
OBSTETRICS

Assessment of Fetal Cardiac Function in Women with Chronic Hypertension

Thanyalak Boonprasit, M.D.*,
Dhirapatara Charoenvidhya, M.D.*

* Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

ABSTRACT

Objectives: The primary objective was to compare the fetal myocardial performance index (MPI) among pregnant women with chronic hypertension and women with normal blood pressure. The secondary objectives were to evaluate whether the fetal MPI can predict adverse perinatal outcomes and to assess uterine, middle cerebral, and umbilical arteries in pregnant women with chronic hypertension and normal blood pressure.

Materials and Methods: A cross-sectional study enrolled singleton pregnancies with a gestational age of 28-32 weeks in the antenatal clinic at King Chulalongkorn Memorial Hospital between April 2020 - April 2021. This study divided pregnant women into two groups, those with normal blood pressure and those with chronic hypertension. The fetuses were evaluated for growth, amniotic fluid volume, and fetal cardiac function.

Results: The median of modified MPI was not different between chronic hypertension and control groups (0.49 vs 0.47, $p = 0.691$, adjusted $p = 0.299$). The median of the Doppler studies showed no differences between groups in the left uterine artery pulsatility index (PI) (0.78 vs 0.76, $p = 0.085$, adjusted $p = 0.902$), right uterine artery PI (0.83 vs 0.75, $p = 0.159$, adjusted $p = 0.442$), umbilical artery PI (0.94 vs 0.93, $p = 0.982$, adjusted $p = 0.060$), middle cerebral artery PI (1.86 vs 1.80, $p = 0.311$, adjusted $p = 0.05$). The chronic hypertension group developed more maternal adverse outcomes, such as gestational age at birth (36.8 ± 2.19 vs 38.2 ± 1.31 , $p < 0.001$, adjusted $p < 0.001$). Women in the chronic hypertension group also experienced more neonatal adverse outcomes, including length of hospital stays (4.0 vs 3.0, $p < 0.001$, adjusted $p = 0.001$). No differences were found in other neonatal adverse outcomes.

Conclusion: There was no difference in the median of the MPI between pregnant women with normal blood pressure and women with chronic hypertension. The Doppler studies of the umbilical artery, middle cerebral artery, and uterine artery were not different between the chronic hypertension group and the control group. The modified MPI may not be predictive of perinatal outcomes.

Keywords: adverse perinatal outcome, chronic hypertension, fetal cardiac function, modified myocardial performance index (Mod-MPI).

Correspondence to: Dhirapatara Charoenvidhya, M.D., Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University, Rama IV Road, Pathumwan, Bangkok 10330, Thailand.
E-mail: dhirapatara.c@chula.ac.th

Received: 21 June 2022, **Revised:** 7 March 2023, **Accepted:** 29 May 2023

การตรวจคลื่นเสียงความถี่สูงเพื่อประเมินการทำงานของหัวใจของทารกในสตรีตั้งครรภ์ที่มีภาวะความดันโลหิตสูงก่อนการตั้งครรภ์

ธัญลักษณ์ บุญประสิทธิ์, ธีระภัทร เจริญวิทย์

บทคัดย่อ

วัตถุประสงค์: เพื่อเปรียบเทียบการทำงานของหัวใจทารกในครรภ์ระหว่างสตรีตั้งครรภ์ที่มีภาวะความดันโลหิตสูงก่อนการตั้งครรภ์กับสตรีตั้งครรภ์ที่มีความดันโลหิตปกติในช่วงอายุครรภ์ 28-32 สัปดาห์ เพื่อศึกษาการทำงานของหัวใจทารกในสตรีตั้งครรภ์ที่มีภาวะความดันโลหิตสูงก่อนการตั้งครรภ์ในช่วงอายุครรภ์ 28-32 สัปดาห์ สามารถทำนายภาวะแทรกซ้อนต่อทารกในครรภ์ และเพื่อศึกษาความต้านทานของเส้นเลือด uterine artery, middle cerebral artery, umbilical artery ในสตรีตั้งครรภ์ที่มีความดันโลหิตสูงก่อนการตั้งครรภ์โดยเปรียบเทียบกับสตรีตั้งครรภ์ที่มีความดันโลหิตปกติในช่วงอายุครรภ์ 28-32 สัปดาห์

