International Journal of Clinical Obstetrics and Gynaecology

ISSN (P): 2522-6614
ISSN (E): 2522-6622

www.gynaecologyjournal.com
2024; 8(2): 35-42
Received: 30-05-2023
Accepted: 25-06-2023

Dr. Rupali Mungase
MBBS, DNB OBGY, Resident, District Hospital, Dharwad, Karnataka, India

Dr. Satish Shetty
MBBS, MD OBGY, Senior Consultant, District Hospital, Dharwad, Karnataka, India

Dr. Suchitra Somkuwar
MBBS, DNB OBGY, IVF Consultant, Indira IVF, Jabalpur, Madhya Pradesh, India

Corresponding Author:
Dr. Rupali Mungase
MBBS, DNB OBGY, Resident, District Hospital, Dharwad, Karnataka, India

A clinical study on Doppler velocimetry of umbilical artery and middle cerebral artery in post-dated pregnancy in the prediction of fetal outcome

Dr. Rupali Mungase, Dr. Satish Shetty and Dr. Suchitra Somkuwar

DOI: https://doi.org/10.33545/gynae.2024.v8.i2a.1433

Abstract
Background: Doppler ultrasound velocimetry of umbilical and fetal vessels has become established method of antenatal monitoring, allowing non-invasive assessment of fetal circulation. The objective is to study the fetal Doppler indices named umbilical artery (UA) - Pulsatility index (PI), Middle cerebral artery (MCA)-Pulsatility index (PI) and MCA -PI/ UA -PI ratio i.e. Cerebroplacental Ratio (CPR) in post-dated pregnancies and their correlation with perinatal outcome.
Methodology: A Prospective observational study conducted on 200 pregnant women having gestational age > 40 weeks in study period from April 2019 to March 2020 at District Hospital, Dharwad. Detailed history of present pregnancy & past obstetric history taken. Thorough examination of patient done. USG Doppler studies were done, above mentioned Doppler parameters were assessed. Apgar score of the neonates were calculated at 1 min and 5 min. They were divided into two groups based on the presence or absence of adverse perinatal outcome.
Results: Women with adverse perinatal outcome shows higher UA-PI (> 0.82) with the specificity of 87% and sensitivity of 50%, had higher cases with oligohydroamnios (61%). Adverse neonatal outcome was much higher in the 41-42 weeks of gestation (33.33%) as compared to the 40-41 weeks of gestation (11.18%).MCA - PI with value (< 1.0) shows good ability to predict the mode of delivery with the specificity of 76% and sensitivity of 44.8%. MCA-PI and CPR were not helpful in predicting the adverse perinatal outcome.
Conclusion: Doppler indices including MCA-PI, CPR were not useful in predicting adverse neonatal outcome in post-dated pregnancies without any high risk factor. However, UA-PI appears to have good ability to predict adverse neonatal outcome and considered best one of them.

