatal outcome	Adverse	18(27.69)	0(0)	18(13.85)	<0.001	Significant
	Normal	47(72.31)	65(100)	112(86.15)		
Total		65(100)	65(100)	130(100)		

Table 3 shows relationship of perinatal outcome between case and control. Out of 65 post-dated mothers, 18 have adverse perinatal outcome but 65 control mothers have normal perinatal outcome.

**Table 4: Doppler indices in women with normal and adverse perinatal outcome in post-dated pregnancy**

	Perinatal outcome		p Value	Significance
	Normal	Adverse		
	Mean ± Std. Deviation	Mean ± Std. Deviation		
UA S/D	2 ± 0.09	1.98 ± 0.06	0.571	Not Significant
UAPI	0.85 ± 0.06	0.88 ± 0.04	0.145	Not Significant
UARI	0.53 ± 0.04	0.52 ± 0.04	0.387	Not Significant
MCAPI	1.2 ± 0.08	1.17 ± 0.09	0.242	Not Significant
MCARI	0.71 ± 0.03	0.7 ± 0.03	0.069	Not Significant
CPR	1.4 ± 0.06	1.34 ± 0.08	0.001	Significant

Table 4 shows relationships of different Doppler indicators (S/D, UA PI, UA RI, MCA S/D, MCA PI, MCA RI and CPR) in women with normal and adverse perinatal outcome. Only CPR shows statistically significant difference for predicting adverse perinatal outcome (p=0.001).

#### 4. Discussion

Our study shows the mean value of UA S/D ratio, UA PI, UA RI, MCA S/D, MCAPI, MCARI, CPR were 1.99 ± 0.08, 0.86 ± 0.05, 0.53 ± 0.04, 2.12 ± 0.12, 1.19 ± 0.09, 0.71 ± 0.03, 1.38 ± 0.07 in post-dated pregnancy whereas it is 1.98 ± 0.1, 0.88 ± 0.05, 0.54 ± 0.04, 2.13 ± 0.17, 1.21 ± 0.08, 0.72 ± 0.05, 1.39 ± 0.04 in dated pregnancy (36-40 weeks) The above Doppler indices show no statistical significance in both case and control groups. Farmakides *et al.* included pregnancies of more than 41

weeks of gestation and reported that impedance to flow in the uterine and umbilical arteries was not altered, even in the presence of other signs suggestive of fetal compromise [16]. Similarly, Stokes *et al* [17] examined 70 pregnancies at more than 41 weeks of gestation and reported that impedance to flow in the umbilical and uteroplacental arteries was not significantly different in pregnancies associated with fetal compromise and abnormal neonatal outcome from those with normal outcome [18]. Zimmermann *et al.* studied 153 pregnancies at 41–43 weeks of gestation and reported that impedance to flow in the umbilical artery, uteroplacental arteries and fetal middle cerebral artery did not change significantly within this gestational range [19]. The majority of Doppler measurements in pregnancies with subsequent asphyxia or otherwise complicated fetal outcome were within the 95% prediction interval for patients with normal fetal outcome.

Bar Hava *et al* [20] in their study measured impedance to flow in the umbilical artery and the fetal middle cerebral and renal arteries in pregnant mothers having gestational age of more than 41 weeks. In 15 pregnancies, there was oligohydramnios and, although in this group the mean birth weight was significantly lower than in the 42 pregnancies with normal amniotic fluid, there were no significant differences between the groups in relation to the Doppler indices. Arstom *et al* [21] observed the blood velocity in the umbilical artery, fetal descending aorta and fetal middle cerebral artery in normal pregnancies between 25-42 weeks of gestation. The blood velocities were analyzed for PI, S/D ratio and RI of UA and MAC and the relation of gestational age and reference value for the variables of the blood velocity were established. The mean UAPI was 0.8 in case of 41 weeks of gestational age and it is 0.75 in 42 weeks of gestational age. Selam *et al* [22] performed a cross sectional study beyond 41 weeks of gestational age. Pulse Doppler imaging was used to determine PI from MCA, renal artery, inferior vena cava, and ductus venosus. The mean UA PI was same (0.86) in both 41 and 42 weeks of gestational age. In the present study the mean UAPI was 0.85 and 0.87 at 40-41 weeks and 41-42 weeks of gestational age. In the present study mean MCAPI was same (i.e.1.19) in both 40-41 weeks and 41-42 weeks of gestational age and it is comparable with above two studies. A cross sectional observational study involving 140 women – 10 women for each gestational day between 287- 300 days of gestation was performed by Palacio *et al* [23]. Fetal Doppler parameters were assessed to construct normal reference range for UAPI, MACPI. CPR was calculated as a ratio of MCA PI/UAPI. CPR was 1.36 and 1.27 in 41 and 42 weeks of gestational age respectively.