วัสดุและวิธีการ: รูปแบบการศึกษาเป็นการศึกษาแบบ cross sectional study ในสตรีตั้งครรภ์เดี่ยวที่มีอายุครรภ์ระหว่าง 28-32 สัปดาห์ ที่มารับการตรวจฝากครรภ์ที่โรงพยาบาลจุฬาลงกรณ์ ในช่วงเดือน เมษายน พ.ศ.2563 - เมษายน 2564 ใน การศึกษานี้แบ่งสตรีตั้งครรภ์เป็น 2 กลุ่ม คือ กลุ่มสตรีตั้งครรภ์ที่มีภาวะความดันโลหิตสูงก่อนการตั้งครรภ์หรือมีความดันโลหิตสูงก่อนอายุครรภ์ 20 สัปดาห์ และกลุ่มสตรีตั้งครรภ์ที่มีความดันโลหิตปกติ สตรีตั้งครรภ์ทั้ง 2 กลุ่มจะได้รับการตรวจคลื่นเสียงความถี่สูงประเมินน้ำหนักรก ปริมาณน้ำคร่ำ ความต้านทานของเส้นเลือด uterine artery, middle cerebral artery, umbilical artery และการทำงานของหัวใจทารก (modified myocardial performance index)

ผลการศึกษา: ค่าการทำงานของหัวใจทารก (modified myocardial performance index) ไม่แตกต่างกันระหว่างสตรีตั้งครรภ์ที่มีความดันโลหิตสูงก่อนการตั้งครรภ์กับสตรีตั้งครรภ์ที่มีความดันโลหิตปกติ (0.49 vs. 0.47, $p=0.691$, adjusted $p=0.299$) ค่ามัธยฐานของค่าความต้านทานของเส้นเลือด left uterine artery PI (0.78 vs. 0.76, $p=0.085$, adjusted $p=0.902$), right uterine artery PI (0.83 vs. 0.75, $p=0.159$, adjusted $p=0.442$), umbilical artery PI (0.94 vs. 0.93, $p=0.982$, adjusted $p=0.060$) และ middle cerebral artery PI (1.86 vs. 1.80, $p=0.311$, adjusted $p=0.050$) ไม่แตกต่างกันระหว่างสตรีตั้งครรภ์ทั้งสองกลุ่ม ในกลุ่มสตรีตั้งครรภ์ที่มีความดันโลหิตสูงก่อนการตั้งครรภ์มีภาวะแทรกซ้อนต่อมารดา มากกว่ากลุ่มสตรีตั้งครรภ์ที่มีความดันโลหิตปกติ ได้แก่ อายุครรภ์ที่คลอดบุตร (36.8 ± 2.19 vs 38.2 ± 1.31 , $p < 0.001$, adjusted $p < 0.001$) และมีภาวะแทรกซ้อนต่อทารกหลังคลอดมากกว่า ได้แก่ ระยะเวลาอนโรงพยาบาลนานกว่า (4.0 vs 3.0 , $p < 0.001$, adjusted $p=0.001$) ส่วนภาวะแทรกซ้อนอื่นๆ ต่อทารกพบว่าไม่แตกต่างกัน

สรุป: ค่าการทำงานของหัวใจทารก (modified myocardial performance index) ความต้านทานของเส้นเลือด umbilical artery, middle cerebral artery และ uterine artery ไม่แตกต่างกันระหว่างสตรีตั้งครรภ์ที่มีความดันโลหิตสูงก่อนการตั้งครรภ์กับสตรีตั้งครรภ์ที่มีความดันโลหิตปกติ และจากการศึกษาแสดงให้เห็นว่าค่าการทำงานของหัวใจทารกในสตรีตั้งครรภ์ที่มีภาวะความดันโลหิตสูงก่อนการตั้งครรภ์ไม่สามารถทำนายภาวะแทรกซ้อนต่อทารกในครรภ์

คำสำคัญ: ภาวะแทรกซ้อนต่อทารกในครรภ์, ภาวะความดันโลหิตสูงก่อนการตั้งครรภ์, ค่าการทำงานของหัวใจทารก, Modified myocardial performance index (Mod-MPI)

Introduction

When hypertension is diagnosed before pregnancy or before 20 weeks of gestation, it is defined as chronic hypertension. Chronic hypertensive disease is reported in 0.5 - 5% of pregnancies^(1,2). The prevalence of chronic hypertension at King Chulalongkorn Memorial Hospital was 3.24% in 2017. The risk of chronic hypertension increases with obesity and advanced maternal age.

Chronic hypertension is related to insulin resistance and endothelial dysfunction. Correspondingly, pregnancy complications such as preeclampsia and gestational diabetes mellitus (GDM) are also associated with insulin resistance and endothelial dysfunction^(3,4,5). The most common comorbidities are pregestational diabetes, thyroid disorders, chronic renal disease, and collagen vascular disease⁽⁶⁾.

