

# Diurnal Variation of Fetomaternal Doppler and Fetal Cardiac Function Parameters in the Hospitalized Pregnancies: A Cross-Sectional Study

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## ABSTRACT

**Introduction:** To assess changes in blood flow in the uterine, fetal cerebral, and umbilical arteries (UA) by Doppler ultrasound and alterations in the variability of fetal heart rate (FHR) as well as fetal cardiac performance by fetal echocardiography between the 7.00 a.m. and 7.00 p.m. periods in pregnancies ranging from 24 to 39 weeks.

**Methods:** Fifty pregnant participants underwent a customized fetal examination on the same day during both study periods, including Doppler measurements of the umbilical artery pulsatility index (UA-PI), fetal middle cerebral artery-pulsatility index (MCA-PI), middle cerebral artery-peak systolic velocity (MCA-PSV), cerebroplacental ratio, uterine artery-pulsatility index (UtA-PI), FHR, and fetal movements as well as various Doppler parameters of the fetal heart such as left isovolumetric contraction and relaxation times, mitral E- and A-wave velocities, the E/A ratio, K-index, filling time, and the myocardial performance index.

**Results:** During the PM period, there was a meaningful increase in the MCA-PSV compared with the AM period. Conversely, the resistance in the MCA, particularly the PI, was found to be lower than that in the AM period. In addition, the FHR measured in the PM period increased compared with that in the AM period. The maternal UtA-PI and fetal UA-PI examined in the AM and PM periods were comparable. In addition, when all cardiac parameters examined in the study periods were compared, no significant difference was observed.

**Conclusion:** The findings reveal that Doppler parameters observed during the study periods may change during the day and that the fetal cardiac function parameters, previously not assessed together, may not change during the day. Subsequent investigations can validate these observations using serial measurements of Doppler parameters in healthy and complicated gravidas.

**Keywords:** Circadian rhythm, Fetomaternal Doppler ultrasound, myocardial performance index

## Introduction

Fetal Doppler ultrasound is crucial in prenatal medicine and obstetrics (1). It is used for screening, evaluating the health of the fetus, and monitoring pregnancies that are problematic. It has been demonstrated to have notable advantages in enhancing perinatal results and functioning as a tool to inform obstetrical decisions and decrease the requirement for neonatal intensive care (2).

Umbilical artery (UA) Doppler provides important information about fetal circulation. During healthy pregnancies, the fetoplacental unit expands as the pregnancy advances, ensuring sufficient oxygen and nutrition transport to support fetal growth (3,4). The umbilical artery pulsatility index (UA-PI) serves as a critical tool for evaluating placental function, where increased resistance within the UA indicates placental impairment and associated with intrauterine growth restriction (5,6).

The middle cerebral artery (MCA) Doppler flow velocity measurement is useful in several clinical scenarios, including the assessment of fetal anemia, fetal hypoxia, and other conditions that might affect the fetal circulatory system. It offers data on how the fetus adapts to decreased oxygen levels. A lower level of middle cerebral artery pulsatility index (MCA-PI) indicates an adaptive decrease in vascular resistance to the fetal brain, which is usually referred to as the “brain-sparing effect” (7,8). The cerebroplacental ratio (CPR) was obtained by dividing the MCA-PI by the UA-PI. This ratio provides valuable information on both the condition of the placenta and the fetal response. It has been found to be a more accurate indicator of perinatal outcome than analyzing the MCA-PI and UA-PI separately (9-11). Peak systolic velocity (PSV) is a significant Doppler blood flow measurement in MCA that holds clinical importance. Fetal anemia increases MCA-PSV when the viscosity of blood decreases because of a decrease in the concentration of red blood cells (12).



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The myocardial performance index (MPI), also commonly referred to as the Tei index, is an echocardiographic parameter used to assess fetal cardiac function. It was first described by Tei et al. (13) and is calculated as the total of isovolumetric contraction time (IVCT) and isovolumetric relaxation time (IVRT) divided by ejection time (ET). If there is an abnormality in the cardiac function of the fetus, it will result in a prolonged isovolumetric time and a shortened ET, leading to an increase in the MPI (14-16).

