

## DOPPLER INDICES OF FETAL MIDDLE-CEREBRAL AND UMBILICAL ARTERIES IN NORMAL 28-40 WEEKS PREGNANCIES

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### ABSTRACT

**Objectives:** The aim of the study was to establish normative data for the pulsatility index (PI), resistive index, and cerebro-placental ratio of umbilical artery (UA), and fetal middle cerebral artery (MCA) of Indian pregnant women in the third trimester of pregnancy using multiples of the median and percentile reference range.

**Methods:** It was a cross-sectional study; the study was carried out at the Department of Obstetrics and Gynaecology and Radiology in MGM Medical College and LSK Hospital, the tertiary care and teaching hospital. A total of 200 cases were enrolled for this study. Patients with Singleton low-risk pregnancies with confirmed gestational age, normal anatomy, normal estimated fetal weight, and born at term with birth weight between 10<sup>th</sup> and 90<sup>th</sup> percentile and gestational age was based on LMP date, corrected if required by trimester first/second (Before 20 weeks) fetal sonographic parameters were included in the study.

**Results:** We found from 28 weeks to 39 weeks of gestational age, MCA PI showed a significantly positive correlation with the cerebro-placental ratio (CPR) 40<sup>th</sup> week of gestational age. We found no significant correlation. While from 28 weeks to 40 weeks of gestational age, UA PI showed a significantly negative correlation with the CPR.

**Conclusion:** Doppler ultrasound is used as a part of the clinical protocol in the surveillance of pregnancies. The UA and MCA Doppler indices and CPR are currently used to modify the scheduling of antepartum surveillance and, in some cases, to timely delivery of the compromised fetus. Researchers measured the pulsatility, resistivity, and cardiac indices of the UA and the fetal MCA between 28 and 40 weeks of gestation to establish a normal range.

**Keywords:** Middle cerebral artery, Umbilical artery, Cerebroplacental ratio, Uterine artery, Doppler.

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### INTRODUCTION

For the placenta to form, it is important for trophoblasts to move into the uterine lining and blood vessels. Normal blood flow in the mother's uterine artery is important for a healthy environment inside the uterus and for keeping the placenta working, which is important for the baby's growth. It is mostly because of two things. First, the mother's blood brings nutrients and eliminates waste. Second, the flow of blood in the uterine artery affects how much oxygen gets to the place where the mother and baby meet [1].

With uterine artery Doppler (UAD), it is possible to predict critical vascular events that will happen during pregnancy (UAD). Changes in the uterine and placental blood vessels can be monitored throughout pregnancy for signs of trouble, beginning at the time of implantation and continuing through to the conclusion [2].

Doppler velocimetry is used to assess small-for-gestational-age fetuses at risk of adverse perinatal outcomes [3]. Doppler abnormalities in the umbilical artery (UA) are closely related to placental disease. More recent work has suggested that the ratio of middle cerebral artery (MCA)-pulsatility index (PI) to UA-PI, the cerebroplacental ratio (CPR), is an independent predictor of fetal compromise, cesarean section, and adverse perinatal outcome. Therefore, UA and MCA Doppler indices and CPR are currently used to modify the scheduling of antepartum surveillance and, in some cases, to timely delivery of the compromised fetus [4].

The study determined normal ranges and reference intervals for MCA and UA Doppler velocities, the S/D ratio, resistive index (RI) and PI, and the CPR in healthy pregnant women.

### METHODS

It was a cross-sectional study. The study was carried out at the Department of OBG and Radiology in MGM Medical College and LSK Hospital, the tertiary care, and teaching hospital. A total of 200 cases were enrolled for this study. Patients with Singleton low-risk pregnancies with confirmed gestational age, normal anatomy, normal estimated fetal weight, and born at term with birth weight between 10<sup>th</sup> and 90<sup>th</sup> percentile and gestational age was based on LMP date, corrected if required by trimester first/second (Before 20 weeks) fetal sonographic parameters were included in the study.