Keywords: Post-dated pregnancy, Doppler velocimetry, perinatal outcome

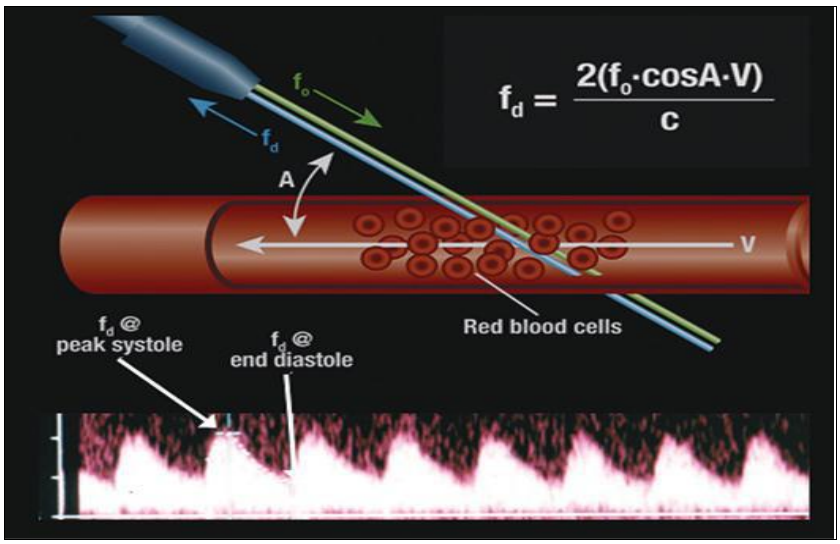
Introduction
Post-dated pregnancy is defined as one which has crossed expected date of delivery. Prolonged pregnancies are those pregnancies advancing beyond expected date of delivery [1].
ACOG (American College Of Obstetricians and Gynaecologists) and The WHO (World Health Organization) had defined post -term pregnancy as that lasts 42weeks (294 days) or more from the first day of the last menstrual period [2-3]. According to ACOG recommendation-Early term - 37-0/7 weeks of gestation through 38 -6/7 weeks of gestation.
Full term - 39-0/7 weeks of gestation through 40 - 6/7 weeks of gestation.
Late term - 41-0/7 weeks of gestation through 41-6/7 weeks of gestation.
Post term - 42-0/7 weeks of gestation and beyond [4].
Incidence of post-dated pregnancy has been reported to be between 4-14% with an average of 10.5% [5].
Incidence of post term pregnancy is about 5.5% of all pregnancies [6].
Prolongation of pregnancy complicates upto 10% of all pregnancy and carries increase risk to mother and fetus [7-8].
Recent studies have shown that the risk to the fetus and to the mother in continuing the pregnancy beyond the estimated date of delivery is higher than what was estimated earlier [9].
The purpose of this study is to assess the effect of pregnancy beyond the 40 weeks on the Doppler flow velocity waveforms in the umbilical artery and middle cerebral artery and CP Ratio and to correlate the flow velocity waveforms with the perinatal outcome.
Doppler ultrasound velocimetry of Uteroplacental, Umbilical and fetal vessels has become

established method of antenatal monitoring, allowing non-invasive assessment of fetal circulation [10].

It's indices provides important information on the hemodynamic of the vascular area under study. Circulatory changes reflected in certain fetal Doppler waveforms predict adverse perinatal outcome [11].

Umbilical arteries are the common vessels assessed by Doppler ultrasound but recent studies confirm the efficacy of middle cerebral artery Doppler assessment for detecting fetal compromise [12-13]. Doppler sonography provides a unique opportunity to investigate human fetal hemodynamics and to use these findings for fetal surveillance. The Doppler effect, first reported by Christian Doppler in 1842 describes the apparent variation in frequency of a light or a sound wave as the source of the wave approaches or moves away relative to an observer. This apparent change in sound pitch (Doppler effect), or what is also termed the frequency shift, is proportional to the speed of movement of the sound-emitting source [14].

Doppler indices that are commonly used in obstetric practice are.



fd = 2(f0.cosA.V)/C
PI = S - D/M
RI = S - D/S
S/D = S/D
CPR = PI of MCA / PI of UA

Fig 1: The Doppler effect (fd) is dependent on the initial frequency of the ultrasound transducer (f0), the velocity of flow (V) of the blood within a vessel, and the cosine of the angle (A) that the ultrasound beam makes with the direction of blood flow. The frequency shift (fd) is displayed as a time-dependent plot within a cardiac cycle and is inversely proportional to the constant (c), which reflects a constant related to the medium in which the sound is traversing. Doppler indices commonly used in obstetric imaging. c, constant related to the medium in which the sound is traversing; D, diastole; M, mean; PI, pulsatility index; RI, resistance index; S, systole