Circadian rhythms are physiological processes that adhere to an approximately 24 h pattern, regulate various physiological functions in our bodies, and are predetermined according to cyclic changes in the environment. The circadian rhythm of pregnancy is intricate; the mother, placenta, and fetus are separate circadian units that communicate with one another (17,18).

The suprachiasmatic nucleus (SNS) is a biological clock that receives information from the environment and imposes a circadian pattern. The SNS develops very early in pregnancy. Therefore, the fetus has a circadian rhythm and receives circadian input from the mother (19). The fetus is invariably subjected to the maternal internal environment's inherent rhythms, such as cortisol, heart rate, body temperature as well as the mother's resting activity; rhythms generated by maternal melatonin crossing placenta unchanged and food intake (20).

The fetal examination needs to be performed at different times of the day according to patient and physician schedules. The various times of the day (morning, afternoon, evening) are not expected to have a major effect on the parameters evaluated, and fetal monitoring is independent of circadian rhythms (21). However, the authors described diurnal variations in several fetal physiological parameters, including heart rate, movements, and breathing (22,23).

There is little information on whether there is a diurnal variation in the parameters of fetal, placental, and maternal uterine blood flow. The objective of this investigation was to ascertain whether day-to-day variations in fetal, placental, and maternal Doppler parameters exist. We also saw if there was any change in intraday fetal cardiac performance, which has not been researched in any previous study.

## Methods

This hospital-based prospective cross-sectional study was conducted at the Perinatology Center of University of Health Sciences Turkey, Haseki Training and Research Hospital, which is associated with the University of Health Sciences, in the Sultangazi community of İstanbul. The study was carried out after receiving consent from the University of Health Sciences Turkey, Haseki Training and Research Hospital Local Ethics Committee (approval number: 240-2023, date: 20.12.2023) in accordance with the relevant clinical ethics guidelines and the current Declaration of Helsinki. Before performing any procedures, each pregnant woman was given detailed explanations regarding the aim and nature of the procedures, and their informed written consent was obtained.

The study included women with 24-39 weeks of singleton pregnancies hospitalized for diagnostic purposes within the indication in our perinatology clinic and were not expected to give birth. The gestational

age was ascertained with the use of first trimester ultrasonography. In addition, age, gravidity, parity, fasting glucose, and body mass index were recorded for all gravidas enrolled in the study.

The study conducted in 2023 had 78 gravidas, each holding a single fetus. Multiple pregnancies, employment of pharmaceutical drugs that potentially impact the fetoplacental and fetal circulatory systems, and fetuses exhibiting malformations and chromosomal anomalies were excluded. The gravidas that participated in the study were first examined by ultrasound at 7 a.m. while fasting, and the following parameters were collected: head circumference (HC), biparietal diameter (BPD), femur length (FL), abdominal circumference (AC), estimated fetal weight (EFW), uterine artery-pulsatility index (UtA-PI), UA-PI, middle cerebral artery peak systolic velocity (MCA-PSV), MCA-PI, CPR, fetal heart rate (FHR), and fetal movements (FM). She was then called back at 7 p.m. when she was full of rested, and the same parameters were checked by ultrasonography. They all ate the same type of food, adjusted to their diet, and served in the hospital at the same time.

All ultrasonography was performed by a single clinician (S.T.). The individual, unaware of subject allocation until the complete collection and analysis of data, conducted each session with a duration of 15 ( $\pm 5$ ) minutes. All sonographic studies were conducted, including color Doppler and pulsed Doppler ultrasound. Doppler assessments were performed without FM or respiration. In addition, the beam angle was maintained at 20°. UA Doppler tracings were taken on the free surface of the umbilical cord. MCA was sampled from the proximal section, close to its origin from the internal carotid artery (24).