Diagnosed fetal anomaly before recruitment, multifetal pregnancy, history of maternal smoking, a known complication in current pregnancy before recruitment, history of any pre-existing maternal conditions such as hypertension, diabetes mellitus, renal disease, and preeclampsia likely to affect the fetus. Cases who develop complications in the subsequent period of their ongoing pregnancy during the study period will be excluded from the study.

#### Study variables

Different UA and MCA Doppler indices.

#### Data collection and interpretation

Doppler velocity waveforms.

#### Methods of data collection

Eligible participants were evaluated through full history taking and detailed anatomical scans to confirm their gestational age. Doppler studies were performed using a Volvoson P8 machine with

124MHz-using the curvilinear transabdominal probe. All patients underwent a Doppler examination. The data were collected prospectively for research purposes. Using clinical information collected routinely to create a reference could be an important source of bias, with over-representation of at-risk cases. Doppler examination was done with the fetus in a quiet state, in the absence of fetal movements and fetal breathing movements. The angle of insonation was optimized as low as possible. The Doppler spectrum was recorded during voluntary maternal apnea. Blood flow velocity waveforms were obtained from the UA and fetal MCA spectral pulsed wave Doppler analysis was done after that. RI and PI were calculated for each vessel. The formulas used for PI and RI were:  $PI = S-D/MEAN$  and  $RI = S-D/S$ , where S is the peak Doppler frequency shift and D is the minimum. At least three uniform waveforms of the spectrum were recorded and analyzed. Blood flow velocity waveforms were recorded from the UA in the free-floating mid-portion of the umbilical cord. Doppler signals were registered from the fetal MCA in its proximal third. For an accurate measurement, the fetal head was in the transverse plane. Using Color Doppler ultrasound, the MCA vessels were pinpointed just above the frontal process of the sphenoid bone, which is located close to the skull's base.

#### Ethical consideration

The research procedure followed was accordance with the approved ethical standards and study was approved by the Institutional Ethics Committee. A written consent was taken from all potentially eligible subjects.

#### Plan for analysis of data

Continuous variable will be analyzed by independent student t-test or Mann-Whitney U test depending on the data normality.  $p < 0.05$  was considered to be statistically significant.

#### RESULTS

In the present study, patients were aged from 18 to 35 years. The majority of the subjects were aged 18–25 years (47.5%), followed by 26–30 years (37.5%) and 31–35 years (15%). The majority of the women were primigravida (49.5%), followed by 2<sup>nd</sup> (40.5%) and 3<sup>rd</sup> gravida (10%). Regarding the birth weight of the neonates of the mothers, we found a majority of them were weighed from 2.5 kg to 3.5 kg (49.5%), followed by >3.5 kg (28.5%) and below 2.5 kg (22%). Out of 200 neonates borne from the mothers included in the study; 102 (51%) were females and 98 (49%) were males. Presented in (Table 1).

The MCA PI percentile values for each gestational age are also plotted in a scatter, and it is shown (Fig. 1). From the gestational age of 28–40 weeks, the percentile values of MCA PI are decreasing gradually in the present study. The scatter plot of MCA PI shows a parabolic curve with a plateau between 28 and 30 weeks and thereafter a turn till 40 weeks of gestation (Tables 2 and 3).

Table 4 presents the mean and standard deviation (SD) values of MCA RI for each gestational age, along with percentile values. The MCA RI percentile values for each gestational age are also plotted in a scatter diagram, which is shown in (Fig. 2). Very likely to the MCA PI, the scatter plot of MCA RI also shows a parabolic curve with a plateau between 28 and 30 weeks and thereafter a turn till 40 weeks of gestation.

Table 5 presents the mean and SD values of UA PI for each gestational age, along with percentile values. The UA PI percentile values for each gestational age are also plotted in a scatter diagram, which is shown in Fig. 3. The scatter plot of UA PI shows a linear curve with a plateau throughout all the gestational weeks from 28 weeks to 40 weeks.