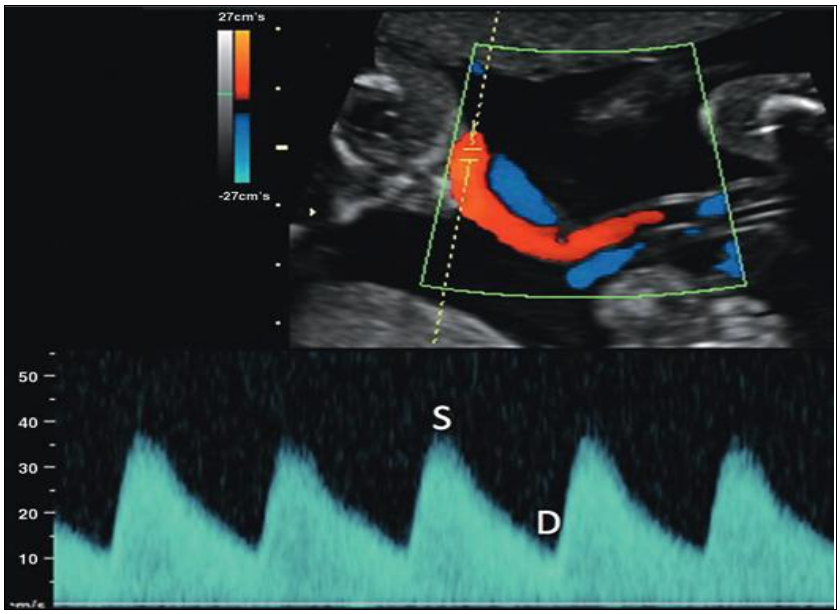


Fig 2: Doppler waveforms of the umbilical artery in a normal fetus in the third trimester of pregnancy. Note the increased end-diastolic velocity (D), consistent with a low impedance circulation. S, peak systole

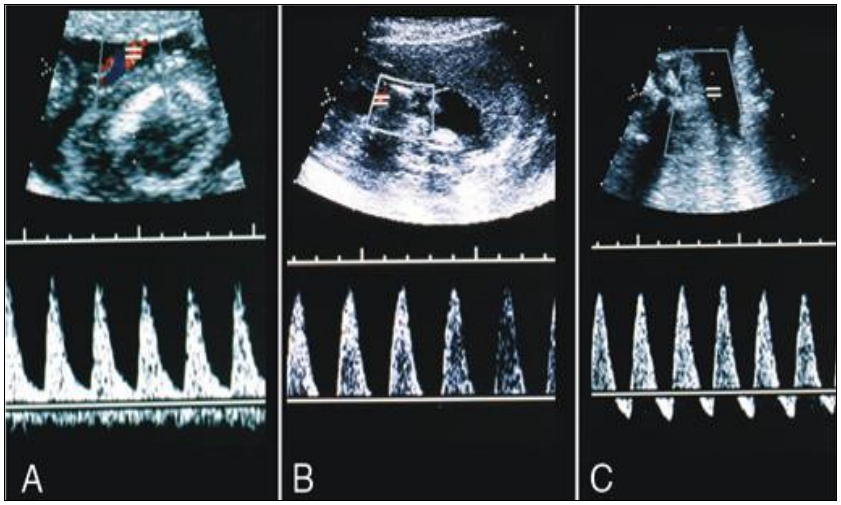


Fig 3: Abnormal umbilical artery Doppler waveforms; decreased end-diastolic velocity (A), absent end-diastolic velocity (B), reversed end-diastolic velocity (C). In 2013, the International Society for Ultrasound in Obstetrics and Gynecology (ISUOG) recommended taking Doppler measurements from a free loop of cord for the sake of simplicity and consistency

