Journal of Neonatal Surgery
ISSN(Online): 2226-0439
Vol. 14, Issue 26s (2025)
https://www.jneonatalsurg.com

OPEN ACCESS

The Role Of Ultrasound In Assessment Of Middle Cerebral Artery In Third Trimester In Pakistani Population

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Cite this paper as: Riffat Bibi, Dr. Avrina Kartika Ririe MD, Temidayo Abiodun Alabi, Godwin Ibiang Obono, Mirza Mohammad Ali Baig, Zareen Fatima, Sadaf Ayesha, Syeda Kiran Aftab, (2025) The Role Of Ultrasound In Assessment Of Middle Cerebral Artery In Third Trimester In Pakistani Population. *Journal of Neonatal Surgery*, 14 (26s), 174-191.

Keywords: *Middle Cerebral Artery (MCA); Doppler Ultrasound; Third Trimester; Fetal Hemodynamics; Pulsatility Index (PI); Resistive Index (RI); Systolic/Diastolic Ratio (S/D Ratio); Fetal Wellbeing; Intrauterine Growth Restriction (IUGR) ,*

ABSTRACT

INTRODUCTION: The purpose of this study was to assess the Doppler indices (Pulsatility Index, Resistive Index and systolic to diastolic ratio) of fetal middle cerebral artery in normal pregnancies with gestation age from 27 to 40 weeks. In this study, the trends of Doppler flow velocity indices were determined.

METHODS: In this cross sectional study, 100 normal pregnant women with gestational age between 27-40 weeks of pregnancy were evaluated by Doppler ultrasound for the assessment of three Doppler indices (PI, RI and S/D ratio) for middle cerebral artery.

RESULTS: All the studied Doppler parameters i.e. resistive index, pulsatility index and systolic to diastolic ratio of middle cerebral arteries decreased continuously in a parabolic pattern with the increase in gestational age. There was a significant correlation between MCA-PI, RI, S/D ratio and gestational age (<0.001). The values obtained were statistically significant

with p-value <0.001 for all Doppler indices. Percentile values were obtained for all the parameters. The regression equation applied which was also significant for all Doppler parameters of middle cerebral artery.

CONCLUSION: The ranges for Doppler indices of middle cerebral artery were calculated and compared with other studies. These ranges are consistent with previous studies on similar topics.

INTRODUCTION

The assessment of middle cerebral artery of fetuses by using Doppler ultrasound has become an important part to assess cardiovascular distress, hypoxia or anaemia in fetus. In the situations that are appropriate to take MCA, it is useful addition to umbilical artery Doppler ultrasound. The Middle cerebral artery is used for the further assessment of intrauterine growth restriction; TAPS (i.e. twin anemia polycythemia sequence) and TTTS (i.e. Twin to Twin Transfusion Syndrome).[1]

If intrauterine growth restriction is due to placental abnormality, then it is mainly a vascular disorder. At first, there will be abnormality in tertiary villous vessels and then it proceeds with distinctive multivessel cardiovascular manifestations in fetus. Such manifestations can be predicted by Doppler sonographic examination of different vessels:

- Uterine arteries of mother and umbilical arteries of the fetus to examine placenta.
- Middle cerebral artery of fetus to assess brain perfusion.
- Precordial veins to predict effects of placenta based functional abnormalities on heart.

In all these vessels, Doppler abnormalities will get worse along with the IUGR. It suggests that there is a chronological sequence in progression of disease. This chronological sequence and the need for prediction of worsening situation of fetus, are foundation of Doppler sonography in growth restricted fetus. Abnormalities in Doppler parameters help and guide for clinical management of growth restricted fetuses and to bring several changes like:

- monitoring frequency is greater than before,
- administering antenatal steroids and
- delivery.[2]

To evaluate the cerebral blood flow is an important step for assessing high risk pregnant women. Extensive studies have been made on the middle cerebral artery for this purpose. The MCA Doppler indices are included on regular basis for managing fetuses that are having threat of increasing abnormalities of placenta and anemia.[3]

Therefore, it is good predictor for early diagnosis of IUGR and fetal anemia. The middle cerebral artery is preferred vessel for evaluating the brain circulation of fetus, because it is unproblematic to recognize it, and it is highly reproducible and provide information on the brain sparing effect.[4]

With the advancing pregnancy, there will be decrease in vascular resistance of middle cerebral artery and causes changes in Doppler indices. In cerebral vessels, the velocity of end diastolic flow is either small or absent during the early stages of pregnancy but the velocity raise as the gestational age proceeds to end. In normal fetal development, there is low vascular resistance in brain area and there is uninterrupted forward flow all through the cardiac cycle. If intrauterine growth restriction is because of placenta based deficiency then it most probably, reason of fetal blood flow redistribution to compensate for brain and stress organs of fetus. This redistribution of blood is at the expense of organs that are less crucial such as kidneys, liver and subcutaneous tissues. As a result, previously less resistance to flow of blood in brain, further decreases and will augment the cerebral circulation. Finally, it results in raised end diastolic velocity and decline in systolic to diastolic ratio of middle cerebral artery (called as “brain sparing effect”). [5]

In this way, intrauterine growth restriction and fetal hypoxia, Doppler ultrasound evaluation of fetal vascular supply, demonstrated the increased flow resistance in umbilical artery and converse in the descending thoracic aorta.[6]

As the growth restricted fetuses shift their blood flow towards the major organs of the body namely brain, heart and adrenal glands, increase in blood supply for the brain is called Brain Sparing and this redistribution can be assessed by MCA Doppler Sonography.[7]

The MCA Doppler examination is a great source in diagnosis and management of fetal anemia and IUGR. As a window into the hemodynamics of the fetal central nervous system, its potential is clearly unlimited. In cases of IUGR, the MCA Doppler flow velocimetry shows early and late changes.[8]

2. MATERIALS AND METHODS

Study Design and Setting

This cross-sectional study was conducted over a period of nine months, from December 2013 to September 2014, at two clinical sites: the Gillani Ultrasound Clinic and Saira Memorial Trust Hospital. The study aimed to analyze Doppler measurements of the middle cerebral artery (MCA) in 100 pregnant women with gestational ages ranging from 27 to 40

weeks. Written informed consent was obtained from all participants prior to their inclusion in the study. Ethical approval was secured from the relevant institutional review board, and the study adhered to the principles outlined in the Declaration of Helsinki.

Study Population

Pregnant women referred for routine prenatal care were recruited for the study. The inclusion criteria were as follows:

- Low-risk pregnancies with normal fetal anatomy.
- Gestational age between 27 and 40 weeks, confirmed by last menstrual period (LMP) and corroborated by first- or early second-trimester ultrasound.
- Normal fetal growth, defined as estimated fetal weight between the 10th and 90th percentiles on standardized growth charts.
- Normal Doppler patterns in the uterine and umbilical arteries.
- Absence of maternal comorbidities such as hypertension, diabetes mellitus, autoimmune disorders, preeclampsia, or abnormal vaginal bleeding.
- No history of smoking, alcohol consumption, or use of hormonal contraceptives.

