

Excursion Index of the Septum Primum in Thai Fetuses of Gestational Diabetic Mothers at 32 to 35 Weeks' Gestation

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Objective: To compare excursion index of the septum primum (EISP) among Thai fetuses of gestational diabetic mothers (FGDMs) with and without septal hypertrophy (SH) and those of nondiabetic mothers from 32 to 35 weeks' gestation.

Material and Method: Fetuses of Thai pregnant women were recruited for prenatal 2-dimensional echocardiographic measurements of the EISP (the ratio between the linear displacement of the flap valve of septum primum and the left atrial diameter) at 32 to 35 weeks' gestation. All had confirmed gestational age and normal structural scanning. The EISP was compared among gestational age - matched 15 FGDMs with SH, 18 FGDMs with normal septal thickness, and 20 fetuses of nondiabetic mothers. The data were presented as mean and standard deviation (SD). Analysis of variance (ANOVA) was used to compare the EISP of the three groups.

Results: Fifty-three measurements were obtained. Comparison among the three groups showed that the mean and SD of the EISP were 0.27 ± 0.04 , 0.50 ± 0.04 and 0.51 ± 0.05 in FGDMs with SH, normal septal thickness and those of nondiabetic mothers, respectively. The analysis demonstrated that the EISP was significantly less than in FGDMs with SH when compared to the FGDMs with normal septal thickness and those of nondiabetic mothers ($p < 0.01$). There was no significant difference in the EISP of the FGDMs with normal septal thickness and those of nondiabetic mothers ($p = 0.16$).

Conclusion: Mobility of the septum primum in FGDMs with septal hypertrophy is reduced. This may indicate a higher preload compared to FGDMs with normal septal thickness and those of nondiabetic mothers.

Keywords: Fetal echocardiography, Left ventricular diastolic function, Gestational diabetes, Septum primum mobility, Excursion index, Septal hypertrophy

J Med Assoc Thai 2007; 90 (9): 1727-32

Full text. e-Journal: <http://www.medassocthai.org/journal>

Children of diabetic mothers present a well-known risk for the development of asymmetrical septal hypertrophy with variable clinical presentation⁽¹⁾. Zielinsky⁽²⁾ suggested that fetal echocardiographic study of fetal cardiac function should be performed in diabetic mothers.

Pathophysiological mechanisms involved in the development of signs and symptoms of cardiac failure in neonates with hypertrophic cardiomyopathy

are mainly related to diastolic dysfunction as a result of changes in ventricular filling, the compliance and relaxation process⁽³⁾. Several authors⁽⁴⁻⁶⁾ have reported that the interventricular septal thickness was greater in the fetuses of insulin-requiring diabetic mothers than those of fetuses in nondiabetic mothers between 32 and 36 weeks' gestation. Recently, Firpo et al^(3,7) demonstrated that the mobility of the septum primum flap valve in the fetus is an appropriate parameter for diastolic function evaluation that is comparable to Doppler analysis of mitral and tricuspid inflow waves.

The purpose of the present study was to compare the septum primum mobility, which was presented

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as the excursion index of the septum primum (EISP), among the FGDMs with and without septal hypertrophy and those of nondiabetic mothers from 32 to 35 weeks' gestation. The hypothesis was the linear displacement of the septum primum flap valve in FGDMs with septal hypertrophy is less than those with normal septal thickness and fetuses of nondiabetic mothers.

Material and Method

The present study was a cross-sectional study as a part of the Gestational Diabetes study project. After obtaining approval from the Faculty Ethical Committee, the authors recruited Thai pregnant women attending the antenatal clinic at the Department of Obstetrics and Gynecology, Faculty of Medicine, King Chulalongkorn Memorial Hospital, Chulalongkorn University, Bangkok, Thailand from August 2004 to June 2006. All of the participants had a reliable menstrual history, singletons, ultrasonographic confirmed gestational age before 20 weeks' gestation and normal structural scanning. Written informed consent was obtained from each mother participating in the present study.

All pregnant women had their blood glucose tested at 24 to 28 weeks' gestation. Diabetic screening method was 50-gram glucose challenge test. The diagnosis of GDM by the 100-gram oral glucose tolerance test was made when two or more venous plasma glucose concentrations met or exceeded the following plasma glucose levels: fasting, 95 mg/dL; 1 hour (h), 180 mg/dL; 2 h, 155 mg/dL; and 3 h, 140 mg/dL as recommended by the American Diabetic Association (ADA)⁽⁸⁾ or the 75-gram oral glucose tolerance test 2 hour plasma glucose is 140 mg/dL or higher⁽⁹⁾ according to World Health Organization diagnostic criteria. Normal pregnancy was defined as an uncomplicated pregnancy with negative diabetic screening at 24 to 28 weeks' gestation. The parameters studied were gestational age and EISP. The study was scheduled at 32⁺⁰-35⁺⁶ weeks' gestation.