Chronic hypertension is a risk factor for many adverse maternal and neonatal outcomes. Significant maternal morbidities are stroke, renal failure, pulmonary edema, severe preeclampsia, and placental abruption. Neonatal morbidities are fetal growth restriction, prematurity, low birth weight, respiratory distress syndrome, and stillbirth^(7, 8, 9,10). Pregnant women with this condition should be managed with appropriate maternal and fetal surveillance.

Chronic hypertension in pregnancy has also been attributed to placenta abnormalities such as decreased placenta vessel numbers, placental infarction, villous fibrinoid necrosis, and avascular villi. When the placenta is abnormal, it can cause fetal hemodynamic change, which can induce changes in fetal cardiac function.

Currently, fetal surveillance is conducted by a nonstress test (NST) and ultrasound. Ultrasound assesses fetal weight, amniotic fluid, Doppler waveform of vessels, and the myocardial performance index (MPI). MPI can be considered a direct

parameter of cardiac dysfunction. In combination with other venous and arterial parameters, MPI helps define the fetal condition⁽¹¹⁾.

Studies have previously used the MPI to evaluate fetal cardiac function and predict adverse neonatal outcomes in conditions such as fetal growth restriction and preeclampsia. In 2019, Lina Zhang et al. reported that fetal growth restriction fetuses had an increased modified MPI which could predict adverse perinatal outcomes⁽¹²⁾. Alici Davutoglu et al⁽¹³⁾ found that early-onset fetal growth restriction and late-onset fetal growth restriction fetuses have significantly higher modified MPI values demonstrating prenatal cardiac dysfunction. Sevket Balli et al⁽¹⁴⁾ also demonstrated that the isovolumic relaxation time and the right and left MPI were higher in fetuses of preeclamptic mothers than in fetuses of non-preeclamptic mothers. Bhorat et al⁽¹⁵⁾ also reported higher MPI values in the preeclamptic group. Fetal cardiac function was significantly impaired in pregnancies complicated by severe early-onset preeclampsia. They concluded that the MPI could be integrated into routine fetal surveillance techniques. No studies have used MPI to evaluate fetal cardiac status in pregnant women with chronic hypertension. This study was performed to compare the MPI of pregnant women with chronic hypertension to those with normal blood pressure and evaluate whether the MPI can predict adverse perinatal outcomes.

Materials and Methods

A cross-sectional study design recruited pregnant patients at the King Chulalongkorn Memorial Hospital antenatal clinic between April 2020 and April 2021. The inclusion criteria were singleton pregnant women above 18 years old with 28 - 32 weeks gestational age. The exclusion criteria were fetal structural or chromosome anomaly, underlying maternal disease (renal, liver, connective tissue disease), and tocolytic agents.

This study was divided into a control group of

pregnant women with normal blood pressure and a case group of pregnant women with chronic hypertension. Chronic hypertension in pregnancy was defined as hypertension diagnosed or present before pregnancy or before 20 weeks of gestation with a systolic blood pressure of 140 mm Hg or more, a diastolic blood pressure of 90 mm Hg or more, or both documented by a minimum of two determinations taken at least 4 hours apart⁽¹⁶⁾.

No study had previously evaluated fetal cardiac function in pregnant women with chronic hypertension. This pilot study estimated the mean MPI in pregnant women with chronic hypertension. The sample size was calculated following Sevket Balli et al⁽¹⁴⁾ and using a sample size calculation from two independent means. A minimum of 34 pregnant women corresponding to the criteria were required for the case and control groups.

The primary outcome of this study was to compare the fetal MPI between pregnant women with chronic hypertension and women with normal blood pressure. The secondary outcomes were to evaluate whether the fetal MPI in pregnant women with chronic hypertension can predict adverse perinatal outcomes and assess the uterine artery, middle cerebral artery, and umbilical artery in pregnant women with chronic hypertension and pregnant women with normal blood pressure.

All the women gave informed consent before enrolling in the study. The study was approved by the Institutional Review Board (IRB) at King Chulalongkorn Memorial Hospital. The fetuses were evaluated for growth, amniotic fluid volume, and fetal cardiac function. Fetal biometric measurements included biparietal diameter, head circumference, abdominal circumference, and femur length. Fetal weight was estimated. Doppler measurements of the umbilical artery (UA), middle cerebral artery (MCA), and uterine artery were assessed. Fetal cardiac function was evaluated using a modified MPI. A single operator (well-trained Maternal-Fetal medicine fellow under supervision by MFM staff) measured all parameters using the GE Voluson E10 (GE Medical Systems,

Kretztechnik, Zipf, Austria). The intraclass correlation coefficient was 0.860 (95% confidence interval (CI) 0.578-0.962).