Table 6 presents the mean and SD values of UA RI for each gestational age, along with percentile values. The UA RI percentile values for each gestational age are also plotted in a scatter diagram and which is shown in Fig. 4. Very likely to the scatter plot of UA PI, the scatter plot of UA RI shows a linear curve with a plateau throughout all the gestational weeks from 28 weeks to 40 weeks.

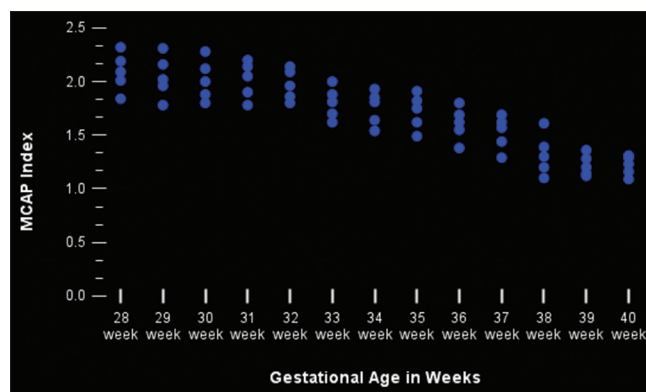


Fig. 1: Middle cerebral artery pulsatility index percentiles according to gestational age

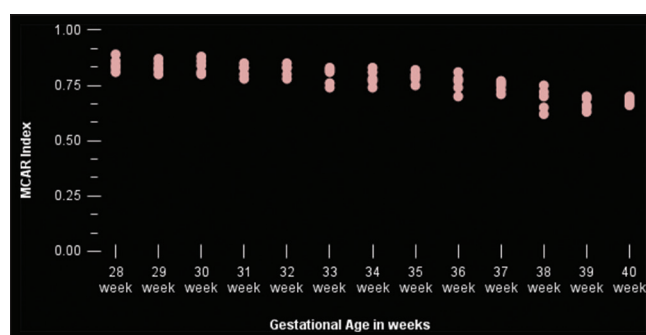


Fig. 2: Middle cerebral artery resistive index percentiles according to gestational age

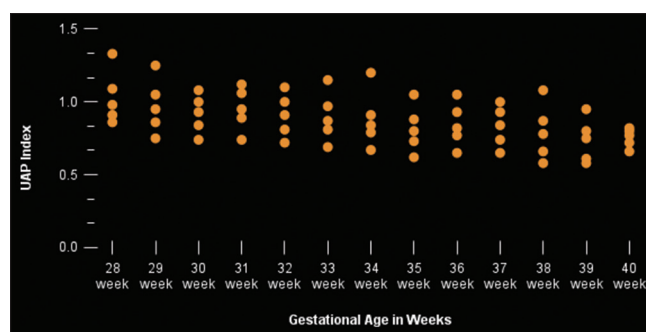


Fig. 3: Umbilical artery pulsatility index percentiles according to gestational age

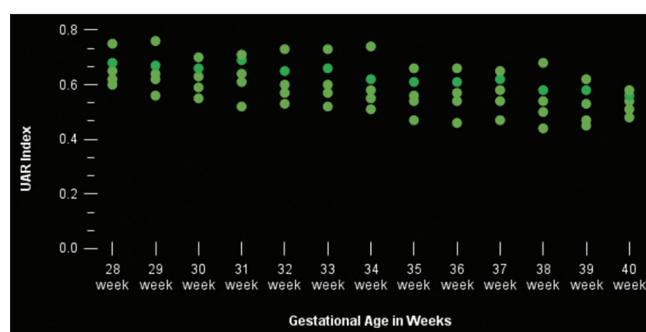


Fig. 4: Umbilical artery resistive index percentiles according to gestational age

Table 7 presents the mean and SD values of the CPR for each gestational age, along with percentile values. The CPR percentile values for each

gestational age are also plotted in a scatter graph, and it is shown in Fig. 5. The scatter plot of the CPR shows a parabolic curve with the plateau from 28 to 32 weeks and thereafter a turn till 40 weeks of gestation.

