Original Article

# Doppler Waveform Indices of Fetal Middle Cerebral Artery in Normal 20 to 40 Weeks Pregnancies

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**Background:** One of the main methods for evaluation of fetal well-being is analysis of Doppler flow velocity waveform of fetal vessels. Evaluation of Doppler wave of the middle cerebral artery can predict most of the at-risk fetuses in high-risk pregnancies. In this study, we tried to determine the normal ranges and their trends during pregnancy of Doppler flow velocity indices (resistive index, pulsatility index, systolic-to-diastolic ratio, and peak systolic velocity) of middle cerebral artery in 20 – 40 weeks normal pregnancies in Iranians.

**Methods:** In this cross-sectional study, 1037 women with normal pregnancy and gestational age of 20 to 40 weeks were investigated for fetal middle cerebral artery Doppler examination.

**Results:** Resistive index, pulsatility index, and systolic-to-diastolic ratio values of middle cerebral artery decreased in a parabolic pattern while the peak systolic velocity value increased linearly with progression of the gestational age. These changes were statistically significant ($P<0.001$ for all four variables) and were more characteristic during late weeks of pregnancy. The mean fetal heart rate was also significantly ($P<0.001$) reduced in correlation with the gestational age.

**Conclusion:** Doppler waveform indices of fetal middle cerebral artery are useful means for determining fetal well-being. Herewith, the normal ranges of Doppler waveform indices for an Iranian population are presented.

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**Keywords:** Doppler ultrasonography • fetus • middle cerebral artery • pregnancy



## Introduction

Currently, Doppler ultrasonography (DU) velocimetry of uteroplacental, umbilical, and fetal vessels has become the established method for antenatal monitoring.[1–3] Circulatory changes, reflected in certain fetal Doppler waveforms, predict adverse perinatal outcome.[4,5]

Although umbilical arteries are the common vessels assessed by DU, recent studies have shown the efficacy of the middle cerebral artery (MCA) Doppler assessment.[6,7] Today, with the advancement of pulsed and color-coded DU combined with better reproducibility, the MCA has emerged as the vessel of choice in the Doppler assessment of fetal intracranial as well as other organs perfusion.[8,9]

Applicability of Doppler indices in the diagnosis of abnormalities is possible only when there are reference normal values for each index. Although various investigators have described and established gestational age-related reference curves,[10–12] this is the first study performed in Iran.

The objective of this study was to determine new DU gestational age-dependent reference curves for the MCA indices including resistive index (RI), pulsatility index (PI), systolic to diastolic (S/D) ratio, peak systolic velocity (PSV), and fetal heart rate (FHR) in a normal Iranian obstetric population of 20 to 40 weeks' gestation.

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## Patients and Methods

In a cross-sectional study conducted between February 2004 and May 2007, we analyzed the Doppler measurements of 1037 low-risk pregnant women with gestational age between 20 and 40 weeks. Those women were referred to our department for routine prenatal care. The research protocol was approved by the local Ethics Committee and an informed written consent was obtained from every subject involved in the study prior to the examination.

Prior to Doppler assessment, routine obstetric ultrasonography was done for each subject.

The examinations were performed by a single investigator in Al-Zahra Obstetrics and Gynecology Hospital using a Hitachi unit EUB-525 (Hitachi Medical Corporation, Tokyo, Japan) with a 3.5 MHz convex transducer. Doppler parameters were optimized in each examination. Every woman underwent only one examination to measure the fetal MCA. After color localization of the MCA, the Doppler flow velocity was measured from the proximal portion of MCA. Securing the best image quality for flow velocity waveforms, at least three waveforms were measured by ultrasonologist and averaged.

Women who met the following criteria were included in the study: I) low-risk pregnancy, II) normal neonatal anatomy, III) accurate gestational age based on the last normal menstruation date adapted with ultrasound parameters, IV) gestational age between 20 and 40 weeks, V) normal fetal growth (between 10th and 90th percentiles of the growth chart), VI) normal Doppler pattern of uterine and umbilical arteries, VII) nonsmoking and nonalcoholic women, and VIII) no history of hypertension, diabetes mellitus, autoimmune conditions, preeclampsia, abnormal vaginal discharge and bleeding, inducted pregnancy, hydrops fetalis, and consumption of hormonal contraceptive agents. Finally, only those who delivered a full-term, healthy baby with birth weight between the 10th and 90th percentiles for gestational age and gender were included for further analysis.

Exclusion criteria were: I) congenital abnormalities, II) oligohydramnios (amniotic fluid index [AFI]<5) according to Phelan's criteria,[13] III) biophysical profile <6, or estimated fetal weight outside the 90% of the normal range,[14] and IV) abnormal fetal biometry with an estimated fetal weight below the 10th percentile or higher than the 90th percentile in comparison with the first trimester or early second trimester ultrasound findings (cases of intrauterine growth retardation [IUGR], small for gestational age [SGA], and large for gestational age[LGA]).