Exclusion criteria included:

- Fetuses with congenital abnormalities or oligohydramnios.
- Abnormal biophysical profile (BPP < 6).
- Fetal biometry inconsistent with first- or early second-trimester ultrasound findings (e.g., intrauterine growth restriction [IUGR]).
- Small-for-gestational-age (SGA) or large-for-gestational-age (LGA) fetuses.

Doppler Ultrasound Protocol

All participants underwent a routine obstetric ultrasound prior to Doppler assessment to confirm normal fetal anatomy, assess gestational age, and rule out any maternal or obstetric abnormalities. The MCA Doppler examination was performed using Mindray and GE ultrasound machines equipped with convex transabdominal probes.

The axial section of the fetal brain, just caudal to the biparietal diameter (BPD) measurement plane, was obtained. Color flow mapping was used to identify the circle of Willis and the proximal segment of the MCA. Pulsed-wave Doppler was then applied near the origin of the MCA at the internal carotid artery to obtain waveforms. If the near-field MCA could not be adequately interrogated, the contralateral MCA was used.

Doppler indices, including the resistive index (RI), pulsatility index (PI), and systolic-to-diastolic (S/D) ratio, were measured. Four to five continuous spectral waveforms were recorded in the absence of fetal breathing or movement. The angle of insonation was maintained below 60 degrees to ensure accuracy. All measurements were recorded on a standardized data collection sheet designed for the study.

Statistical Analysis

Data were analyzed using SPSS version 13.0. Continuous variables were expressed as mean ± standard deviation (SD). The relationship between Doppler indices and gestational age was assessed using Pearson's correlation and regression analysis. A quadratic regression model was fitted to estimate the association between Doppler variables and gestational age (in weeks). Percentile values were calculated, with the 90% normal reference range defined between the 5th and 95th percentiles. A p-value of <0.05 was considered statistically significant.

3. CHAPTER-V TABLES AND GRAPHS

Table-1 Mean±SD and Range of the maternal age

	N	Range	Minimum	Maximum	Mean		Std. Deviation
	Statistic	Statistic	Statistic	Statistic	Statistic	Std. Error	Statistic
Age	100	17.00	21.00	38.00	28.4900	.32582	3.25823

Graph-1; Histogram for maternal age, showing frequency of the patients

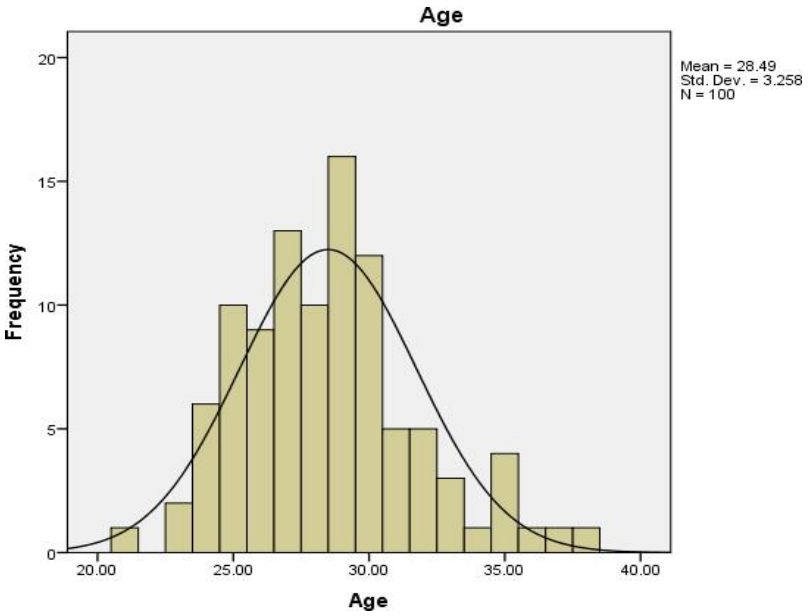


Table-2; Mean±SD and Range of gestational age

	N	Range	Minimum	Maximum	Mean		Std. Deviation
	Statistic	Statistic	Statistic	Statistic	Statistic	Std. Error	Statistic
Gestational age (weeks)	100	12.00	27.00	39.00	32.7900	.35027	3.50265

Graph-2; Histogram for Gestational age (GA), showing frequency of the patients according to gestation age

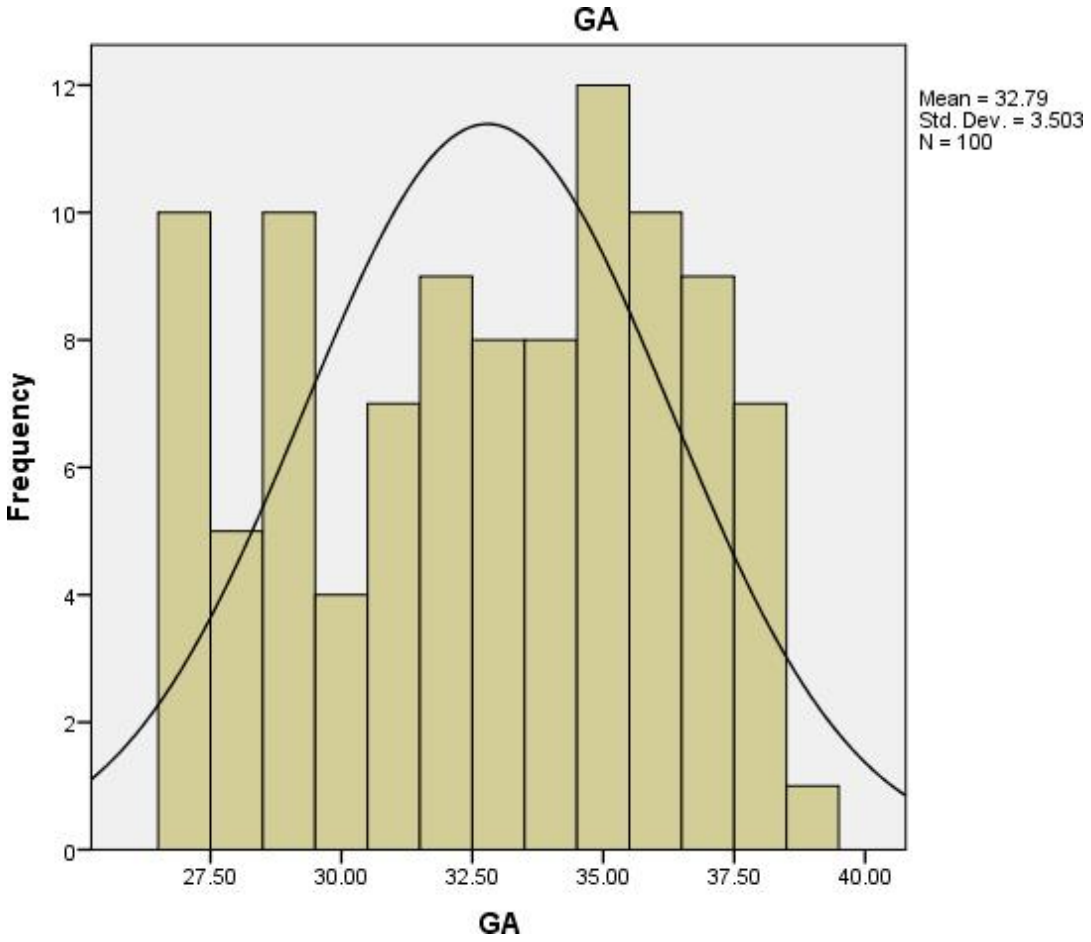


Table-3; Mean±SD and range of pulstality index

	N	Range	Minimum	Maximum	Mean		Std. Deviation
	Statistic	Statistic	Statistic	Statistic	Statistic	Std. Error	Statistic
PI	100	3.22	.74	3.96	1.7692	.05149	.51494