Table 8 presents the correlation between MCA PI with CPR and UA PI with CPR. Above analysis, we found from 28 weeks to 39 weeks of gestational age, MCA PI showed a significantly positive correlation with the CPR 40<sup>th</sup> week of gestational age. We found no significant correlation. While from 28 weeks to 40 weeks of gestational age, UA PI showed a significantly negative correlation with the CPR.

## DISCUSSION

The current research was performed at the Obstetrics and Gynecology and Radiology, M.G.M. Medical College and L.S.K. Hospital, Kishanganj,

Bihar. This study comprised 200 antenatal cases registered during the study period at OBG Department of tertiary care and teaching hospital.

Two hundred pregnant women were enrolled in the present study, all of whom were between 28 and 40 weeks along in their pregnancies.

In the present study, patients were aged from 18 to 35 years. The majority of the subjects were aged 18–25 years (47.5%), followed by 26–30 years (37.5%) and 31–35 years (15%). The majority of the women were primigravida (49.5%) followed by 2<sup>nd</sup> (40.5%) and 3<sup>rd</sup> gravida (10%). Regarding the birth weight of the neonates of the mothers included in the present study, we found the majority of them were weighed from 2.5 kg to 3.5 kg (49.5%) followed by >3.5 kg (28.5%) and below 2.5 kg (22%). Out of 200 neonates borne from the mothers included in the study; 102 (51%) were females and 98 (49%) were males.

Regarding the RI and PI of MCA and UA and CPR, we observed the following:

From the gestational age of 28 weeks to 40 weeks, the percentile values of MCA PI are decreasing gradually in the present study. The scatter plot of MCA PI shows a parabolic curve with a plateau between 28 and 30 weeks and thereafter a turn till 40 weeks of gestation. Very likely to the MCA PI, the scatter plot of MCA RI also shows a parabolic curve with a plateau between 28 and 30 weeks and thereafter a turn till 40 weeks of gestation. The scatter plot of UA PI shows a linear curve with a plateau throughout all the gestational weeks from 28 weeks to 40 weeks. Very likely to the scatter plot of UA PI the scatter plot of UA RI shows a linear curve with a plateau throughout all the gestational weeks from 28 weeks to 40 weeks. The scatter plot of the CPR shows a parabolic curve with the plateau from 28 to 32 weeks and thereafter a turn till 40 weeks of gestation.

Above analysis, we found from 28 weeks to 39 weeks of gestational age. MCA PI showed a significantly positive correlation with the CPR 40<sup>th</sup> week gestational age. We found no significant correlation.

**Table 1: Demographic characteristics**

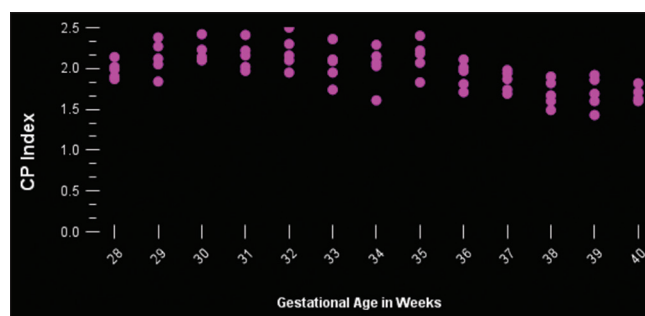
Variables	Number of Cases	Percentage
Age group		
18–25 years	95	47.5
26–30 years	75	37.5
31–35 years	30	15.0
Gravidity		
Primigravida	99	49.5
2 <sup>nd</sup> Gravida	81	40.5
3 <sup>rd</sup> Gravida	20	10.0
Birth weight		
<2.5 kg	44	22.0
2.5–3.5 kg	99	49.5
>3.5 kg	57	28.5
Fetal sex		
Male	98	49.0
Female	102	51.0

**Table 2: Distribution according to gestational age**

Gestational Age	Number of Females	Percentage
28 week	16	8.0
29 week	16	8.0
30 week	16	8.0
31 week	16	8.0
32 week	16	8.0
33 week	15	7.5
34 week	15	7.5
35 week	15	7.5
36 week	15	7.5
37 week	15	7.5
38 week	15	7.5
39 week	15	7.5
40 week	15	7.5
Total	200	100.0