To obtain the left MPI and other fetal cardiac parameters; initially, a 4-chamber perspective of the fetal heart was acquired, followed by a slight angled probe toward the apex to capture the aorta's origin. The Doppler sample volume was opened to 3 mm and positioned on the ascending aorta's lateral wall, situated beneath the aortic valve (AV) and just above the mitral valve (MV). The insonation angle was kept as close to 0° as possible and was always less than 30° (Figure 1). In addition, the E/A waveform consistently exhibited positive flow. However, the aortic blood flow waveforms were negative. The subsequent time intervals were estimated as follows: IVCT was estimated from the moment MV closed to AV opening, ET from AV opening to closure, and IVRT from AV closure to MV opening. MPI was determined by dividing the sum of IVCT and IVRT by ET.

## Statistical Analysis

Analyses were performed using IBM SPSS v22.0 (USA). For descriptive statistics, the values of mean with standard deviation and median with range were used to present the numeric data. After Kolmogorov-Smirnov test to examine the normality of clinical and Doppler ultrasound parameters, the comparisons of study parameters were performed using the paired t-test or Wilcoxon signed-rank test. For categorical variables, the McNemar's test was used. To determine significances, p-value of less than 0.05 was chosen.

## Results

In 2023, a cohort of 78 gravidas with singleton gestations was enrolled in this study. However, only 50 gravidas could be included in the study.

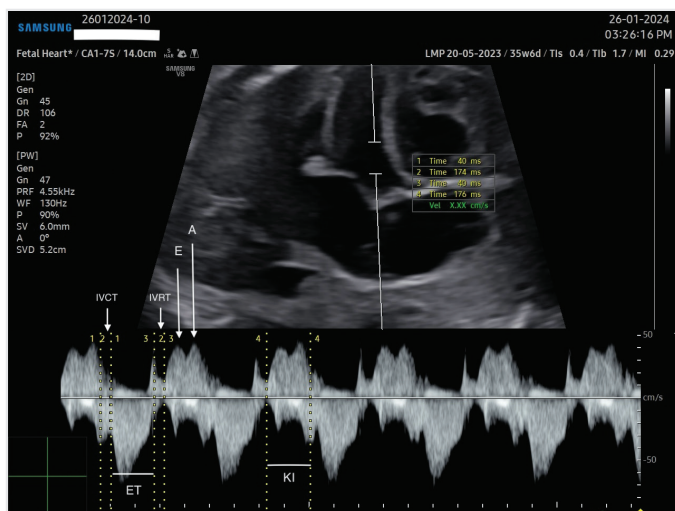
Of the remaining 28 subjects, they were excluded because of unsuitable fetal heart position or difficult assessment of the fetal heart.

The findings of 50 gravidas whose data could be fully collected during the study period were analyzed. In this study of 50 cases, 8 (16%) were normal healthy gravidas, 13 (26%) were gravidas with threatened preterm labor, 11 (22%) were gravidas with gestational diabetes (GDM), 8 (16%) were gravidas with fetal growth restriction, 5 (10%) were gravidas with anemia, and 5 (10%) were gravidas with type 2 diabetes.

Maternal and fetal characteristics are listed in Table 1. The mean values for the maternal age were 30.0±5.9 years. The median values for gravidity were 2 (1-11), parity was 1 (0-3), gestational age was 33 (24-39) weeks, BPD was 34 (25-38) weeks, HC was 33 (24-38) weeks, AC was 33 (23-41) weeks, FL was 33 (24-38) weeks, and EFW was 1950 (649-3210) g. The median values for body mass index were 27.4 (20.1-45.8) and fasting glucose was 76 (62-135) mg/dL. There were no abnormal findings related

to amniotic fluid and placenta and except for 3 fetuses, all others were head presentation.