Graph-3; Histogram for MCA-PI, showing frequency of the patients

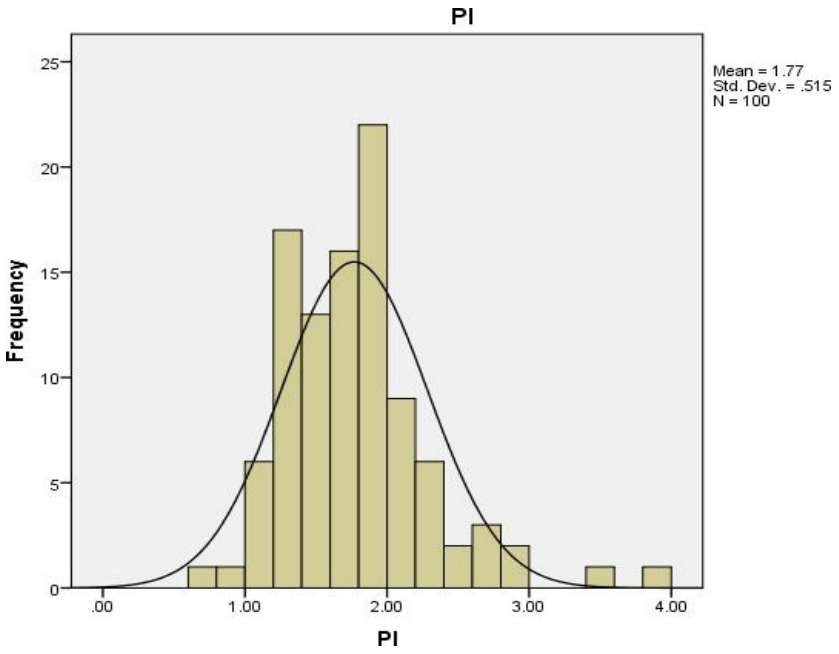


Table-4; Mean±SD and range of Resistive Index (RI)

	N	Range	Minimum	Maximum	Mean		Std. Deviation
	Statistic	Statistic	Statistic	Statistic	Statistic	Std. Error	Statistic
RI	100	.38	.53	.91	.7586	.00807	.08065

Graph-4; Histogram for MCA-RI, showing frequency of the patients

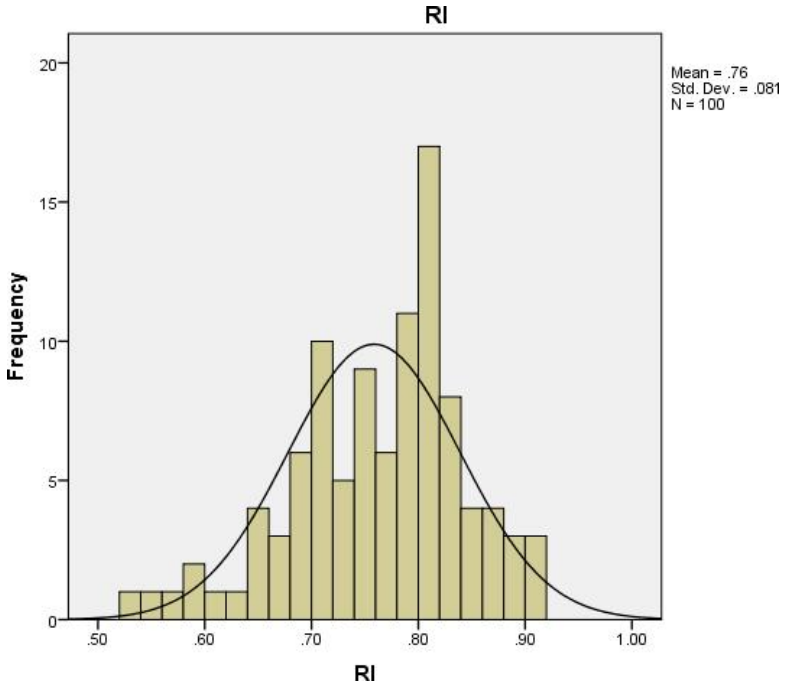


Table-5; Mean±SD and range of systolic to diastolic (S/D) ratio

	N	Range	Minimum	Maximum	Mean		Std. Deviation
	Statistic	Statistic	Statistic	Statistic	Statistic	Std. Error	Statistic
S_D	100	9.50	2.10	11.60	5.0328	.18156	1.81564

Graph-5; Histogram for MCA-S/D, showing frequency of the patients

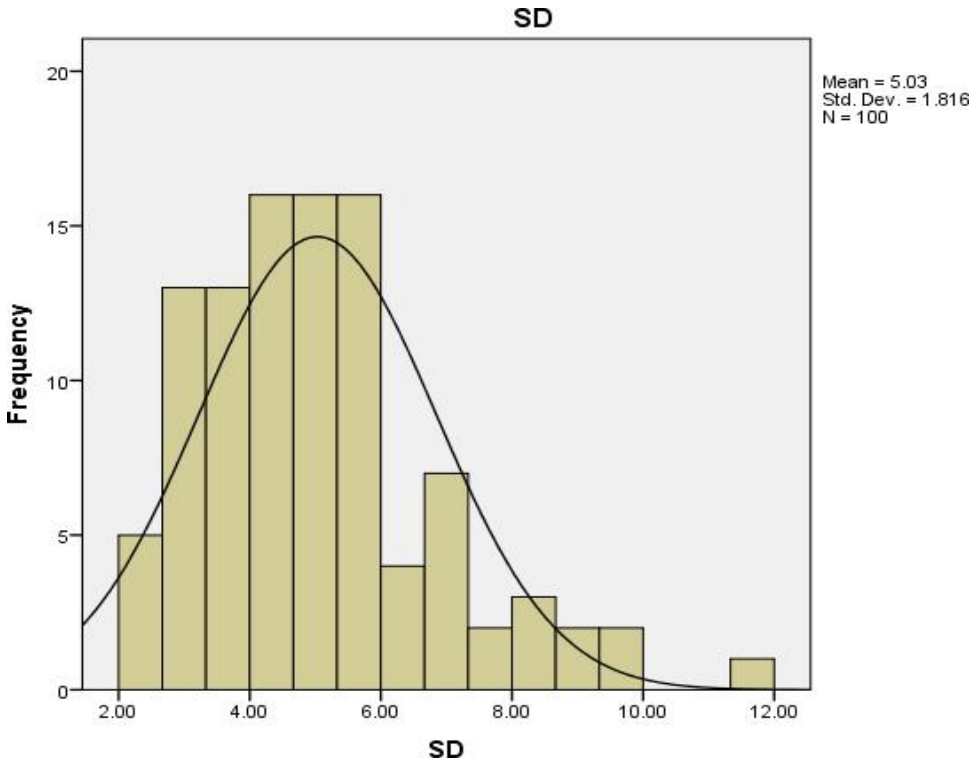


Table-6; Grouped data of Maternal Age

Age	Frequency	Percent	Valid Percent	Cumulative Percent
21-24	9	9	9	9
25-28	42	42	42	51
29-32	38	38	38	89
33-36	9	9	9	98
37-40	2	2	2	100

Graph-6; Graph showing Frequency and Percentage of grouped maternal age.