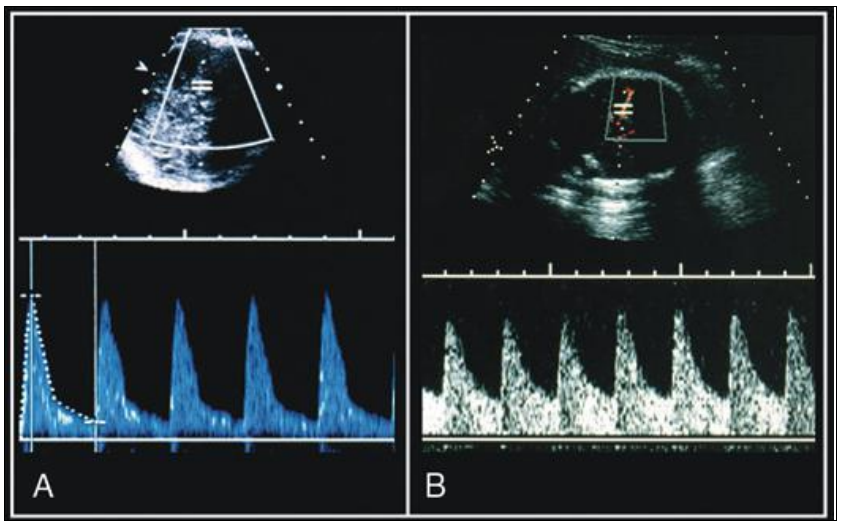


Fig 4: Doppler waveforms of the middle cerebral artery in a normal fetus (A) and in a hypoxemic fetus (B). Note the increase in end-diastolic velocity in fetus B resulting from a low-impedance cerebral circulation as part of the brain-sparing reflex

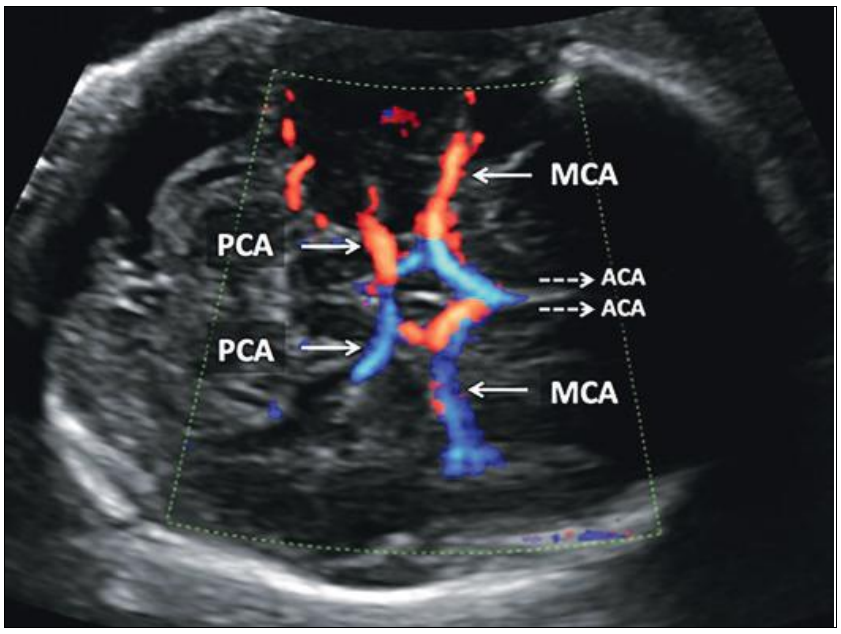


Fig 5: Circle of Willis shown on color Doppler imaging. ACA, anterior cerebral artery; MCA, middle cerebral artery; PCA, posterior cerebral artery. (From Ultrasound in Obstetrics & Gynecology: A Practical Approach. Available at www.openultrasound.com

MCA Doppler waveforms, obtained from the proximal third portion of the vessel, immediately after its origin from the circle of Willis, have shown the best reproducibility.

Cerebroplacental Ratio: CPR is emerging as an important predictor of adverse pregnancy outcome, and it is used for the assessment of fetal wellbeing. It is the ratio of Pulsatility Index of Middle Cerebral Artery to the Pulsatility Index of Umbilical Artery.

Aim: To predict and improve fetal outcome by doing Doppler study

Materials and methods

This study was conducted in department of Obstetrics and Gynecology, District hospital, Dharwad accredited to DNB course.

Study Design: A Prospective Observational study.

Sample Size: 200 patients.