Table 2 shows that the mean values for FHR was 135±7 beats/min in the AM period and 141±5.6 beats/min in the PM period. The mean FHR difference between the AM and PM periods was statistically significant (p=0.001). There was also a significant difference in the number of FM observed on ultrasound at 15 min between the AM and PM periods. The median MCA-PSV values were 41 (24-57) cm/s in the AM period and 51 (31-61) cm/s in the PM period. The mean difference in MCA-PSV between AM and PM was statistically significant (p=0.001) and the MCA-PI values measured in the PM period were significantly lower than the MCA-PI values measured at the AM period (1.4±0.19 vs. 1.6±0.2; p=0.001). The median values of CPR measured during the PM period. were significantly lower than those during the AM period [1.4 (0.4-3.6) vs. 1.5 (0.4-4.2); p=0.001]. Maternal UtA-PI and UA-PI were not statistically different between the AM and PM periods. The fetal cardiac parameters measured at the AM and PM periods are depicted in the Table 3. There were no significant differences in the Doppler parameters E, A, IVCT, IVRT, MPI, and filling time measured at the AM and PM periods (p>0.05).



**Figure 1.** Measuring and calculating the myocardial performance index. A representative image indicating measurements of myocardial performance index  
 IVCT: Isovolumetric contraction time, IVRT: Isovolumetric relaxation time, KI: Filling time, E: Mitral E wave velocity, A: Mitral A wave velocity, ET: Ejection time

**Table 1. Baseline clinical maternal and fetal characteristics (n=50)**

Characteristics	Value
Maternal age, y	30.0±5.9
Gravidity	2 (1-11)
Parity	1 (0-3)
Gestational age at study, week	33 (24-39)
BMI, kg/m <sup>2</sup>	27.4 (20.1-45.8)
Fasting glucose, mg/dL	76 (62-135)
BPD, mm	34 (25-38)
HC, mm	33 (24-38)
AC, mm	33 (23-41)
FL, mm	33 (24-38)
EFW, g	1950 (649-3210)

BMI: Body mass index, BPD: Biparietal diameter, HC: Head circumference, AC: Abdominal circumference, FL: Femur length, EFW: Estimated fetal weight

## Discussion

In our study, the MCA-PSV measured at 7 p.m. was significantly higher than that measured at 7 a.m., whereas the MCA-PI was significantly lower. As a result, CPR at 7 p.m. was significantly lower than that at 7 a.m. In addition, the FHR and movement in the afternoon were significantly

**Table 2. B-mode and Doppler ultrasonographic findings of the study population (n=50)**

	AM	PM	p
Mean UtA-PI	1.1 (0.4-2.1)	1.1 (0.5-1.9)	0.848
UA-PI	1 (0.4-4.2)	1.1 (0.6-2)	0.651
MCA-PI	1.6±0.2	1.4±0.19	0.001
MCA-PSV, cm/s	41 (24-57)	51 (31-61)	0.001
CPR	1.5 (0.4-4.2)	1.4 (0.4-3.6)	0.001
FHR, bpm	135±7	141±5.6	0.001
<b>FM</b>			
No	20 (40%)	5 (10%)	0.001
Yes	30 (60%)	45 (90%)	

UtA: Uterin artery, PI: Pulsatility index, UA-PI: Umbilical artery-pulsatility index, MCA-PI: Middle cerebral artery-pulsatility index, MCA-PSV: Middle cerebral artery-peak systolic velocity, CPR: Cerebroplacental ratio, FHR: Fetal heart rate, FM: Fetal movements

**Table 3. Fetal cardiac parameters of the study population (n=50)**

	AM	PM	p
E, cm/s	33±7	33±5	0.759
A, cm/s	45±9	44±8	0.863
E/A	0.7±0.1	0.7±0.1	0.246
IVCT, ms	31 (24-38)	33 (24-40)	0.021
IVRT, ms	36±4.3	36±4.3	0.824
MPI, ms	0.4 (0.35-0.43)	0.4 (0.35-0.44)	0.126
KI	0.3±0.04	0.3±0.04	0.175

E: Mitral E wave velocity, A: Mitral A wave velocity, IVCT: Isovolumetric contraction time, IVRT: Isovolumetric relaxation time, MPI: Myocardial performance index, KI: Filling time

higher than those in the morning. In our study, the UA-PI and mean UtA-PI in the morning and afternoon were not significantly different.