Modified myocardial performance index

A cross-sectional image of the five-chamber view of the fetal heart and an apical projection of the heart were obtained. The Doppler sample volume was placed on the lateral wall of the ascending aorta, below the aortic valve (AV), and above the mitral valve (MV). The ascending aorta aligns with an angle of insonation < 20 degrees. The Doppler trace showed an echo corresponding to the opening and closure of the mitral valve and aortic valve waveforms. The periods were estimated as follows: the isovolumetric contraction time (ICT) was estimated from the closure of the mitral valve to the opening of the aortic valve, the ejection time (ET) from the opening to the closure of the aortic valve, and the isovolumetric relaxation time (IRT) from the closure of the aortic valve to the opening of the mitral valve. The modified MPI was calculated as $(ICT + IRT)/ET$ ^(17, 18).

Uterine artery Doppler assessment

The probe was placed longitudinally in the lower lateral quadrant of the abdomen. Color flow mapping is useful for identifying the uterine artery as it crosses the external iliac artery. The pulsed-wave Doppler sampling gate should be narrow (~ 2 mm). The insonation angle should be < 30°, and the peak systolic velocity should be > 60 cm/s. The PI was measured when at least three identical waveforms were obtained^(19, 20).

Middle cerebral artery Doppler assessment

An axial brain section, including the thalami and the sphenoid bone wings, should be obtained and magnified. The circle of Willis and the proximal MCA was identified using color flow mapping. The pulsed-wave Doppler gate should then be placed at the proximal third of the MCA, and the angle of insonation should be kept as close as possible to 0°. The PI was measured when at least three identical

waveforms were obtained^(20, 21).

Umbilical artery Doppler assessment

The umbilical cord was visualized in a longitudinal section in a free loop and magnified to the maximum possible extent without fetal movements or breathing. The angle of insonation was less than 60°. The PI was measured when at least three identical waveforms were obtained^(20,22).

Statistical analysis

SPSS (IBM Corp. IBM SPSS Statistics for Windows, version 22.0, Armonk, NY: IBM Corp) was used for statistical analysis. The Kolmogorov-Smirnov test was used to check the normality of the variable distribution. Data are presented with mean ± standard deviation (SD) and median (interquartile range, IQR). Pearson's chi-square or Fisher's exact test was used to compare categorical data. An independent t-test was used in a comparison of parametric variables, and a Mann-Whitney U test was used for comparing continuous data with non-normal distributions. Multiple regression was used to model the effect of different baseline characteristics on each response

variable. Multiple logistic regression was established to determine the association between binary outcomes and chronic hypertension group adjusted with maternal age, gestational diabetes (GDM) and body mass index (BMI). A p-value of < 0.05 was considered statistically significant.

Results

A total of 140 pregnant women were enrolled in this study. Forty women had chronic hypertension, and 100 women had normal blood pressure. All the fetuses were evaluated for growth, amniotic fluid volume, fetal cardiac function, and Doppler measurement between 28-32 weeks of gestational age and followed up by adverse maternal and neonatal outcomes.

The two groups' baseline characteristics were compared (Table 1). The chronic hypertension group were older (35.73 ± 4.27 vs 32.81 ± 5.50 , $p = 0.003$) and had a higher BMI (32.42 ± 6.15 kg/m² vs 21.95 ± 3.69 kg/m², $p < 0.001$). Gestational diabetes mellitus was also more prevalent in the chronic hypertension group compared to the normal group (45% vs 0%, $p < 0.001$) (Table1).

Table 1. Baseline characteristics.

	Chronic hypertension (n = 40)	Normal blood pressure (n = 100)	p value
Maternal age (years)	35.73 ± 4.27	32.81 ± 5.50	0.003 [†]
Gravida (%)			0.433 [*]
- Primigravida	12 (30.0%)	37 (37%)	
- Multigravida	28 (70.0%)	63 (63%)	
Other underlying disease (%)			
- Heart disease	0 (0%)	2 (2%)	1.000 [*]
- Chronic Hepatitis B infection	0 (0%)	1 (1%)	1.000 [*]
- GDM	18 (45.0%)	0 (0%)	< 0.001 [*]
- No underlying disease	22 (55.0%)	97 (97%)	< 0.001 [*]
BMI (kg/m ²)	32.42 ± 6.15	21.95 ± 3.69	< 0.001 [†]

BMI: body mass index, GDM: gestational diabetes mellitus

Data are presented as the mean ± standard deviation or n (%).