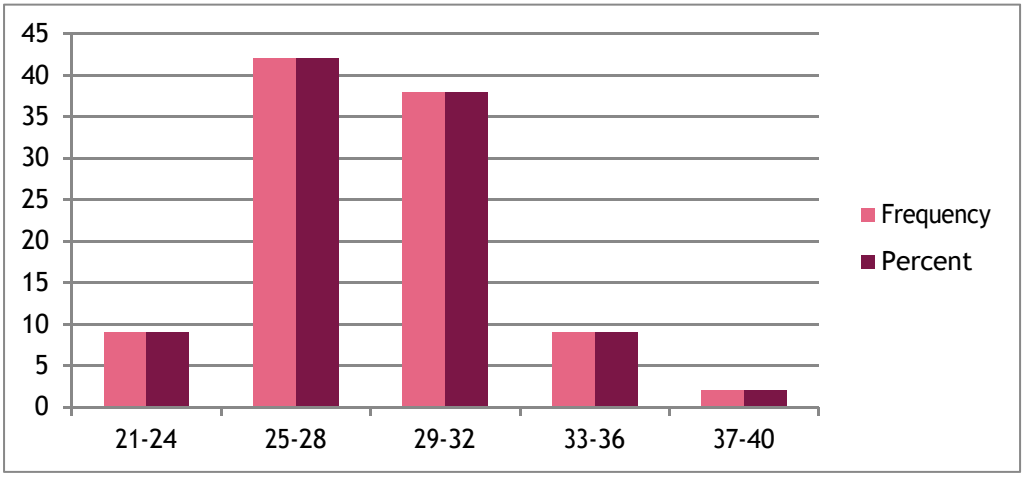


Table-7; Grouped data of Gestational age

Gestational age (wks)	Frequency	Percent	Valid Percent	Cumulative Percent
27-30	**29**	**29**	**29**	**29**
31-34	**32**	**32**	**32**	**61**
35-38	**38**	**38**	**38**	**99**
39-40	**1**	**1**	**1**	**100**

Graph-7; Showing frequency and percentage of grouped data of gestational age (GA)

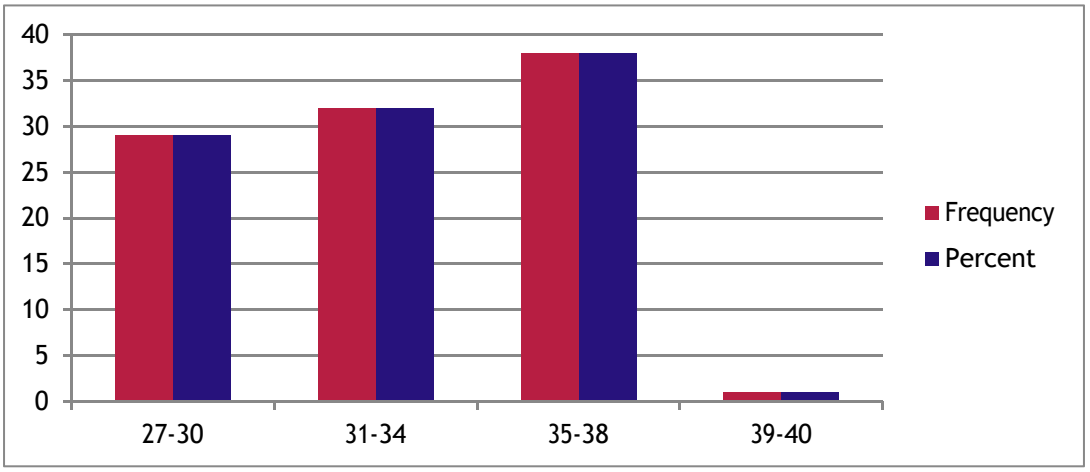
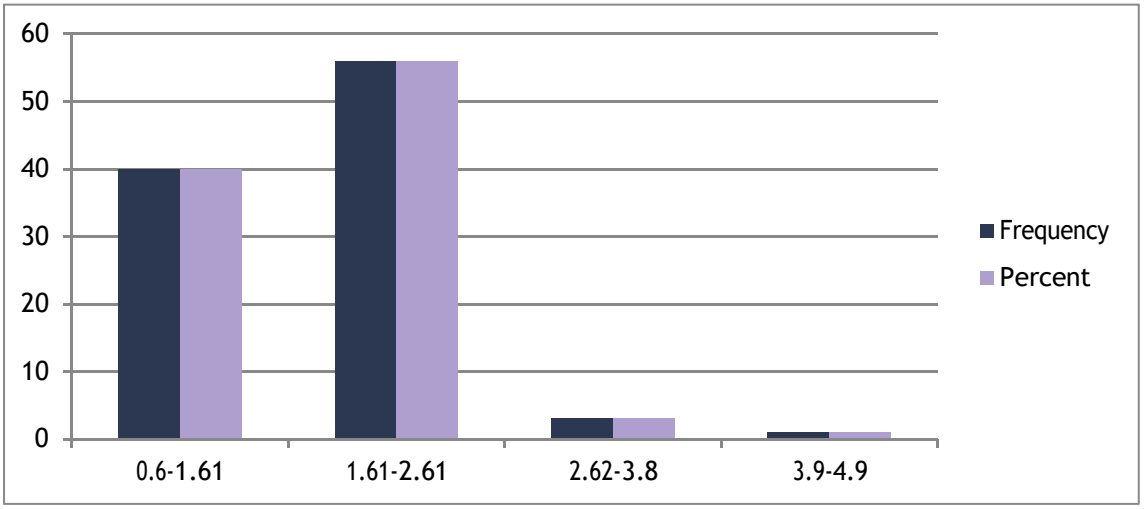