Inclusion criteria: This study included the singleton pregnancy with cephalic presentation with gestational age more than 40 weeks without any high risk factor. Careful and detail history including the information regarding the age, details about previous conception, antenatal care, and booking status was collected. Complete general physical examination, systemic examination and obstetric examination was done. Routine and relevant investigations such as Haemoglobin, Blood Grouping and Rh typing, VDRL, HIV, HBsAg, RBS, analysis of urine (albumin, sugar, microscopy) were all done. Period of gestation was derived from history of LMP and clinical examination and confirmed by 1st trimester ultrasound.

Ultrasound Examination - The following ultrasound parameters were assessed

1. Routine ultrasound for fetal biometry which includes BPD (Biparietal diameter), Femur Length (FL), Abdominal circumference (AC), Head circumference (HC), Estimated fetal weight calculated automatically using Hadlocks formula, AFI were calculated.
2. USG Doppler studies - a) Umbilical artery pulsatility index
   b) Middle cerebral artery pulsatility index.
   c) Cerebroplacental ratio (CPR) i.e. MCA PI /UA PI for the evaluation of fetal status in utero.
3. APGAR score - The neonates were subjected to APGAR scoring at 1 and 5 min.

Doppler indices were calculated by using

https://medicinafetalbarcelona.org/calc/ the app.

Single Doppler study of MCA and UA was done. The apparatus used were 1) Aloka SSD 1100 prosound alpha 6 ultrasound machine.

Mindray DC-N2 ultrasound machine, with the Doppler unit and convex linear transducer 3.5 MHz.

The technique of UA and MCA Doppler measurement:

All the examination were made with the patient lying in semi recumbent position with a lateral tilt. Doppler transducer was placed on the abdominal wall over the uterus and carefully manipulated till Doppler signals appropriate for that particular vessels were identified. All the examinations were performed only during foetal apnoea and foetal inactivity.

The signal was recorded for a minimum of 5 to 8 cycles with the blood flow velocity waveforms of equal shape and amplitude and satisfactory quality. Then the image was frozen and measurements were taken. An area of amniotic cavity with several loops of umbilical cord was selected for the Umbilical artery Doppler indices. A minimum of 3 separate readings were recorded and averaged before the final values obtained.

The standard plane for the measurement of Middle cerebral artery Doppler indices was transthalamic plane which contains the thalami and cavum septum pellucidum. Care was taken not to exert pressure on the fetal head because this will alter the flow velocity waveforms from the MCA.

The patient were followed up till delivery. Mode of delivery were noted in each case.

The study population was divided into 2 groups with 1) normal Doppler indices 2) Abnormal Doppler indices and their perinatal outcome was studied.

Adverse perinatal outcome was defined as the presence of 1 or more of the following: caesarean delivery for fetal distress, Apgar score <7 at 1 and 5 min, Meconium aspiration syndrome, Neonatal intensive care unit admission and perinatal mortality.

Results and Discussion

Age distribution

The average age was 23.85 +/- 2.81 years.

The age distribution is shown in figure number.