* Fisher's exact test or Pearson's chi-square test. † Independent t-test.

Sonographic data, including the mean of gestational age at the time of ultrasound (29.70 ± 1.29 vs 30.05 ± 0.97 , $p = 0.082$, adjusted $p = 0.108$), median estimated fetal weight (1389.50 vs 1521.00, $p = 0.039$, adjusted $p = 0.006$), median deep vertical pocket (5.50 vs 4.90, $p = 0.109$, adjusted $p = 0.698$) as well as the median of the Doppler studies including

left uterine artery PI (0.78 vs 0.76, $p = 0.085$, adjusted $p = 0.902$), right uterine artery PI (0.83 vs 0.75, $p = 0.159$, adjusted $p = 0.442$), umbilical artery PI (0.94 vs 0.93, $p = 0.982$, adjusted $p = 0.060$), middle cerebral artery PI (1.86 vs 1.80, $p = 0.311$, adjusted $p = 0.05$), were not different between chronic hypertension group and control group (Table 2).

Table 2. Sonographic data and comparison of UtAPI, UAPI, MCA PI.

	Chronic hypertension (n = 40)	Normal blood pressure (n = 100)	p value	Adjusted p value ^ψ
GA at USG (weeks)	29.70 ± 1.29	30.05 ± 0.97	0.082 [†]	0.108
EFW (grams)	1389.50 (1232.00 - 1623.00)	1521.00 (1368.75 - 1637.75)	0.039 [‡]	0.006
DVP (cm)	5.50 (4.45 - 6.28)	4.90 (4.35 - 5.85)	0.109 [‡]	0.698
Left Uterine artery PI	0.78 (0.61 - 1.31)	0.76 (0.59 - 0.92)	0.085 [‡]	0.902
Right Uterine artery PI	0.83 (0.63 - 1.31)	0.75 (0.63 - 1.30)	0.159 [‡]	0.442
Umbilical artery PI	0.94 (0.86 - 1.03)	0.93 (0.82 - 0.93)	0.982 [‡]	0.060
Middle cerebral artery PI	1.86 (1.62 - 2.37)	1.80 (1.63 - 2.07)	0.311 [‡]	0.050

USG: ultrasound, EFW: estimate fetal weight, DVP: deep vertical pocket, PI: pulsatility index

Data are presented as the mean ± standard deviation or median (interquartile range) or n (%).

[†] Independent t-test. [‡] Mann Whitney U test, ^ψ Adjusted p value for maternal age, GDM, BMI, using multivariate linear regression.

No significant differences were found in the median MPI (0.49 vs 0.47, $p = 0.691$, adjusted $p = 0.299$), isovolumetric relaxation time (44.00 vs 47.00, $p = 0.785$, adjusted $p = 0.232$), ejection time (173.00

vs 178.00, $p = 0.133$, adjusted $p = 0.179$) but isovolumetric contraction time was decreased in chronic hypertension group (36.00 vs 36.00, $p = 0.380$, adjusted $p = 0.019$) (Table 3).

Table 3. Modified myocardial performance index.

	Chronic hypertension (n = 40)	Normal blood pressure (n = 100)	p value	Adjusted p value ^ψ
ICT, ms	36.00 (29.25 - 40.00)	36.00 (27.00 - 49.00)	0.380 [‡]	0.019
IRT, ms	44.00 (40.00 - 53.00)	47.00 (40.00 - 58.00)	0.785 [‡]	0.232
ET, ms	173.00 (157.00 - 182.00)	178.00 (169.00 - 187.00)	0.133 [‡]	0.179
Modified MPI	0.49 (0.40 - 0.55)	0.47 (0.40 - 0.57)	0.691 [‡]	0.299

ICT: isovolumetric contraction time, IRT: isovolumetric relaxation time, ET: ejection time, modified MPI: modified myocardial performance index. Data are presented as the median (interquartile range)

[‡] Mann Whitney U test. ^ψ Adjusted p value for maternal age, GDM, BMI, using multivariate linear regression

Thirty-seven pregnant women delivered and collected data for maternal and neonatal outcomes in the chronic hypertension group. Results showed that pregnant women with chronic hypertension had more maternal adverse outcomes, such as the mean gestational age at delivery was lower in the chronic hypertension group (36.8 ± 2.19 vs 38.2 ± 1.31 , $p <$

0.001 , adjusted $p < 0.001$). The other maternal adverse outcomes were not different (Table 4).