The ultrasound machine used in the present study was Aloka Prosound 5000 (Aloka Co., Ltd., Tokyo, Japan). The system was interfaced with either 3 or 5 MHz abdominal transducers. Each fetus was examined only once by PL blinded to gestational age, patient's diabetic status and identification number. All measurements were recorded on VHS for later playback and analysis. The quality of all pictures and the measurements were reviewed by UB.

The linear displacement of the septum primum measurement by two-dimensional echocardiography

During the examination, the mother reclined

supinely, with some rotation either to the right or left side to facilitate the evaluation as described elsewhere^(10,11). The measurement was made during fetal apnea. The interventricular septal thickness was measured in millimeters (mm), using M-mode echocardiography during diastole and systole as previously reported⁽¹²⁾. The septal thickness during diastole (IVSD) and systole (IVSS) obtained from each fetus were compared to a nomogram of the authors' institute⁽¹²⁾. The septal hypertrophy was diagnosed when the value of IVSD > 4.50 mm and IVSS > 6.20 mm⁽¹²⁾. The fetuses were then classified into three groups: Group 1, fetuses of gestational diabetic mothers (FGDMs) with septal hypertrophy; Group 2, FGDMs with normal septal thickness; and Group 3, fetuses of nondiabetic mothers (normal control fetuses).

To assess the mobility of the septum primum, the authors measured its "excursion index", which is the ratio between the maximal linear displacement of the atrial flap valve in diastole and the left atrial diameter in 4-chamber view^(11,13) (Fig. 1A and 1B).

Statistical analysis

Statistical analysis was carried out using SPSS software package version 11.0 (SPSS Inc., Chicago, IL, USA). Obstetric characteristics are presented as mean and standard deviation (SD). The analysis of variance (ANOVA) was used to compare variables in the three groups. A p-value < 0.05 was considered statistically significant. The intraobserver variability was calculated.

Sample size calculation⁽¹⁴⁾ was based on the data from the pilot study. There are three independent groups of fetuses in the present study. The continuous variable was EISP. The authors found that the standard deviation of EISP was approximately 0.08 from each measurement. The sample size of at least 15 subjects per group was required to obtain the power of the test over 80%.

Results

There was no significant difference in the obstetric characteristics and fetal heart rate among the three groups as shown in Table 1 and Table 2. In group 1, the mean and standard deviation of the IVSD and IVSS were 6.80 ± 0.83 mm and 8.40 ± 0.41 mm, respectively. There was no significant difference in IVSD and IVSS of the subjects in group 2 and group 3 as shown in Table 2. The mean and standard deviation of EISP in group 1 was significantly decreased when compared to group 2 and group 3 (p < 0.01). There was no significant difference in the EISP of the FGDMs

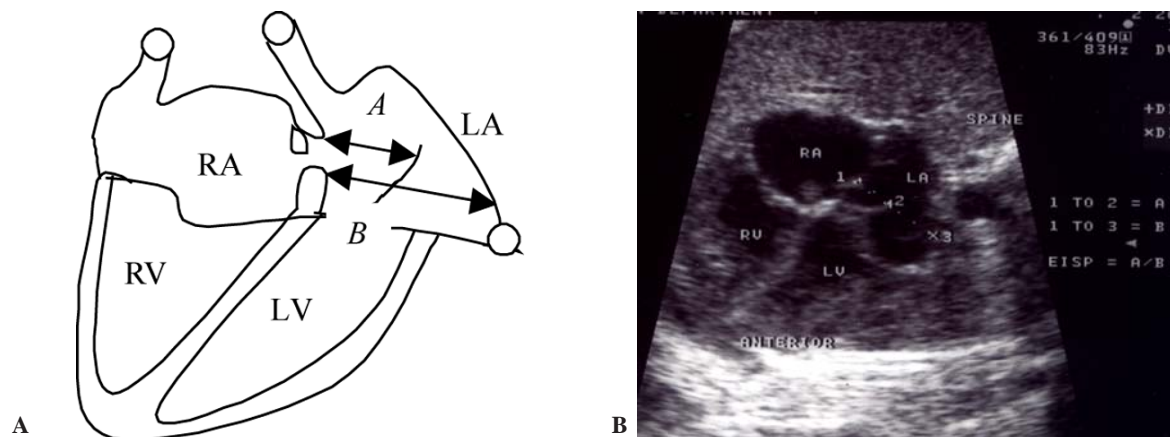


Fig. 1 The excursion index of the septum primum
 (A) Diagram showing how the excursion index of the septum primum is obtained from the ratio A/B
 The flap valve of the septum primum projecting into the left atrium during atrial diastole:
 A is the maximal diastolic excursion of the flap valve in a four - chamber view
 B is the maximal left atrial diameter
 (B) The measurement of excursion index of the septum primum by 2-dimensional echocardiography:
 A is the distance between point 1 to point 2
 B is the distance between point 1 to point 3