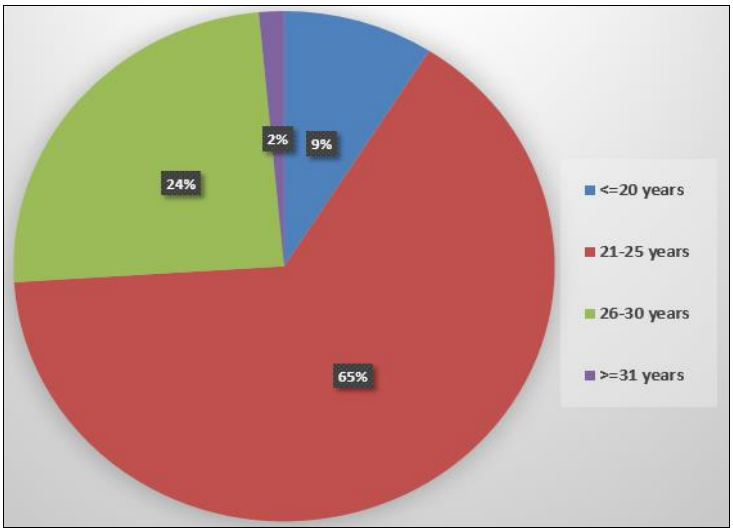


Fig 6: Age distribution

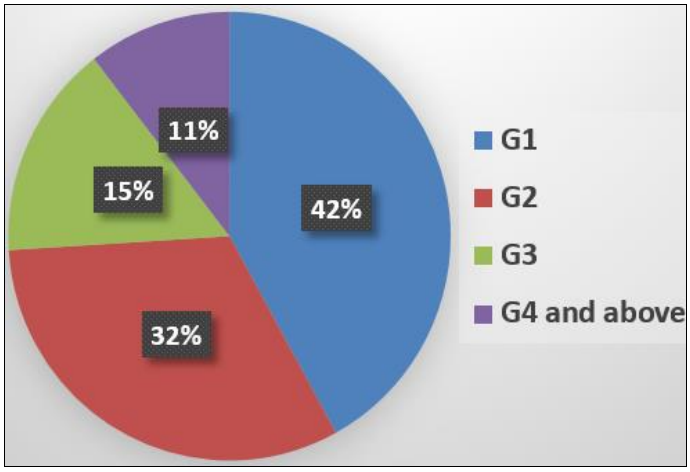


Fig 7: Gravidity distribution

Table 1: Demographic data of the two studied group

Parameter	Adverse (n=31)	Normal (n=169)	
Maternal age	22.67 +/-2.885	24.09 +/-2.071	0.009 Statistically significant difference
Gestational age at delivery	284 +/-14.81	286 +/-13.22	0.0002 statistically significant difference
Gravidity	1.58 +/- 1.13	2.05 +/-0.76	0.02 statistically significant difference
Parity	0.85+/- 0.95	1.25+/- 0.599	0.210 not statistically significant

The average age of the patients in the group which had adverse neonatal outcomes was 22.67 years, whereas that of the patients in the group which had normal neonatal outcomes was 24.09 years. The gestational age (in days) at delivery was 284 in those with adverse neonatal outcomes and 286 in those with normal neonatal outcomes. While the parity between the two groups were comparable (p value 0.21), the gravidity was lower in the group with adverse events (1.58) as compared to those with normal outcomes (2.05) with statistically significant difference (p value 0.02). These observations are explained by the fact that this was an observational study of an unselected population with no matching process to ensure the comparability of the groups.

Table 2: Comparison between both the groups as regards: UA-PI, MCA-PI, MCA-PI/UA-PI ratio and EFW

Parameter	Adverse (n=31)	Normal (n=169)	
EFW on USG	3.11 +/-0.239	3.0+/-0.294	0.058 Not statistically significant
Neonatal birthweight	3.06+/-2.54	3.0+/-0.26	0.19 Not statistically significant
Umbilical artery PI	0.81+/-0.169	0.76 +/- 0.138	0.08 Not statistically significant
MCA PI	1.2 +/- 0.178	1.19 +/- 0.167	0.65 Not statistically significant
CPR	1.5+/- 0.276	1.55+/- 0.291	0.29 Not statistically significant

The estimated fetal weight on ultrasonography was 3.11 kg in those with adverse neonatal outcomes while that with normal neonatal outcomes was 3.0 kg, with no statistically significant difference between the groups.

The actual neonatal birth weights was 3.06 kg in those with adverse neonatal outcomes while that with normal neonatal outcomes was 3.0 kg, with no statistically significant difference between the groups. The umbilical artery PI was 0.81 in those with adverse neonatal outcomes while that with normal neonatal outcomes was 0.76, with no statistically significant difference between the groups.

The MCA PI was 1.2 in those with adverse neonatal outcomes while that with normal neonatal outcomes was 1.19, with no statistically significant difference between the groups. The CPR was 1.5 in those with adverse neonatal outcomes while that with normal neonatal outcomes was 1.55, with no statistically significant difference between the groups.