**Table 3: Middle cerebral artery pulsatility index percentiles according to gestational age**

Gestational age	5 <sup>th</sup> Percentile	25 <sup>th</sup> Percentile	50 <sup>th</sup> Percentile	75 <sup>th</sup> Percentile	95 <sup>th</sup> Percentile	Mean±SD
28 week	1.84	2.01	2.09	2.19	2.32	2.09±0.16
29 week	1.78	1.96	2.02	2.16	2.31	2.04±0.18
30 week	1.80	1.88	2.00	2.12	2.28	2.01±0.17
31 week	1.78	1.90	2.05	2.14	2.20	2.01±0.16
32 week	1.80	1.86	1.96	2.09	2.14	1.97±0.14
33 week	1.62	1.70	1.81	1.88	2.00	1.80±0.14
34 week	1.54	1.64	1.81	1.85	1.93	1.75±0.15
35 week	1.49	1.62	1.75	1.82	1.91	1.71±0.15
36 week	1.38	1.55	1.62	1.69	1.80	1.60±0.15
37 week	1.29	1.44	1.57	1.62	1.69	1.52±0.22
38 week	1.10	1.20	1.30	1.39	1.61	1.32±0.17
39 week	1.12	1.14	1.20	1.28	1.36	1.22±0.09
40 week	1.09	1.16	1.23	1.29	1.31	1.21±0.09



**Fig. 5: Cerebroplacental ratio index percentiles according to gestational age**

Table 4: Middle cerebral artery resistive index percentiles according to gestational age

gestational age	5 <sup>th</sup> Percentile	25 <sup>th</sup> Percentile	50 <sup>th</sup> Percentile	75 <sup>th</sup> Percentile	95 <sup>th</sup> Percentile	Mean±SD
28 week	0.81	0.83	0.84	0.86	0.89	0.85±0.03
29 week	0.80	0.82	0.83	0.85	0.87	1.12±0.60
30 week	0.80	0.81	0.84	0.86	0.88	0.83±0.03
31 week	0.78	0.80	0.83	0.83	0.85	0.81±0.02
32 week	0.78	0.80	0.83	0.83	0.85	0.81±0.03
33 week	0.74	0.76	0.81	0.82	0.83	0.79±0.04
34 week	0.74	0.77	0.78	0.81	0.83	0.78±0.03
35 week	0.75	0.78	0.79	0.80	0.82	0.78±0.02
36 week	0.70	0.74	0.77	0.78	0.81	0.76±0.03
37 week	0.71	0.73	0.75	0.76	0.77	0.74±0.02
38 week	0.62	0.65	0.70	0.72	0.75	0.68±0.04
39 week	0.63	0.65	0.66	0.69	0.70	0.66±0.02
40 week	0.66	0.67	0.68	0.69	0.70	0.68±0.01

Table 5: Umbilical artery pulsatility index percentiles according to gestational age

Gestational age	5 <sup>th</sup> Percentile	25 <sup>th</sup> Percentile	50 <sup>th</sup> Percentile	75 <sup>th</sup> Percentile	95 <sup>th</sup> Percentile	Mean±SD
28 week	0.86	0.91	0.98	1.09	1.33	1.035±0.22
29 week	0.75	0.86	0.95	1.05	1.25	0.97±0.18
30 week	0.74	0.84	0.93	1.00	1.08	0.92±0.15
31 week	0.74	0.89	0.95	1.06	1.12	0.95±0.15
32 week	0.72	0.81	0.91	1.00	1.10	0.90±0.14
33 week	0.69	0.81	0.87	0.97	1.15	0.89±0.15
34 week	0.67	0.79	0.84	0.91	1.20	0.88±0.18
35 week	0.62	0.73	0.80	0.88	1.05	0.81±0.15
36 week	0.65	0.77	0.82	0.93	1.05	0.84±0.16
37 week	0.65	0.74	0.84	0.93	1.00	0.83±0.13
38 week	0.58	0.66	0.78	0.87	1.08	0.79±0.17
39 week	0.58	0.61	0.75	0.80	0.95	0.74±0.13
40 week	0.66	0.72	0.77	0.80	0.82	0.75±0.05