The chronic hypertension group showed more neonatal adverse outcomes, including length of hospital stays (4.0 vs 3.0 , $p < 0.001$, adjusted $p = 0.001$). Although, other neonatal adverse outcomes were not distinct (Table 5).

Table 4. Maternal adverse outcomes.

	Chronic hypertension (n = 37)	Normal blood pressure (n = 100)	p value	Adjusted p value
GA at birth (weeks)	36.8 ± 2.19	38.2 ± 1.31	$< 0.001^\dagger$	$< 0.001^\psi$
Preterm delivery indicated from preeclampsia with severe features (%)	3 (8.1%)	0 (0%)	0.019*	0.996 [‡]
Preeclampsia with severe feature (%)	7 (18.9%)	1 (1.0%)	$< 0.001^*$	0.382 [‡]
Preterm delivery (%)	5 (13.5%)	8 (8.0%)	0.337*	0.536 [‡]
Placenta previa (%)	0 (0%)	1 (1.0%)	1.000*	1.000 [‡]

Data are presented as the mean \pm standard deviation or n (%).

* Fisher's exact test or Pearson's chi-square test. [†] Independent t-test.

^ψ Adjusted p value for maternal age, GDM, BMI, using multivariate linear regression.

[‡] Adjusted p value for maternal age, GDM, BMI, using multiple logistic regression.

Table 5. Maternal adverse outcomes.

	Chronic hypertension (n = 37)	Normal blood pressure (n = 100)	p value	Adjusted p value
TTNB (%)	1 (2.7)	1 (1.0)	0.469*	0.571 [‡]
RDS (%)	3 (8.1)	4 (4.0)	0.387*	0.309 [‡]
EOS (%)	5 (13.5)	4 (4.0)	0.060*	0.638 [‡]
IUGR (%)	0 (0)	0 (0)	1.000*	1.000 [‡]
Jaundice (%)	7 (18.9)	5 (5.0)	0.017*	0.148 [‡]
Hypoglycemia (%)	4 (10.8)	1 (1.0)	0.019*	0.444 [‡]
No adverse outcome (%)	17 (45.9)	85 (85.0)	$< 0.001^*$	0.042 [‡]
NICU admission (%)	1 (2.7)	3 (3.0)	1.000*	0.633 [‡]
Need for ventilator (%)	6 (16.2)	4 (4.0)	0.024*	0.225 [‡]
Length of hospital stay (days) median (IQR)	4.00 (3.00 - 7.00)	3.00 (3.00 - 3.50)	$< 0.001^\ddagger$	0.001 [‡]

TTNB: transient tachypnea of newborn, RDS: respiratory distress syndrome, EOS: early onset neonatal sepsis, IUGR: intrauterine growth restriction

Data are presented as the median (interquartile range) or n (%). * Fisher's exact test or Pearson's chi-square test. [‡] Mann Whitney U test.

^ψ Adjusted p value for maternal age, GDM, BMI, using multivariate linear regression.

[‡] Adjusted p value for maternal age, GDM, BMI, using multiple logistic regression

Discussion

Chronic hypertension is a risk factor for many adverse maternal and neonatal outcomes. Pregnant women with this condition should be managed with appropriate maternal and fetal surveillance. A nonstress test and ultrasound should be performed to assess fetal weight, amniotic fluid, Doppler waveform of vessels and to calculate the MPI.

Pregnancy with chronic hypertension can cause fetal growth restriction that decreases and impairs fetal cardiac function, such as MPI, from cardiac growth interference caused by nutrient supply and oxygen reduction, rising placental impedance, and chronic fetal cardiac afterload⁽²³⁾. We conducted a study comparing fetal cardiac function between pregnant women with chronic hypertension and women with normal blood pressure. Our study found differences in baseline characteristics between the two groups. The prevalence of GDM was higher in the chronic hypertension group, related to insulin resistance and endothelial dysfunction. Maternal age and BMI were also higher in the chronic hypertension group. Both groups also differed in data collected by sonograph, including gestational age at the time of ultrasound, estimated fetal weight, deep vertical pocket, and Doppler studies.

Our results corresponded with a study from Api et al⁽²⁴⁾ that fetal global myocardial functioning assessed by modified MPI did not change in mild or severe preeclampsia between the two groups, which might have resulted from fetuses in the study not having complications that impacted fetal cardiac function such as placental insufficiency or fetal growth restriction. In contrast, Sevket Balli et al⁽¹⁴⁾ and Bhorat et al⁽¹⁵⁾ reported higher fetal MPI values in pregnant women with preeclampsia.