Table 3: Comparison between both the groups as regards the amniotic fluid volume

	Adverse (31)	Normal (n=169)	
AFI value	6.13+/- 2.27	7.97 +/- 3.02	0.001 Statistically significant
Normal AFI	12/ 31	141/169	0.001 Statistically significant
Oligohydramnios	19/31 (61%)	28/169(16.5%)	

Table 3A: Relation between the AFI and mode of delivery

Amniotic fluid	Normal (>5 cm)	Abnormal (<=5 cm)	
Vaginal delivery	130	16	0.0001
LSCS	29	25	

The average AFI of those with adverse neonatal outcomes was 6.13cm while that with normal neonatal outcomes was 7.97 cm, and the difference between the groups was statistically significant. Among those who had an adverse neonatal outcome, 61% had oligohydramnios. Whereas among those who had normal neonatal outcomes, only 16.5% had oligohydramnios. The difference between the groups was statistically significant. The proportion of patients with oligohydramnios who had a LSCS was 60.9% (25/41), whereas the proportion of patients with normal AFI who had an LSCS was 18.2%, and the difference between the groups was statistically significant.

Table 4: Comparison between both the groups as regards the indications of CS

	Adverse (31)	Normal (n=169)	
LSCS	31/31	23/169	<0.0001
Meconium stained liquor	23/31		<0.0001
Non-reactive FHR	8/31		
CPD		8	
Failed IOL		4	
Severe oligo		10	
Obstructed labour		1	

Among those who had an adverse outcome, all of them were delivered by LSCS. However, among those who had normal neonatal outcome, only 13% delivered by LSCS. All those who had an adverse neonatal outcome underwent an LSCS due to meconium stained liquor or non-reactive fetal heart rate pattern. Whereas, those who had a normal neonatal outcome, underwent LSCS due to CPD, failed IOL, severe oligohydramnios and obstructed labour.

Table 5: Relation between the period of gestation at delivery and adverse perinatal outcome.

Gestational age	Number	Percentage	Mean birth weight	Apgar score at 1 minute	Apgar score at 5 minutes	NICU admission
40-41	161	80.5%	3007 grams	7	8	18/161
41-42	39	19.5%	3021 grams	7	8	13/39

The adverse neonatal outcome was much higher in the 41-42 weeks gestation group (33.33%), as compared to the 40-41 weeks gestation group (11.18%). The mean birth weight and Apgar score (Both 1 minute and 5 minutes) were similar in both the 40-41 weeks gestation age and 41-42 weeks gestational age groups.

Table 6: Relation between the UA-PI, MCA-PI and MCA-PI /UA-PI ratio (CPR) to perinatal outcome and the mode of delivery.

	UA-PI			MCA-PI			CPR		
	Normal <0.82	Abnormal >0.82		Normal >1.0	Abnormal <1.0		>10th percentile	<10th centile	
Vaginal delivery	86	60	0.747	130	16	0.024	134	12	0.3207
LSCS	30	24		41	13		56	8	
Adverse outcome	15	16	0.0001	26	5	0.782	27	4	0.509
Normal outcome	101	16		145	24		154	15	

We used UA-PI cut off value was 0.82 based on the study by Ahmed Maged *et al*. The UA-PI was not useful in predicting the mode of delivery. (p value 0.747). The UA-PI appeared to have a good ability to "rule out" the adverse neonatal outcome, considering that it has a specificity of 87% (101/116). However, the sensitivity of the test is quite poor at 50% (16/32). The MCA PI appeared to have a good ability to "rule out" CS, considering that it has a specificity of 76% (130/171). However, the sensitivity of the test is quite poor at 44.8% (16/29). The proportion of patients with a CPR <10th percentile who had a poor neonatal outcome was 21.05% (4/19) and those with a CPR >10th percentile who had a poor neonatal outcome was 14.91% (27/154) and there was no statistically significant difference between the groups. This implies that CPR does.

Table 7: The details values are presented below

	UA - PI Normal<0.82	UA-PI Abnormal>0.82	
Vaginal delivery	86	60	Chi-square test p value = 0.747
LSCS	30	24	

As shown in table number, it can be seen that there was no correlation between an Umbilical Artery PI value (using cut off 0.82) and the mode of delivery. (p value 0.747).
For the UA PI to predict vaginal delivery, the following accuracy statistics are noted.