Table 1. Obstetric characteristics

Parameters	Group 1 n = 15 (Mean ± SD)	Group 2 n = 18 (Mean ± SD)	Group 3 n = 20 (Mean ± SD)
Age (years)	33.20 ± 8.90	33.20 ± 8.96	33.27 ± 7.27
GA (weeks)	33.60 ± 1.24	33.60 ± 1.14	33.33 ± 1.05
Gravidity	1.20 ± 0.30	1.22 ± 0.38	1.20 ± 0.77
Fetal heart rate (bpm)	144.78 ± 7.76	140.37 ± 7.29	142.37 ± 7.24

Group 1: FGDMs with septal hypertrophy, Group 2: FGDMs with normal septal thickness, Group 3: Fetuses of nondiabetic mothers, SD: standard deviation; GA: gestational age; bpm: beat per minute

Table 2. Echocardiographic parameters

Parameters	Group 1 n = 15 (Mean ± SD)	Group 2 n = 18 (Mean ± SD)	Group 3 n = 20 (Mean ± SD)
IVSD (mm)	6.80 ± 0.83	3.07 ± 0.50	2.84±0.35
IVSS (mm)	8.40 ± 0.41	4.70 ± 0.81	4.40±0.68
EISP	0.27 ± 0.04*,**	0.50 ± 0.04*,+	0.51 ± 0.05**,+

Group 1: FGDMs with septal hypertrophy (IVSD ≥ 4.50 mm and IVSS ≥ 6.20 mm)

Group 2: FGDMs with normal septal thickness

Group 3: Fetuses of nondiabetic mothers

SD: standard deviation; IVSD: interventricular septal thickness during diastole; IVSS: interventricular septal thickness during systole; mm: millimeters; EISP: excursion index of the septum primum

* p < 0.01 (group1 vs 2)

** p < 0.01 (group1 vs 3)

+ p = 0.16 (group2 vs 3)

with normal septal thickness and those of nondiabetic mothers ($p = 0.16$). The intraobserver variability of the EISP measurements was 6.6%.

Discussion

Prenatal assessment of diastolic abnormalities may be important in prediction of the prognosis of fetuses of diabetic mothers. Subtle early clinical and radiological findings, such as tachypnea and mild pulmonary congestion may be due to diastolic alterations of the left ventricle in such babies⁽¹⁵⁾. Even though overt heart failure is not a common clinical outcome in neonates with myocardial hypertrophy secondary to maternal diabetes, the presence of diastolic dysfunction is somewhat common⁽¹⁵⁾. Recently EISP was shown to be well correlated with diastolic function^(3,16). A significant decrease EISP was observed with increasing gestational age among the normal fetuses⁽³⁾.

The present study design was gestational age matched control analysis evaluating the mobility of the flap valve of the septum primum. The authors chose to study during 32 to 35 weeks' gestation because it encompassed a period of a significant increase in septal thickness distinct from those who were proved to have normal septal thickness at birth⁽⁴⁻⁶⁾. Comparing to the normal fetuses and FGDMs with normal septal thickness; the mobility of the flap valve of the septum primum was significantly reduced in the fetuses of diabetic mothers with septal hypertrophy. This could be due to a decrease in compliance and an altered relaxation of the left ventricle. Increased filling pressure would trigger an elevation of the mean pressure in both atria, with a trend to equalizing pressures throughout the cardiac cycle and to reducing the flap excursion within the left atrium. Decreased distensibility of the ventricular myocardium would cause a less marked linear displacement of the septum primum flap valve. The results obtained in the present population confirmed the hypothesis that, in the third trimester, fetuses of diabetic mothers with septal hypertrophy have a less mobile septum primum flap valve inside the left atrium, compared to the fetuses of nondiabetic mothers and FGDMs with normal septal thickness.

The present report confirms that septum primum mobility behaves differently in situations in which the ventricular compliance is reduced, such as in myocardial hypertrophy secondary to maternal diabetes. The findings suggested that reduced EISP in association with septal hypertrophy which may be due to the increase in left atrial diastolic pressure as a result of the hypertrophic left ventricle interferes with

the normal mobility of the atrial flap valve, limiting its expansion. The advantage of using EISP over conventional atrioventricular flow velocity is that it is simpler and is probably more easily accessible since it requires only real-time 2-dimensional ultrasound without the need for a Doppler capacity. Besides, instead of a need for sophisticated Doppler interrogation by highly skilled sonographers, it requires only a simple real-time scanning, which is available throughout the country. Nevertheless, further cohort studies, which are designed to compare the usefulness between atrioventricular flow velocities and the excursion index of the septum primum, are desired so that appropriate parameter would be employed in this condition.