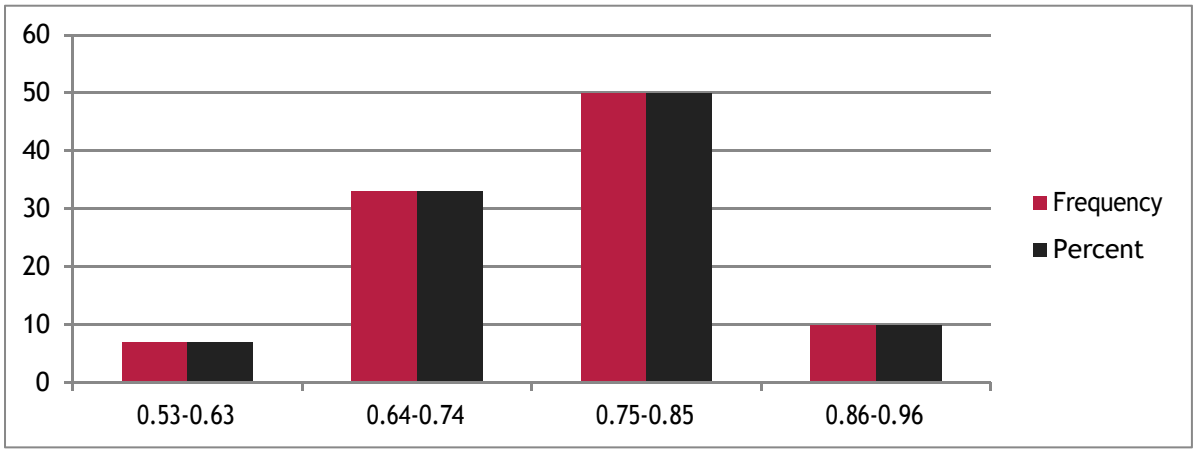
Table-8; Grouped data of Pulstality index of middle cerebral artery

Pulstality Index (PI)	Frequency	Percent	Valid Percent	Cumulative Percent
0.6-1.61	40	40	40	40
1.61-2.61	56	56	56	96
2.62-3.8	3	3	3	99
3.9-4.9	1	1	1	100

Graph-8; Frequency and Percentage of grouped MCA- Pulstality Index



Graph-9; Frequency and percentage of grouped Resistive Index of middle cerebral artery



Graph-10; Frequency and Percentage of grouped S/D ratio of middle cerebral artery.

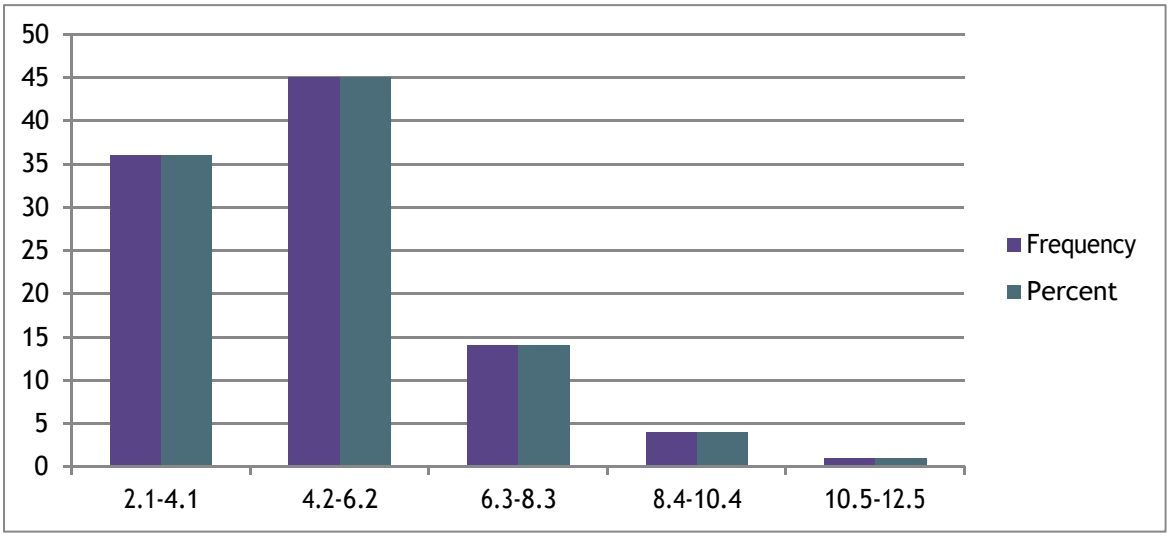


Table-9; Means and standard deviations of demographic and Doppler ultrasonographic findings in study population

Gestation Age	N	PI		RI		S/D	
		Mean	Sd	Mean	Sd	Mean	Sd
27	10	2.0540	0.65429	0.8040	0.06346	6.2200	1.66520
28	5	1.6740	0.14724	0.7600	0.04000	5.0600	0.64265
29	10	1.9830	0.70462	0.7950	0.06637	5.7170	1.89015
30	4	1.6975	0.40302	0.7975	0.07632	5.5500	2.32164
31	7	1.7943	0.63794	0.7943	0.07390	5.8214	2.93057
32	9	1.9067	0.58093	0.7578	0.08378	5.1644	2.02531
33	8	1.7075	0.38044	0.7737	0.07558	4.8425	1.47227
34	8	1.8450	0.35901	0.7950	0.04504	5.4850	1.70615
35	12	1.9367	0.52412	0.7567	0.08988	5.0250	1.53985
36	10	1.6710	0.24488	0.7300	0.0532	4.2130	0.89427
37	9	1.3133	0.42585	0.6767	0.09566	3.7933	1.40309
38	7	1.3600	0.20897	0.6771	0.06317	3.7557	1.93556

Table-10; 5th, 50th and 75th percentile values for Doppler waveform indices according to gestation age.

Week of Gestation (GA)	Sample (N)	Pulstality Index (PI) Percentiles			Resistive Index (RI) Percentiles			Systolic to Diastolic Ratio (S/D) Percentiles		
		5th	50th	75th	5th	50th	75th	5th	50th	75th
27	**10**	1.0400	1.9000	2.3500	0.6900	0.8000	0.8500	3.2000	5.9000	7.4250
28	**5**	1.4600	1.7000	1.8050	0.7000	0.7800	0.7900	4.4000	5.0000	5.7000
29	**10**	1.5800	1.8050	1.8950	0.6900	0.8100	0.8425	3.2000	5.5500	6.6425
30	**4**	1.3200	1.6250	2.1150	0.7100	0.7950	0.8725	3.4000	5.0500	7.9750
31	**7**	1.0700	1.5000	2.5000	0.7100	0.7800	0.8700	3.4000	4.4500	7.7000
32	**9**	1.0800	1.8400	2.3450	0.5700	0.7900	0.8100	2.3000	4.7000	5.6500
33	**8**	1.3000	1.5850	2.1150	0.6900	0.7700	0.8375	3.2000	4.4700	6.2250
34	**8**	1.2800	1.9050	2.1425	0.7200	0.8050	0.8175	3.5000	5.2000	7.2000
35	**12**	1.0700	2.0050	2.1925	0.5900	0.7800	0.8275	2.4000	4.8000	6.6500
36	**10**	1.3600	1.6800	1.9425	0.5800	0.7350	0.7850	2.4000	4.3050	5.0075
37	**9**	0.7400	1.3000	1.6450	0.5300	0.6900	0.7500	2.1000	3.9000	4.8530
38	**7**	1.1300	1.3000	1.6100	0.6300	0.6500	0.7000	2.1000	3.9000	3.6000

Table-13; Correlation between Doppler Indices

Parameters	Pierson Correlation (r)	p value
PI &RI	0.521	0.000
RI & S/D	0.845	0.000
S/D & PI	0.559	0.000

Correlation is significant at the 0.01 level (2-tailed).

Table-14; Correlation 0f Doppler Indices PI, RI and S/D of Middle cerebral artery with gestational age

Parameters	Pierson correlation	p value
PI & GA	-0.294	0.003
RI & GA	-0.418	0.000
S/D & GA	-0.375	0.000

Correlation is significant at the 0.01 level (2-tailed).