Statistical analysis was performed using SPSS version 13.0. Variables were presented as mean±SD. A $P$ value of <0.05 was considered statistically significant. Pearson's correlation coefficient and regression were used for evaluation of correlation between indices and gestational age. Reference ranges (90% range between the 5th and 95th percentiles) and the 95% confidence interval were calculated for each parameter and presented as graphs. Linear, quadratic, and cubic regression models were fitted to estimate the relationship between fetal Doppler variables and gestational age (in weeks). The best fitting model for each variable was then selected.

## Results

A total of 1037 women were evaluated for this study of whom only 978 (94.31%) were enrolled in the final analysis and 59 were excluded from the study for the previously-mentioned criteria.

The number of patients according to gestational age in weeks, patients' characteristics, mean±SD for the MCA RI, PI, S/D ratio, and PSV are shown in Table 1. Values and nomograms of RI, PI at 5, 50, and 95th percentiles for each gestational age are shown in Figures 1 and 2, respectively. The reference curve of the RI follows a parabolic pattern, increasing from 0.76 at 20th week of gestation to 0.85 at 28th week and decreasing to 0.67 at 40th week of gestation (Figure 1). A similar pattern was also observed for the PI (from 1.72 to a maximum of 2.05 at 28th week to 1.23; Figure 2) and S/D ratio (from 5.34 to a maximum of 7.13 at 30th week to 3.16). Regarding PSV, an increase of 20 to 54.42 cm/s with a peak PSV of 60.85 at 39th week was noted for the observation interval. However, the reference curve of FHR demonstrated a decreasing trend from 151.69 to 136.5 beats per minute from 20th to 40th weeks of gestation.

There was a strong positive linear correlation between RI and PI ($P$<0.001, r=0.886), RI and S/D ratio ($P$<0.001, r=0.860), and PI and S/D ratio ($P$<0.001, r =0.863) and a negative linear correlation between PSV and PI ($P$<0.001, r =-0.170) and PSV and S/D ratio ($P$=0.012, r =-0.125). None of the RI, PI, PSV, or S/D ratio was correlated to the FHR.

**Table 1.** Mean±SD of demographic and Doppler ultrasonographic findings in the study group.

| Gestational age (wk) | No. of patients | Age of patients | Heart rate of fetus | Patients gravidity | RI | PI | PSV | S/D ratio |
|---|---|---|---|---|---|---|---|---|
| 20 | 41 | 23.25±3.41 | 151.69±5.88 | 1.31±0.6 | 0.76±0.04 | 1.72±0.29 | 20±12.23 | 5.34±1.55 |
| 21 | 48 | 27.38±6.34 | 149.63±5.72 | 1.79±0.88 | 0.77±0.06 | 1.79±0.26 | 23.15±12.69 | 5.81±1.9 |
| 22 | 43 | 26.38±6.37 | 149.77±7.39 | 1.69±0.85 | 0.76±0.05 | 1.82±0.28 | 23.77±11.69 | 5.91±1.79 |
| 23 | 54 | 26.74±6.7 | 144.48±8.04 | 1.81±1.03 | 0.78±0.04 | 1.94±0.28 | 22.72±11.02 | 6.31±1.97 |
| 24 | 45 | 27.36±5.95 | 146.43±6.92 | 2±1.35 | 0.81±0.05 | 1.94±0.43 | 27.92±11.38 | 6.21±1.61 |
| 25 | 52 | 25.23±5.21 | 148.54±7 | 1.81±0.98 | 0.81±0.05 | 1.9±0.36 | 27.14±9.2 | 6.38±1.59 |
| 26 | 44 | 27.79±4.51 | 142±7.4 | 1.74±0.8 | 0.82±0.05 | 1.95±0.39 | 30.56±10.14 | 6.36±1.47 |
| 27 | 42 | 27.1±5.31 | 144.24±7.75 | 2.1±1.04 | 0.83±0.04 | 2.03±0.38 | 36.13±9.37 | 6.69±1.37 |
| 28 | 41 | 26.5±3.62 | 143.7±7.57 | 1.6±0.69 | 0.85±0.07 | 2.05±0.49 | 37.24±6.6 | 6.95±1.64 |
| 29 | 55 | 25.97±5.56 | 141.43±8.59 | 1.6±0.85 | 0.84±0.05 | 2.02±0.4 | 36.54±9.7 | 6.87±1.46 |
| 30 | 46 | 26.5±4.47 | 140.6±11.06 | 1.7±0.82 | 0.83±0.04 | 1.98±0.34 | 46.42±11.16 | 7.13±1.35 |
| 31 | 50 | 27.53±7.7 | 138.77±10.67 | 1.57±0.77 | 0.82±0.04 | 1.97±0.35 | 41.24±10.14 | 6.6±1.66 |
| 32 | 46 | 27.29±5.97 | 140.76±8.28 | 2.06±0.82 | 0.82±0.07 | 1.92±0.33 | 49.28±9.77 | 7.09±2.21 |
| 33 | 47 | 27.3±4.78 | 138.39±8.78 | 1.52±0.73 | 0.79±0.06 | 1.76±0.3 | 47.3±10.73 | 5.84±2.00 |
| 34 | 42 | 27.05±6.02 | 138.67±9.91 | 1.81±0.98 | 0.79±0.04 | 1.79±0.28 | 57.1±9.29 | 5.1±1.18 |
| 35 | 49 | 29.21±4.65 | 136.37±10.13 | 2.26±1.36 | 0.8±0.05 | 1.75±0.33 | 52.06±9.61 | 5.33±1.84 |
| 36 | 48 | 27.92±5.62 | 139.88±9.52 | 2.33±1.09 | 0.75±0.05 | 1.54±0.26 | 56.65±12.2 | 4.31±1.15 |
| 37 | 43 | 27.94±5.05 | 137±9.66 | 1.63±0.88 | 0.73±0.07 | 1.43±0.31 | 53.93±16.34 | 4.12±1.31 |
| 38 | 51 | 25.29±5.65 | 134.71±7.76 | 1.53±0.8 | 0.68±0.06 | 1.25±0.21 | 56.97±15.91 | 3.22±0.67 |
| 39 | 45 | 28.33±5.66 | 136.33±9.3 | 2.27±1.43 | 0.68±0.05 | 1.23±0.15 | 60.85±18.96 | 3.22±0.46 |
| 40 | 46 | 26.50±2.33 | 136.50±10.19 | 1.63±0.51 | 0.67±0.04 | 1.23±0.16 | 54.42±23.48 | 3.16±0.44 |