Our Doppler studies of the UA, MCA, and uterine artery did not reveal any differences between the chronic hypertension group and control group due to the absence of placental insufficiency or fetal growth restriction in both groups, which do not affect placental impedance and fetal cardiac afterload. On the contrary, Sevket Balli et al⁽¹⁴⁾ found a decreased MCA PI in the

preeclampsia group compared to the healthy group. Api et al⁽²⁴⁾ reported that uterine artery PI increased, and MCA PI decreased in severe preeclampsia mothers due to redistribution of fetal cardiac output secondary to increased placental vascular resistance. Our study showed that compared to women with normal blood pressure, pregnant women with chronic hypertension experienced more maternal adverse outcomes. The mean gestational age at the delivery time was lower in the chronic hypertension group (36.8 ± 2.19 vs 38.2 ± 1.31 , $p < 0.001$, adjusted $p < 0.001$). The chronic hypertension group was also associated with more neonatal adverse outcomes, including length of hospital stay; however, other neonatal adverse outcomes were not different. Six newborns needed ventilators in the chronic hypertension group. Three newborns were diagnosed with respiratory distress syndrome, and others were diagnosed with early onset of neonatal sepsis, transient tachypnea of newborns, and hypoglycemia. Most were put in an oxygen box at 5 liters per minute (LPM) for 1-2 days. Only one preterm newborn with respiratory distress syndrome was on continuous positive airway pressure (CPAP) for two days. There were two newborns with respiratory distress syndrome in the normal blood pressure group, one newborn with transient tachypnea of the newborn, and one newborn with early onset of neonatal sepsis. All of them were put in an oxygen box at 5 LPM for 1-2 days. However, the two groups had no significant correlations in the MPI with neonatal adverse outcomes.

In addition to the lack of significant difference in the MPI between chronic hypertension and normal blood pressure groups (0.49 vs 0.47 , $p = 0.691$, adjusted $p = 0.299$), we also found no difference in the MPI between chronic hypertension with neonatal adverse outcomes and chronic hypertension without neonatal adverse outcomes (0.47 vs 0.49 , $p = 0.784$, adjusted $p = 0.710$).

This study's strength was that no studies had used MPI to evaluate fetal cardiac status in pregnant women with chronic hypertension, and few have used MPI to predict perinatal outcomes. Since our study

only enrolled 40 women with chronic hypertension and some variables of interest had low incidence, our results need to be confirmed by a more extensive study with a larger sample.

Conclusion

There was no difference in the modified MPI between pregnant women with normal blood pressure and women with chronic hypertension. The Doppler studies of the UA, MCA, and uterine artery were also not different between chronic hypertension and control groups. Based on our results, the modified MPI may not be predictive of perinatal outcomes.

Acknowledgments

The authors thank the Division of Maternal-Fetal Medicine staff and nurses, Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University, for their helpful suggestions and assistance. We also thank Dr. Michael Ullman, English editor, for reviewing of the manuscript.

Potential conflicts of interest

The authors declare no conflicts of interest.