Table-15; Gestation Age and MCA-PI Crosstabulation

Gestational Age (GA)	MCA-Pulsatility Index (PI)				Total
	1.00	2.00	3	4.00	
27-30	7	20	1	1	29
31-34	14	17	1	0	32
35-38	19	18	1	0	38
39-42	0	1	0	0	1
Total	40	56	3	1	100

Graph-11; Calculated reference ranges for MCA-PI. The standard boundaries include 90% of the normal patient population.

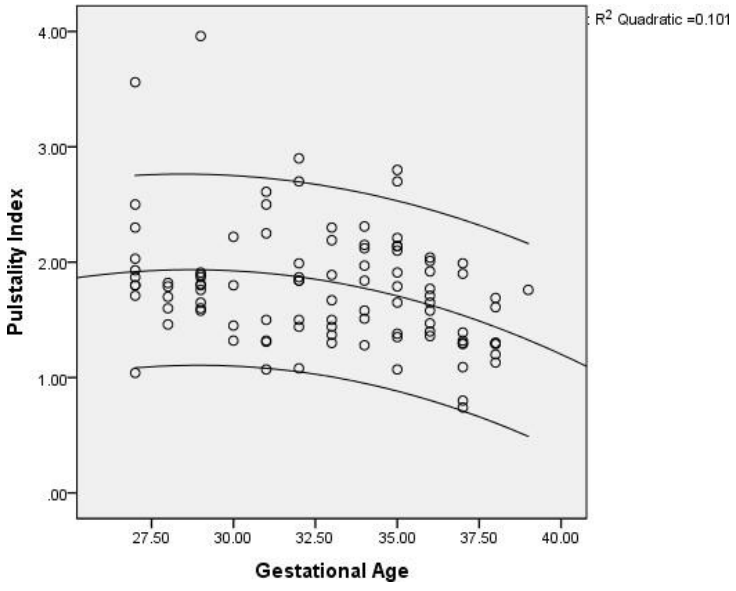


Table- 16; Gestation Age and MCA-Resistive Index Crosstabulation

Gestational age (GA) in weeks	MCA-Resistive Index (RI)				Total
	0.53-0.63	0.64-0.74	0.75-0.85	0.86-0.96	
27-30	0	8	17	4	29
31-34	1	7	20	4	32
35-38	6	17	13	2	38
39-42	0	1	0	0	1
Total	7	33	50	10	100

Graph-12; Calculated reference ranges for MCA-RI. The standard boundaries include 90% of the normal patient population.

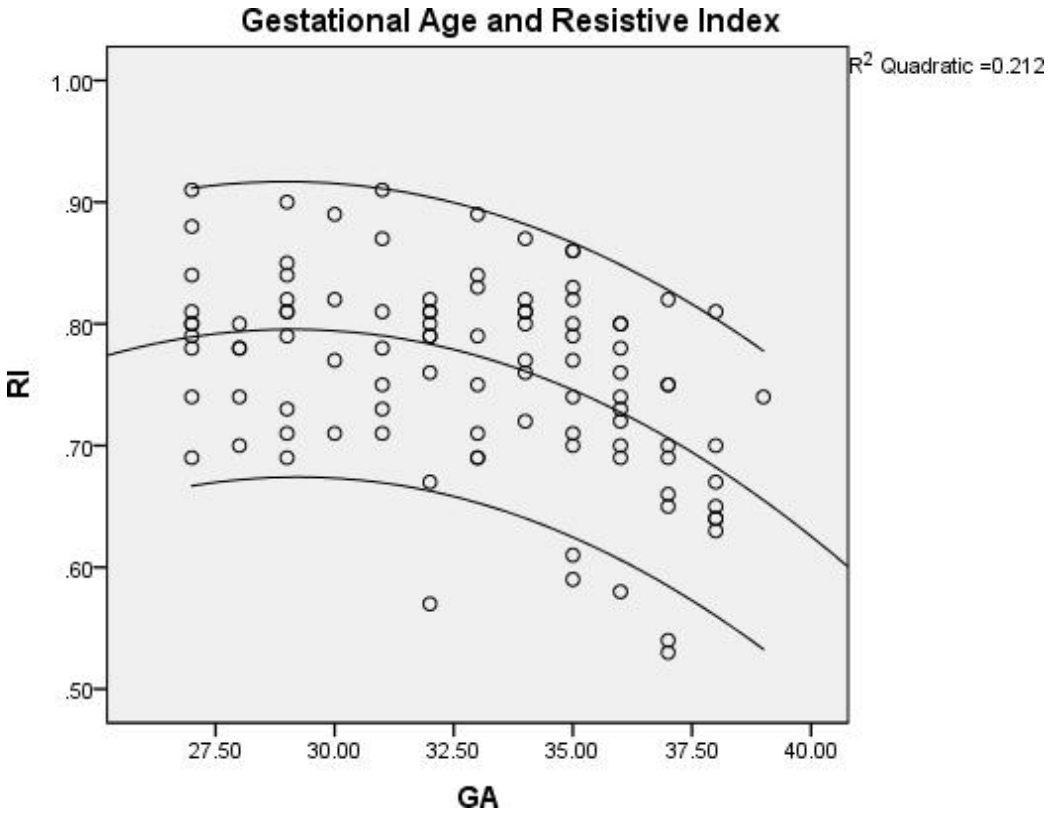


Table-17; Gestation Age and MCA-Systolic to Diastolic ratio Crosstabulation

Gestational Age (GA) in weeks	MCA-S/D					Total
	2.2-4.1	4.2-6.2	6.3-8.3	8.4-10.4	10.5-12.5	
27-30	3	18	5	3	0	29
31-34	10	15	6	1	1	33
35-38	21	12	4	0	0	37
39-42	1	0	0	0	0	1
Total	35	45	15	4	1	100

Graph-13; Plotting for reference ranges of MCA-S/D. The standard boundaries include 90% of the normal patient population.