RI= resistive index; PI=pulsatility index; S/D ratio=systolic-to-diastolic ratio; PSV=peak systolic velocity; FHR=fetal heart rate.

## Discussion

In fetal intracranial circulation, diastolic blood flow appears earlier than the fetal aorta and umbilical artery representing redistribution of the flow to the most vital fetal organ.[15] Also, comparing changes in the fetal cerebral circulation with changes in the systemic circulation or the umbilical arteries have shown that fetal cerebral circulation changes to be more promising as a predictor of the condition of the fetus.[6,16] So, the MCA has been the vessel of choice to assess fetal cerebral circulation.

Comparing the RI as found in our reference curves with that published by Kurmanavicius et al.[17] it is clear that reference limits during 24th to 40th weeks of gestation are lower (about 0.6 – 1.1) for our curves. A reason for these conflicting results may be the different mathematical methods used for derivation of the indices. With similar

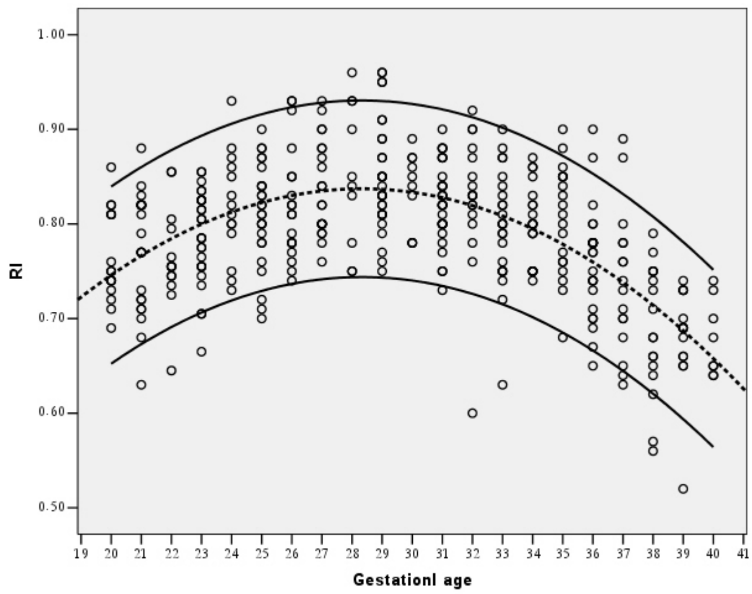


**Figure 1.** Individual measurements and calculated reference ranges for the resistive index (RI) in the MCA. The standard boundaries include 90% of the normal patient population ($r^2$=0.386, *P*<0.001).