Table 6: Umbilical artery resistive index percentiles according to gestational age

Gestational age	5 <sup>th</sup> Percentile	25 <sup>th</sup> Percentile	50 <sup>th</sup> Percentile	75 <sup>th</sup> Percentile	95 <sup>th</sup> Percentile	Mean±SD
28 week	0.60	0.62	0.65	0.68	0.75	0.657±0.05
29 week	0.56	0.62	0.64	0.67	0.76	0.65±0.07
30 week	0.55	0.59	0.63	0.66	0.70	0.62±0.05
31 week	0.52	0.61	0.64	0.69	0.71	0.63±0.07
32 week	0.53	0.57	0.60	0.65	0.73	0.21±0.27
33 week	0.52	0.57	0.60	0.66	0.73	0.61±0.07
34 week	0.51	0.55	0.58	0.62	0.74	0.61±0.07
35 week	0.47	0.54	0.56	0.61	0.66	0.56±0.06
36 week	0.46	0.54	0.57	0.61	0.66	0.56±0.07
37 week	0.47	0.54	0.58	0.62	0.65	0.56±0.06
38 week	0.44	0.50	0.54	0.58	0.68	0.55±0.88
39 week	0.45	0.47	0.53	0.58	0.62	0.52±0.06
40 week	0.48	0.51	0.54	0.56	0.58	0.53±0.03

Table 7: Cerebroplacental ratio index percentiles according to gestational age

Gestational Age	5 <sup>th</sup> Percentile	25 <sup>th</sup> Percentile	50 <sup>th</sup> Percentile	75 <sup>th</sup> Percentile	95 <sup>th</sup> Percentile	Mean±SD
28 week	1.87	1.90	1.99	2.02	2.14	2.33±0.36
29 week	1.84	2.05	2.12	2.27	2.38	2.24±0.21
30 week	2.10	2.11	2.14	2.23	2.42	2.22±0.21
31 week	1.97	2.02	2.16	2.22	2.41	2.19±0.20
32 week	1.95	2.10	2.16	2.30	2.50	2.21±0.27
33 week	1.74	1.95	2.09	2.11	2.36	2.14±0.19
34 week	1.61	2.03	2.15	2.07	2.29	2.03±0.24
35 week	1.83	2.07	2.18	2.22	2.40	2.14±0.28
36 week	1.71	1.81	1.97	2.01	2.11	1.94±0.29
37 week	1.69	1.74	1.87	1.94	1.98	1.84±0.34
38 week	1.49	1.60	1.67	1.82	1.90	1.79±0.23
39 week	1.43	1.60	1.69	1.86	1.92	1.71±0.22
40 week	1.60	1.61	1.63	1.71	1.82	1.69±0.12

**Table 8: Correlation between MCA PI and CP ratio and UA PI and CP ratio according to gestational age**

Gestational Age	Correlation between MCA PI and CP Ratio		Correlation between UA PI and CP Ratio	
	Correlation factor	p-value	Correlation factor	p-value
28 week	0.047	0.524	-0.657	0.014
29 week	0.594	<0.0001	-0.922	<0.0001
30 week	0.688	<0.0001	-0.871	<0.0001
31 week	0.737	<0.0001	-0.825	<0.0001
32 week	0.728	<0.0001	-0.752	<0.0001
33 week	0.829	<0.0001	-0.709	<0.0001
34 week	0.823	<0.0001	-0.742	<0.0001
35 week	0.874	<0.0001	-0.623	<0.0001
36 week	0.921	<0.0001	-0.594	<0.0001
37 week	0.919	<0.0001	-0.521	<0.0001
38 week	0.921	<0.0001	-0.588	<0.0001
39 week	0.915	<0.0001	-0.564	<0.0001
40 week	0.170	0.146	-0.398	0.047

MCA: Middle cerebral artery, PI: Pulsatility index, UA: Umbilical artery, CP: Cerebro-placental

While from 28 weeks to 40 weeks of gestational age UA PI showed a significantly negative correlation with the CPR.