Sensitivity is 24 / (24+30) = 44.44% (95% CI - 30.92% to 58.60%).
Specificity is 86/ (86+60) =58.90% (95% CI- 50.47% to 66. 97%).

	UA - PI Normal <0.82	UA - PI Abnormal >0.82	
Adverse outcome	15	16	Chi-square test P value 0.0001
Normal outcome	101	16	

For the UA PI to predict adverse neonatal outcomes, the following accuracy statistics are noted

Sensitivity is 16/ (16+16)) = 50% (95% CI - 31.89% to 68.11%

	MCA PI Normal >1.0	MCA PI Abnormal <1.0	
Vaginal delivery	130	16	Chi-square test P value 0.024 Statistically significant
LSCS	41	13	

Specificity is101 / (101+16) =86.21% (95% CI- 78.74% to 91.98%). As shown in table number, it can be seen that there was a statistically significant correlation between Middle Cerebral Artery PI value (using cut off 0.82) and the mode of

delivery. (p value 0.024). For the MCA PI to predict vaginal delivery, the following accuracy statistics are noted

	MCA PI Normal >1.0	MCA PI Abnormal <1.0	
Adverse outcome	26	5	Chi-square test P value 0.782 Statistically significant
Normal outcome	145	24	

Sensitivity 24.07% (13/13+41) 13.49% to 37.64% Specificity 89.04% (130/130+16) 82.81% to 93.60% For the MCA PI to predict adverse neonatal outcomes, the following accuracy statistics are noted Sensitivity 16.13% (5/5+26) (95% CI 5.45% to 33.73%) Specificity 85.80% (145+24) (95% CI 79.61% to 90.68%).

	CPR		
	>10th centile	<10th centile	Chi-square test p value 0.3207 Not statistically significant
Vaginal delivery	134	12	
LSCS	56	8	

As can be seen in table number, there is no statistically significant correlation between a CPR <10th centile and mode of delivery (p value 0.3207). For a CPR <10th centile, the following accuracy statistics are noted. Sensitivity 12.50% (8/8+56) 5.55% to 23.15%.

	CPR >10th percentile	CPR <10th centile	
Adverse outcome	27	4	Chi-square test p value 0.509 Not statistically significant
Normal outcome	154	15	

Specificity 91.78% (134/134+12) 86.08% to 95.68% as can be seen in table number, there is no statistically significant correlation between a CPR <10th centile and adverse neonatal outcomes (p value 0.3207).
For a CPR <10th centile in its ability to predict adverse neonatal outcomes, the following accuracy statistics are noted.
Sensitivity 12.90% (4/4+27) 3.63% to 29.83% Specificity 91.12% (154/15+154) 85.78% to 94.95%.

Conclusion

From this study it is concluded that UA PI values, MCA PI values, CPR values are similar between the neonates who had good and adverse neonatal outcome in low risk post-dated pregnancies.
UA PI value of > 0.82 is helpful in predicting adverse neonatal outcome.
UA PI value of > 0.82 is not helpful in predicting the mode of delivery.
MCA PI value of > 1.0 is not helpful in predicting the adverse neonatal outcome.
MCA PI value of > 1.0 is helpful in predicting the mode of delivery.
CPR < 10th percentile is not helpful in predicting the adverse perinatal outcome.
CPR < 10th percentile is not helpful in predicting the mode of delivery.

Recommendation

Ultrasound Doppler parameters are to be used cautiously and on selected basis in the management of post-dated pregnancies. Further large scale prospective studies are required in the topic of Ultrasound Doppler study in post-dated pregnancy.

Acknowledgement: Not available.

Author's Contribution: Not available.

Conflict of Interest: Not available.

Financial Support: Not available.

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How to Cite This Article
Mungase R, Shetty S. A clinical study on Doppler velocimetry of umbilical artery and middle cerebral artery in post-dated pregnancy in the prediction of fetal outcome. International Journal of Clinical Obstetrics and Gynaecology. 2024;8(2):35-42.