References

1. Martin JA, Hamilton BE, Ventura SJ, Osterman MJ, Kirmeyer S, Mathews TJ, et al. Births: final data for 2009. *Natl Vital Stat Rep* 2011; 60:1-70.
2. Zetterstrom K, Lindeberg SN, Haglund B, Hanson U. Maternal complications in women with chronic hypertension: a population-based cohort study. *Acta Obstet Gynecol Scand* 2005; 84:419-24.
3. Gilbert WM, Young AL, Danielsen B. Pregnancy outcomes in women with chronic hypertension: a population-based study. *J Reprod Med* 2007; 52:1046-51.
4. Leon MG, Moussa HN, Longo M, Pedroza C, Haidar ZA, Mendez-Figueroa H, et al. Rate of gestational diabetes mellitus and pregnancy outcomes in patients with chronic hypertension. *Am J Perinatol* 2016; 33:745-50.
5. Robertson WB, Brosens I, Dixon HG. The pathological response of the vessels of the placental bed to hypertensive pregnancy. *J Pathol Bacteriol* 1967; 93:581-92.
6. Bateman BT, Bansil P, Hernandez-Diaz S, Mhyre JM, Callaghan WM, Kuklina EV. Prevalence, trends, and outcomes of chronic hypertension: a nationwide sample of delivery admissions. *Am J Obstet Gynecol* 2012;206:e.1-8.
7. Vanek M, Sheiner E, Levy A, Mazor M. Chronic hypertension and the risk for adverse pregnancy outcome after superimposed preeclampsia. *Int J Gynaecol Obstet* 2004;86:7-11.
8. Panaitescu AM, Syngelaki A, Prodan N, Akolekar R, Nicolaides KH. Chronic hypertension and adverse pregnancy outcome: a cohort study. *Ultrasound Obstet Gynecol* 2017;50:228-35.
9. Bramham K, Parnell B, Nelson-Piercy C, Seed PT, Poston L, Chappell LC. Chronic hypertension and pregnancy outcomes: systematic review and meta-analysis. *BMJ* 2014;348:g2301.
10. Tervilä L, Goecke C, Timonen S. Estimation of gestosis of pregnancy (EPH-gestosis). *Acta Obstet Gynecol Scand* 1973;52:235-43.
11. Hernandez-Andrade E, Benavides-Serralde JA, Cruz-Martinez R, Welsh A, Mancilla-Ramirez J. Evaluation of conventional doppler fetal cardiac function parameters: E/A ratios, outflow tracts, and myocardial performance index. *Fetal Diagn Ther* 2012;32:22-9.
12. Zhang L, Han J, Zhang N, Li Z, Wang J, Xuan Y, et al. Assessment of fetal modified myocardial performance index in early-onset and late-onset fetal growth restriction. *Echocardiography* 2019;36:1159-64.
13. Alici Davutoglu E, Ozel A, Oztunc F, Madazli R. Modified myocardial performance index and its prognostic significance for adverse perinatal outcome in early and late onset fetal growth restriction. *J Matern Fetal Neonatal Med* 2020;33:277-82.
14. Balli S, Kibar AE, Ece I, Oflaz MB, Yilmaz O. Assessment of fetal cardiac function in mild preeclampsia. *Pediatr Cardiol* 2013;34:1674-9.
15. Bhorat IE, Bagratee JS, Reddy T. Assessment of fetal myocardial performance in severe early onset preeclampsia (EO-PET) with and without intrauterine growth restriction across deteriorating stages of placental vascular resistance and links to adverse outcomes. *Eur J Obstet Gynecol Reprod Biol* 2017; 210:325-33.
16. American College of Obstetricians and Gynecologists' Committee on Practice Bulletins-Obstetrics. ACOG Practice Bulletin No. 203: Chronic Hypertension in Pregnancy. *Obstet Gynecol* 2019;133: e26-e50.
17. Hernandez-Andrade E, López-Tenorio J, Figueroa-Diesel H, Sanin-Blair J, Carreras E, Cabero L, et al. A modified myocardial performance (Tei) index based

on the use of valve clicks improves reproducibility of fetal left cardiac function assessment. *Ultrasound Obstet Gynecol* 2005; 26:227-32.

18. Alfred Z. Abuhamad RC. *A practical guide to fetal echocardiography normal and abnormal hearts*. 3rd ed. Philadelphia: Lippincott Williams & Wilkins;2016.
19. MacDonald TM, Hui L, Robinson AJ, Dane KM, Middleton AL, Tong S, et al. Cerebral-placental-uterine ratio as novel predictor of late fetal growth restriction: prospective cohort study. *Ultrasound Obstet Gynecol* 2019;54:367-75.
20. G M. Doppler ultrasonography in obstetrics: from the diagnosis of fetal anemia to the treatment of intrauterine growth-restricted fetuses. *Am J Obstet Gynecol* 2009;200:613.e1-e9.
21. Moise KJ Jr. The usefulness of middle cerebral artery Doppler assessment in the treatment of the fetus at risk for anemia. *Am J Obstet Gynecol* 2008;198:161.e1-4.
22. Dias T, Abeykoon S, Kumarasiri S, Mendis P, Gunawardena C, Pragasan G, et al. Fetal Doppler reference values in women with a normal body mass index. *Ceylon Medical J* 2019; 64:59-65.
23. Crispi F, Miranda J, Gratacós E. Long-term cardiovascular consequences of fetal growth restriction: biology, clinical implications, and opportunities for prevention of adult disease. *Am J Obstet Gynecol* 2018;218:S869-S879.
24. Api O, Balsin Emeksiz M, Api M, Ugurel V, Unal O. Modified myocardial performance index for evaluation of fetal cardiac function in pre-eclampsia. *Ultrasound Obstet Gynecol* 2009;33:51-7.