In our study 130 pregnant women having gestational age of  $\geq 36$  week to 42 weeks were participated. Study group consists of 65 pregnant women with gestational age of  $\geq 40$  weeks. Out of them 18 pregnant mothers had an adverse perinatal outcome and 65 control mothers having gestational age of 36-40 weeks had normal perinatal outcome. Among post dated pregnancies 40 mothers were between gestational age of 40-41 weeks and 25 mothers were between 41-42 weeks. Adverse perinatal outcome was noted in 12 pregnant mothers in the gestational age of 41-42 weeks where as only 6 pregnant mother of gestational age of 40-41 weeks have adverse perinatal outcome. It is seen that pregnant mother of 41-42 weeks gestational age had more adverse perinatal outcome as compared to 40-41 weeks and it is statistically significant ( $P=0.004$ ). Gupta *et al*[24] conducted a study on 31 women of gestational age of  $\geq 40$  weeks and found 5 (16.1%) had an adverse perinatal outcome. There were 5 pregnancies with meconium stain of the liquor and 2 of these require admission to NICU for MAS. In our study 18(13.85%) had adverse perinatal outcome and all needed admission to

NICU. In the present study the value of mean UA S/D ratio in women with normal and adverse perinatal outcome is ( $2 \pm 0.09$  vs.  $1.98 \pm 0.06$ ) and it was no statistically significant between the groups. The mean MCAPI value in women with normal and adverse perinatal outcome is ( $1.2 \pm 0.08$  vs.  $1.17 \pm 0.09$ ) and it shows no significant correlation. The mean MCARI and UARI in pregnancies with normal and adverse perinatal outcome is ( $0.71 \pm 0.03$  vs.  $0.7 \pm 0.03$ ) and ( $0.53 \pm 0.04$  vs.  $0.52 \pm 0.04$ ) and the mean UAPI value in pregnancies with normal and adverse perinatal outcome was ( $0.85 \pm 0.06$  vs.  $0.88 \pm 0.04$ ) and all these are not statistically significant. The mean CP ratio was  $1.4 \pm 0.06$  and  $1.34 \pm 0.08$  in pregnancies with normal and adverse perinatal outcome respectively and was statistically significant ( $p=.001$ ). Sensitivity, Specificity, PPV, NPV and diagnostic accuracy of different Doppler parameters are calculated by using reference cut-off value published by El Sökkary *et al* [25]. The sensitivity of MCA PI, UA-S/D and UARI for predicting adverse outcome was found nil as all the women for adverse outcome had normal Doppler value. UAPI sensitivity was very low i.e. 5.56%. MCA RI sensitivity and specificity is 60% and 75% respectively. So, these Doppler parameters are not sensitive and specific enough for predicting adverse outcome in post-dated pregnancy.

Doppler study conducted by Gupta *et al* [24], found that the value of umbilical artery S/D ratio was not statistically different in women with normal and abnormal perinatal outcome ( $2.64 \pm 0.84$  vs.  $2.43 \pm 0.50$ ). Four of the five women with adverse perinatal outcome had normal UA / S/D ratio of  $< 3$ . Similarly, there was no statistically significant difference in the MCA PI values in the pregnancies with normal and adverse perinatal outcome ( $1.30 \pm 0.27$  vs.  $1.33 \pm 0.21$ ). The sensitivity of MCA PI for predicting adverse perinatal outcome was found to be nil as all the women with adverse perinatal outcome had normal MCA PI values. The mean CPR was  $1.39 \pm 0.26$  and  $1.23 \pm 0.12$  in pregnancies with normal and adverse perinatal outcome respectively, and the difference was not significant. MCA PI was normal in the study of all women with adverse perinatal outcome; hence it is an insensitive test for predicting adverse perinatal outcome. The CPR quantifies the redistribution of cardiac output by dividing Doppler indices from representative cerebral and fetoplacental vessels, and has been considered superior to the MCA-PI alone in predicting adverse fetal outcome. Baschat and Gembruch *et al* [26] constructed a reference range for CPR which is not constant throughout gestation, and hypothesized that reference ranges constructed by a standardized Doppler technique may be of benefit for monitoring high-risk pregnancies. Bahado-Singh *et al*[27] reported that CPR is superior to MCA-PI or UA-PI alone in predicting adverse outcome in growth-restricted fetuses, but that CPR does not appear to correlate significantly with

outcome in fetuses after 34 weeks' of gestation. Studies on CPR in uncomplicated prolonged pregnancies have led to conflicting result.

Gramellini *et al* [28] and Devine *et al* [29] found that a CPR of less than 1.08 in term and 1.05 in post-term pregnancies, respectively, was an accurate predictor of perinatal outcome. Gramellini *et al* [28] used the ratio of MCA-PI to UA-PI between 30 and 41 weeks' gestation, but used a single cut-off of 1.08.

Among 65 post-dated pregnancies in the present study, 47 pregnant mother had CPR >1.335 and 18 <1.335. Eleven out of 18 (CPR<1.335) have adverse perinatal outcome. The CPR screening efficiency for prediction of adverse perinatal outcome in post-dated pregnancy is 85.11% sensitive and 85.11% PPV. The Specificity and NPV of CPR are however very low (i.e. 61.11%). Its false positive rate is also very high (38.88%). Its low specificity and high false positive value lead to unnecessary test and intervention.

## 5. Conclusion

Knowledge about Doppler indices in post-dated pregnancy is poor. None of the Doppler indices except CPR is sensitive enough. Although CPR cut-off value of 1.335 assures the obstetrician of fetal wellbeing, its low specificity and high false positive results lead to unnecessary tests, undue concern and unnecessary interference. Hence, it is not an ideal test for routine antepartum fetal surveillance in low risk post-dated pregnancy.

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