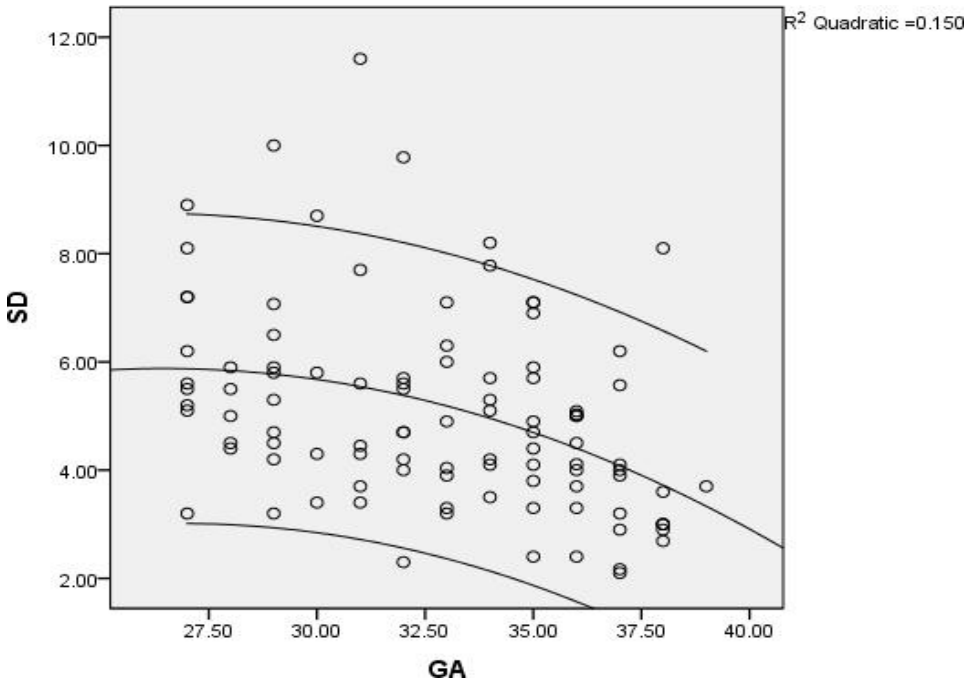


Table-18; Regression equations applied for MCA-PI and gestation age

Independent variable: GA

Dependent Variable: PI

Coefficients[a]						
Model		**Unstandardized Coefficients**		**Standardized Coefficients**	**t**	**Sig.**
		B	**Std. Error**	**Beta**		
1	**(Constant)**	**3.186**	**.468**		**6.808**	**.000**
	GA	**-.043**	**.014**	**-.294**	**-3.045**	**.003**

Coefficients[a]			
Model		**95.0% Confidence Interval for B**	
		Lower Bound	**Upper Bound**
1	**(Constant)**	**2.258**	**4.115**
	GA	**-.071**	**-.015**

Graph-14; Regression line fitted on the scatter plot of MCA-PI and gestation age

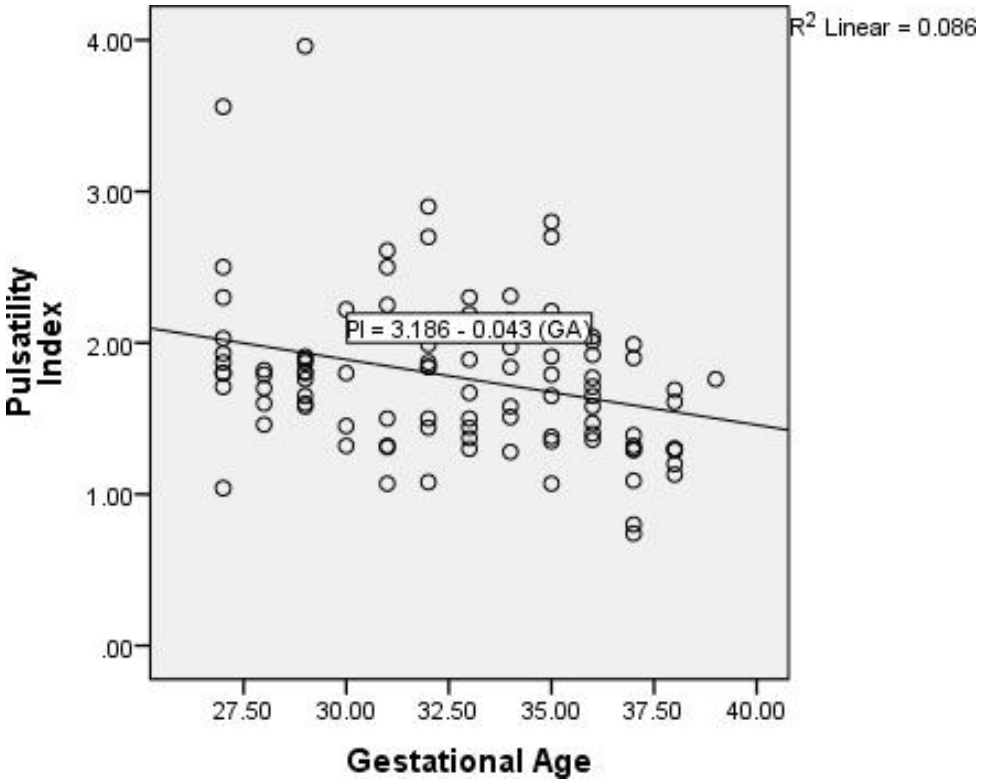


Table-19; Regression equations applied for MCA-RI and gestation age

Independent variable: GA

Dependent Variable: RI

Coefficients[a]						
Model		**Unstandardized Coefficients**		**Standardized Coefficients**	**T**	**Sig.**
		B	**Std. Error**	**Beta**		
1	**(Constant)**	**1.074**	**.070**		**15.423**	**.000**
	GA	**-.010**	**.002**	**-.418**	**-4.559**	**.000**

Coefficients[a]			
Model		**95.0% Confidence Interval for B**	
		Lower Bound	**Upper Bound**
1	**(Constant)**	**.936**	**1.213**
	GA	**-.014**	**-.005**