Our study has also shown a similar parabolic curve with a peak at 30 weeks and then a gradual fall compared with the previously described studies [5].

Researchers Bahlmann *et al.* looked at found that the RI's reference curve had a parabolic shape (18 weeks - 0.68, 28 weeks - 0.8, 42 weeks - 0.61) [6].

After 11-20 weeks, MCA RI showed a decreasing trend that was not parabolic, as depicted by Rujiwetpongstorn's Nomogram [7].

The MCA PI and RI value ranges in our study in different gestation are similar to what was found by Tarzamni *et al.* [8]. However, there were lower as compared to what was recorded by Ebbing *et al.*, Mari and Deter, Komwilaisak *et al.* [5,9,10]. The exact cause for this deviation needs to be clarified. However, this may be due to a different subset of the population, socioeconomic status, demographic indices, and statistical methods. A strong positive correlation was noted between MCA PI and RI in our study, as was also seen in the study done by Tarzamni *et al.* [8].

Normal values and their nomograms were sought for Doppler flow velocity indices of MCA in 20-40 week pregnancies in the Iranian population in 2008, and the pattern was compared to nomograms from other countries. In their study, they reported that RI, PI, and S/D ratio values of MCA decreased with a parabolic pattern and PSV value increased with a simple pattern as gestational age progressed. These changes were statistically significant ( $p=0.000$  for all of the indices) and more characteristic during the late weeks of pregnancy [8].

In 2019, Zohav *et al.* aimed to determine third-trimester reference ranges for UA-PI, MCA-PI, and CPR in low-risk, normal-growth singleton fetuses. They also noted that the MCA-PI and CPR values, during the third trimester of pregnancy, followed a similar parabolic curve, with peaks at 32 and 33 weeks of gestation, respectively. The UA-PI decreased in a linear fashion with advancing maternal age [11].

Consistent with earlier research, ours suggests that alterations in the fetal MCA reflect cardiovascular adaptations to hypoxia or blood flow redistribution [12]. Thus, decreased PI has been considered a compensatory phenomenon to protect the fetal brain in the context of intrauterine growth restriction [13]. The observation of the recent studies and the present study as well suggested that the ratio of MCA-PI

to UA-PI, the CPR, is an independent predictor of fetal compromise [14], Cesarean section [15] and adverse perinatal outcome [16]. Therefore, UA and MCA Doppler indices and CPR should be used to modify the scheduling of antepartum surveillance and, in some cases, to timely delivery of the compromised fetus.

## CONCLUSION

Doppler ultrasound is used as a part of the clinical protocol in the surveillance of pregnancies. It gives direct information on fetoplacental circulation and identifies the placental circulatory failure. The advantage of Doppler ultrasound is that the technique is fast, reproducible, and can be performed on a daily basis.

The UA and MCA Doppler indices and CPR are currently used to modify the scheduling of antepartum surveillance and, in some cases, to timely delivery of the compromised fetus. To provide a range within which these Doppler values can be interpreted, this study aimed to determine the values of the PI and the RI of the UA and the MCA of the fetus, along with the CPR for a normal pregnancy of 28-40 weeks. It is fair to characterize the progression of MCA PI and RI as a parabolic curve, with a plateau between 28 and 30 weeks and a subsequent turn until 40 weeks of gestation. The scatter plot of UA PI and RI shows a linear graph with a plateau from 28 weeks to 40 weeks of pregnancy. The scatter plot of the CPR shows a parabolic curve with a plateau between 28 and 32 weeks and a turn between 32 and 40 weeks.

## AUTHORS CONTRIBUTIONS

Equal contribution.

## COMPETING INTERESTS

Nil.

## AUTHORS FUNDING

Nil.

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