We found two studies that noted the effect of circadian rhythm on fetal and maternal Doppler. The first study, having a considerably similar design, had a wide range of gestational weeks and included both healthy and complicated gravidas like our participants. In this study, no significant change in the circadian rhythm was found in any of the Doppler parameters (25). In the other study involving healthy pregnant women in their third trimester, the increase in MCA-PSV and decrease MCA-PI in the afternoon are similar to our study (21). MPI and other cardiac parameters were not evaluated in either study.

In the current study, Doppler parameters at 7 a.m. were evaluated when the patient was fasting. The values at 7 p.m. were evaluated when the patient was full. Because the gravidas in the study were hospitalized, they all ate the same meals at the same time according to their diet. Opheim et al. (26) evaluated Doppler parameters before and after a meal. In this study, MCA-PSV evaluated when the pregnant woman was full was found to be high and MCA-PI was found to be low. In our study, the increase in PSV and decrease in PI of the MCA evaluated in the afternoon, when the pregnant woman was satiated, were similar to those found in this study (26).

The fetal Doppler waveform can be influenced by many factors (27). The factors involved are the angle of insonation and the region of measurement (28), technical factors like ultrasound settings, gestational age, FHR (29,30), fetal breathing (31,32) or hiccups, FM, and circadian rhythm (25). In our study, it is likely that technical factors did not significantly influence our study. Measurements were conducted using an identical instrument and by the same clinician. Measurements were obtained when fetal breathing and movement were not present.

In our study, FHR increased significantly in the afternoon, which may affect Doppler parameters. A limitation of our study is that we did not adjust the MCA Doppler parameters according to FHR. With the exception of a few studies (33), previous studies have ignored this. Another limitation of this study is the lack of neonatal outcomes and the relatively small number of cases. However, the number of cases was kept small because each patient was examined twice and the appropriate position for cardiac evaluation was waited. If the position was not favorable for fetal heart evaluation, the patient was given two more chances for a favorable position. If the fetal heart was not in the appropriate position, the patient was excluded.

When fetal cardiac parameters measured at 7 a.m. and 7 p.m. were compared, there were no significant differences. Studies on MPI, previously used to assess fetal cardiac function, have been shown that Oral Glucose Tolerance testing does not affect MPI (34), but some conditions such as fetal growth restriction (35), oligohydramnios (36) and maternal diabetes (tip 1, tip 2 and unregulated GDM) (37) increase MPI. In this study, we observed that circadian rhythm did not significantly affect fetal cardiac function. However, as this is the first study on this subject, further studies with a larger number of cases are needed.

This study demonstrated that circadian rhythms influence some Doppler parameters but not those related to cardiac function. Therefore, time of

day should be taken into account when evaluating Doppler parameters. However, larger studies are necessary to develop a definitive nomogram for this purpose.

## Conclusion

In conclusion, among the Doppler parameters examined in AM and PM in gravidas at 24 to 39 weeks of gestation, MCA-PSV was found to be significantly increased in PM, whereas MCA-PI was found to be significantly decreased. FHR was found to be increased in PM, contrary to other studies. As shown in previous studies, circadian rhythm affects Doppler parameters. However, more work is needed on this. However, fetal cardiac parameters did not change significantly in the AM and PM periods, and circadian rhythm did not affect fetal performance. As this is the first study on this topic, further studies are required.

**Ethics Committee Approval:** The study was carried out after receiving consent from the University of Health Sciences Turkey, Haseki Training and Research Hospital Local Ethics Committee (approval number: 240-2023, date: 20.12.2023) in accordance with the relevant clinical ethics guidelines and the current Declaration of Helsinki.

**Informed Consent:** Informed written consent was obtained.

**Authorship Contributions:** Concept - A.Ö.; Design - A.Ö.; Data Collection or Processing - S.T.; Analysis or Interpretation - S.T., A.Ö.; Literature Search - S.T., A.Ö.; Writing - S.T., A.Ö.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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