Graph-15; Regression line fitted on the scatter plot of MCA-RI and gestation age

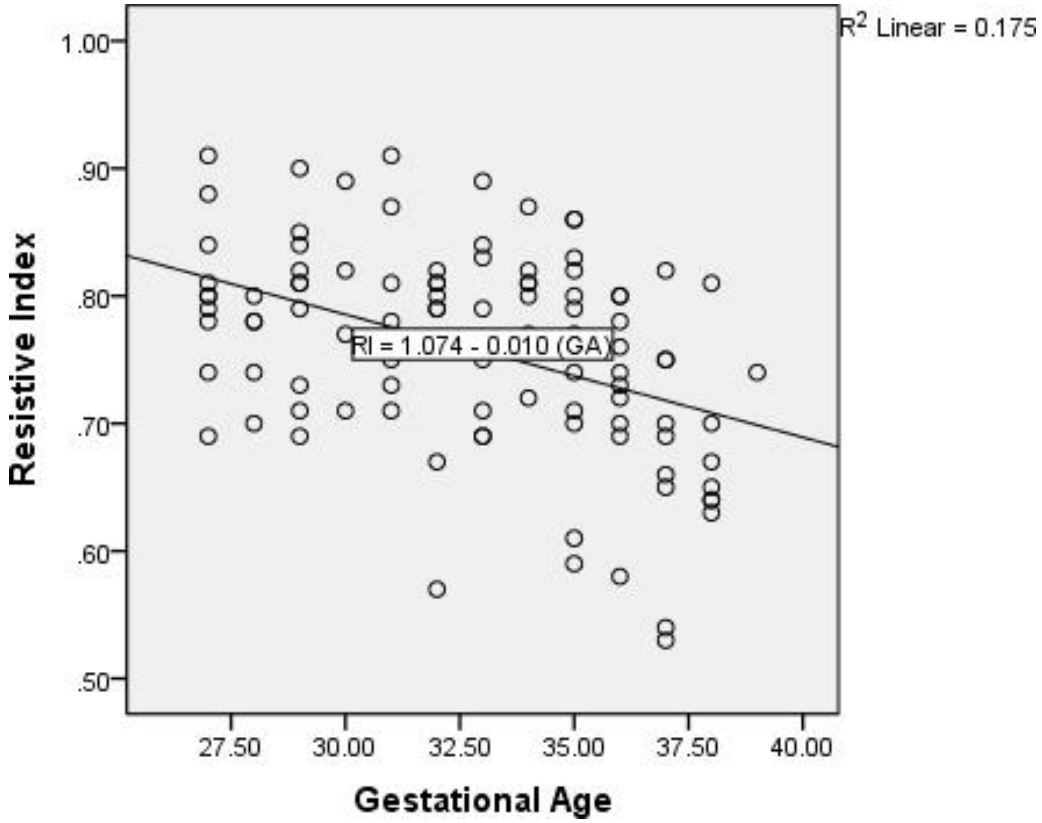


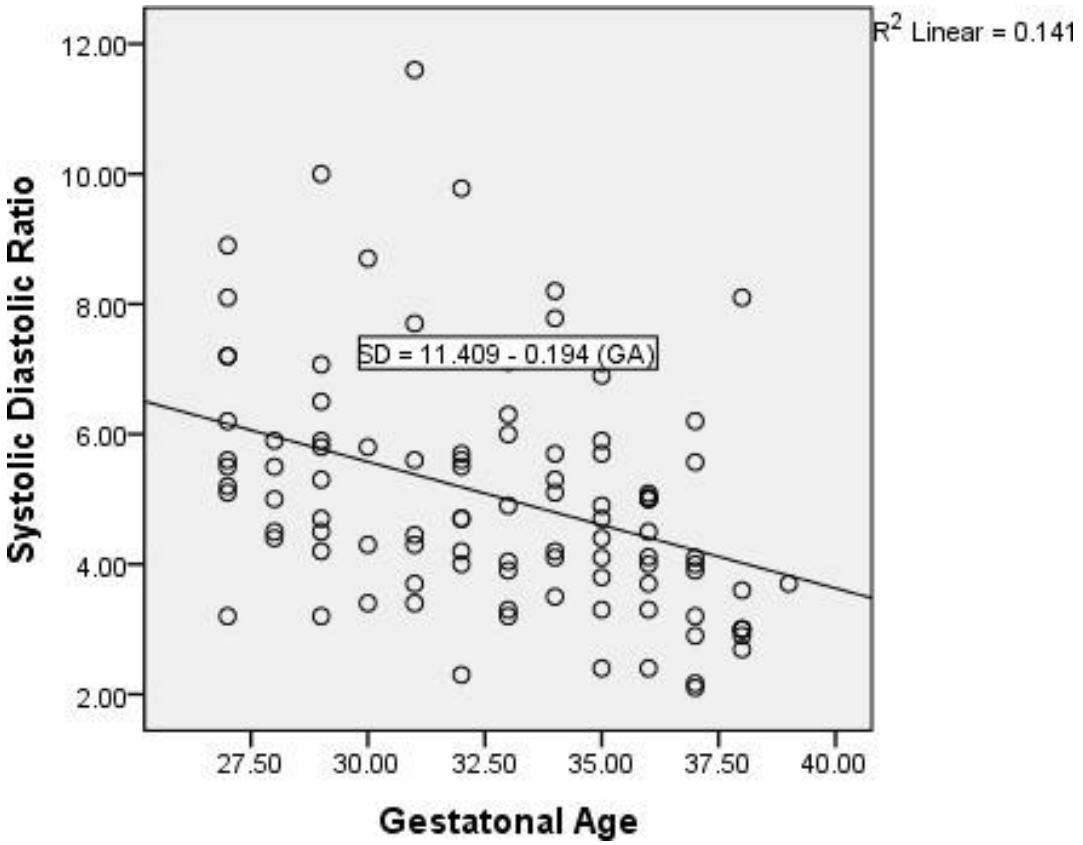
Table-20; Regression equations applied for MCA-S/D and gestation age

Independent variable: GA

Dependent variable: S/D

Coefficients[a]						
Model			**95.0% Confidence Interval for B**			
			Lower Bound	**Upper Bound**		
1	**(Constant)**		**8.233**	**14.585**		
	GA		**-.291**	**-.098**		
Coefficients[a]						
Model		**Unstandardized Coefficients**		**Standardized Coefficients**	**T**	**Sig.**
		B	**Std. Error**	**Beta**		
1	**(Constant)**	**11.409**	**1.601**		**7.128**	**.000**
	GA	**-.194**	**.049**	**-.375**	**-4.006**	**.000**

Graph-16; Regression line fitted on the scatter plot of MCA-S/D and gestational age



4. CHAPTER-VI DISCUSSION

Observations were obtained in 100 pregnant women. All were normal third trimester pregnancies between 27 and 40 weeks of gestation. Relying on these observations, the reference ranges were constructed for three Doppler indices PI, RI and S/D ratio of fetal middle cerebra artery. All the curves show parabolic pattern with continuous reduction in all Doppler indices with the gestation age. Significant correlation PI with gestation age was obtained -0.294 (p value=0.003<0.01), between RI and gestation age, -0.418 (p value=0.000<0.01) and between S/D ratio and gestation age -0.375 (p value=0.000 < 0.01).

The diastolic flow of fetal cerebral circulation appears earlier than fetal aorta and umbilical artery. It represents the redistribution of the blood flow towards most vital organs of the fetus.[43]

Comparing the PI as found in our reference curves with that published by Tarzamni etal.[36] It reveals that the reference limits during 27 to 39 weeks of gestation, are consistent with our study and our ranges were closer to that study. Not only MCA-PI but also the MCA-RI and S/D ratio were consistent with that study having parabolic pattern. The reference values of MCA-PI were also similar to that of C. Ebbing etal.[3] But our sample size was small as compared to that study.

Despite the parabolic shape of our PI curve generally there was a decrease in fetal MCA-PI with advancing gestation age that is comparable to other studies. This reduction might show the decreasing vascular impedance with advancing gestation age. There may be an association with the production of deoxyribonucleic acid in fetal brain.[36] Resistive Index of the MCA in our study follows the decreasing trend with increase in gestation age (r=-0.418,p=0.000). However it shows parabolic pattern and consistent with Tarzamani etal, but its range is slightly lower than that of paudal S, etal. Although MCA-PI reference curves of our studies are consistent with that of Paudal S, etal,[44] the S/D ratio reference curve is also slightly higher for Paudal S, etal. While this result is similar to that obtained by Antonio Gadelho etal.[26]

S/D ratio of MCA shows significant correlation with increasing gestational age (r= -0.375, p=0.000), in our study. However these values are slightly lower than that obtained by Justin C. Konje etal.[45]

From 26th week of gestation, the brain maturity begins at greater extent.[44] As brain is maturing during third trimester of

pregnancy, Greater cerebral blood flow is provided due to reduced vascular impedance which causes decrease in PI, RI and S/D ratio.

Due to reduction in oxygen supply, there is fetal response to central redistribution and preferential perfusion of fetal brain, myocardium and adrenal glands. Doppler velocimetry of middle cerebral artery is used to assess the redistribution. Normally, the MCA is high resistance vessel but in case of redistribution its resistance is decreased causing increased flow in it. If fetal compromise continues, the redistribution may reverse and become preterminal for the fetus.[46]

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