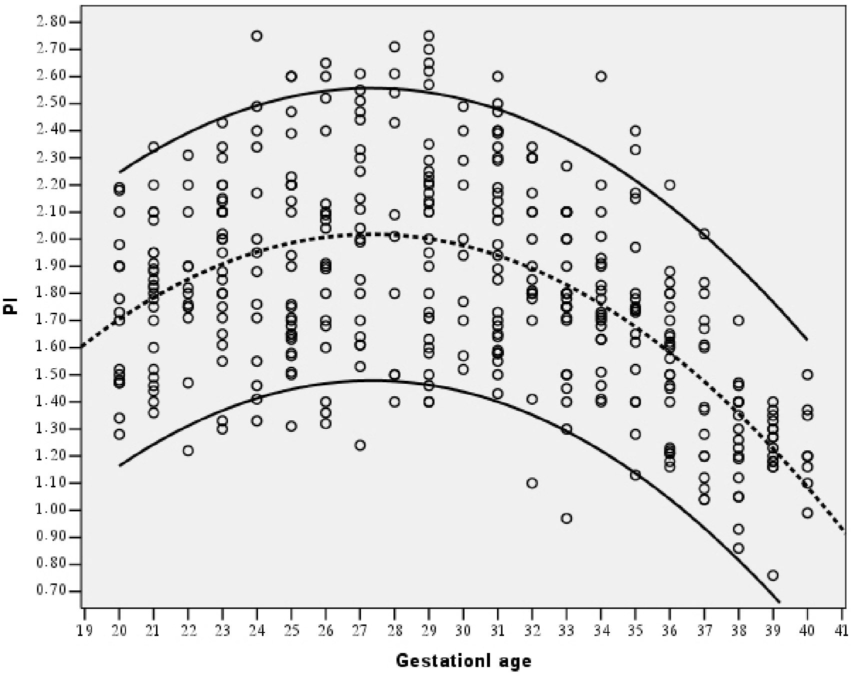


**Figure 2.** Individual measurements and calculated reference ranges for the pulsatility index (PI) in the MCA. The standard boundaries include 90% of the normal patient population ($r^2$=0.340, $P$<0.001).

parabolic pattern, our ranges were closer to the Bahlmann et al.'s report.[7]

Despite the parabolic shape of our PI curve and the presence of a peak at 28th week of gestation, generally, there was a fall in the fetal MCA PI with advancing gestational age (Figure 2) which is comparable with other studies.[18,19] This decrease probably reflects a decreasing vascular resistance with advancement of gestational age or an association with deoxyribonucleic acid production in fetal brain.[18,19]

A comparison of the reference ranges established in this study with those obtained in the USA[20] and Germany[3] shows almost identical parabolic pattern and reference values for the PI over the entire observation period. Conversely, the results reported by Vyas et al.,[21] Mari and Deter,[22] Komwilaisak et al.,[23] and Bahlmann et al.,[7] show higher PI values, despite the similarity of their curves with our chart. This discrepancy may be due to the eight- to 11-fold smaller number of patients included in Vyas et al.'s and Mari and Deter's studies and the different statistical methods used for analyses.

There are no available studies on S/D ratio range and pattern, expect that of Ertan et al.[24] who have reported a chart with decreasing slope toward the end of gestation. In our study, S/D ratio chart had a parabolic pattern similar to those obtained for RI and PI (20th week: 5.34, 40th week: 3.16, and peak in 30th week: 7.13). Because the same factors were used to calculate the RI, PI, and S/D ratio, these indices showed a similar pattern.

Our study demonstrated that the MCA PSV was increased during the second half of pregnancy. Although patterns were similar, values were different and showed an average of 6 cm/s higher than that reported by Bahlmann et al.[7] Comparison of the PSV ranges in the MCA measured in this study with those reported by Kurmanavicius et al.[25] and Mari and Deter[26] demonstrates good agreement, although there are minor differences in values. Marked disparity, especially for the upper reference limits, become apparent in the period prior to 28 weeks of gestation. Explanations for this phenomenon were the use of different statistical methods, and different sample sizes. An inverse correlation between PSV and the fetal hemoglobin concentration or hematocrit may also interfere with the results of studies.[26]

Although studies in early periods of gestation (first trimester) showed that FHR increases as pregnancy progresses,[27,28] but we demonstrated that after 20th week of gestation (during late second and third trimesters), the rate decreases as gestational age increases. Similar results were reported by Snijders et al. and Park et al.[29,30]

This is of clinical importance to determine whether given MCA Doppler indices are normal or not; so, normal MCA Doppler indices must be defined for each week of gestational age. Since these parameters may be varied among different populations, population-specific charts may be needed. The DU reference curves for the MCA described in this paper (especially, the lower reference limits of the PI and RI) can be used in assessment of fetal hypoxemic, anemic disorders, and IUGR,[22,31] because these processes are identified by demonstration of low-impedance Doppler waveforms of the MCA.[21]

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