Acknowledgements

The authors wish to thank Professor Sompop Limpongsanurak, Chairman of the Department of Obstetrics and Gynecology, Associate Professor Dhiraphongs Charoenvidhya, Head of the Division of Maternal - Fetal Medicine, Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University for their permission to conduct and report the present study.

With the support of Ratchadapiseksompotch Fund, Faculty of Medicine, Chulalongkorn University, the present study was successfully done and delivered academic knowledge of an alternative parameter for prenatal evaluation of fetal diastolic function in diabetic pregnancies.

References

1. Oberhoffer R, Hogel J, Stoz F, Kohne E, Lang D. Cardiac and extracardiac complications in infants of diabetic mothers and their relation to parameters of carbohydrate metabolism. *Eur J Pediatr* 1997; 156: 262-5.
2. Zielinsky P. Role of prenatal echocardiography in the study of hypertrophic cardiomyopathy in the fetus. *Echocardiography* 1991; 8: 661-8.
3. Firpo C, Zielinsky P. Behavior of septum primum mobility in third-trimester fetuses with myocardial hypertrophy. *Ultrasound Obstet Gynecol* 2003; 21: 445-50.
4. Cooper MJ, Enderlein MA, Tarnoff H, Roge CL. Asymmetric septal hypertrophy in infants of diabetic mothers. Fetal echocardiography and the impact of maternal diabetic control. *Am J Dis Child* 1992; 146: 226-9.
5. Gandhi JA, Zhang XY, Maidman JE. Fetal cardiac hypertrophy and cardiac function in diabetic

- pregnancies. *Am J Obstet Gynecol* 1995; 173: 1132-6.
6. Jaeggi ET, Fouron JC, Proulx F. Fetal cardiac performance in uncomplicated and well-controlled maternal type I diabetes. *Ultrasound Obstet Gynecol* 2001; 17: 311-5.
 7. Zielinsky P, Nicoloso LH, Firpo C, Marcantonio S, Scheid M, Gus EI, et al. Alternative parameters for echocardiographic assessment of fetal diastolic function. *Braz J Med Biol Res* 2004; 37: 31-6.
 8. American Diabetic Association. Diagnosis and classification of diabetes mellitus *Diabetes Care* 2004; 27(Suppl 1): S5-10.
 9. Metzger BE, Coustan DR. Summary and recommendations of the Fourth International Workshop-Conference on Gestational Diabetes Mellitus. The Organizing Committee. *Diabetes Care* 1998; 21 (Suppl 2): B161-7.
 10. Veille JC, Sivakoff M, Hanson R, Fanaroff AA. Interventricular septal thickness in fetuses of diabetic mothers. *Obstet Gynecol* 1992; 79: 51-4.
 11. Firpo C, Zielinsky P. Mobility of the flap valve of the primary atrial septum in the developing human fetus. *Cardiol Young* 1998; 8: 67-70.
 12. Patchakapat L, Uerpairojkit B, Wacharaprechanont T, Manotaya S, Tanawattanacharoen S, Charoenvidhya D. Interventricular septal thickness of Thai fetuses: at 32 to 35 weeks' gestation. *J Med Assoc Thai* 2006; 89: 748-54.
 13. Patchakapat L, Uerpairojkit B, Wacharaprechanont T, Tanawattanacharoen S, Manotaya S, Charoenvidhya D. Excursion index of the septum primum as a parameter for diastolic function assessment of thai fetuses: at 32 to 35 weeks' gestation. *J Med Assoc Thai* 2007; 90: 1047-52.
 14. Dawson B, Trapp RG. Research questions about means in three or more groups. In: Dawson B, Trapp RG, editors. *Basic and clinical biostatistics*. 3rd ed. New York: McGraw-Hill; 2001: 161-82.
 15. Rizzo G, Pietropolli A, Capponi A, Cacciatore C, Arduini D, Romanini C. Analysis of factors influencing ventricular filling patterns in fetuses of type I diabetic mothers. *J Perinat Med* 1994; 22: 149-57.

**Excursion index ของ septum primum ของทารกไทยในครรภ์ที่มารดาเป็นโรคเบาหวานขณะตั้ง
ครรภ์ที่มีอายุครรภ์ 32 ถึง 35 สัปดาห์**

ลาวัลย์ ปัจฉักขภิติ, บุญชัย เชื้อไพโรจน์กิจ, ธิระ วัชรปรีชานนท์

วัตถุประสงค์: เปรียบเทียบ excursion index ของ septum primum ของทารกไทยในครรภ์ 3 กลุ่ม ที่มีอายุครรภ์ 32 ถึง 35 สัปดาห์ ได้แก่ทารกในครรภ์ของมารดาที่เป็นโรคเบาหวานขณะตั้งครรภ์ ซึ่งมีและไม่มีภาวะ septal hypertrophy และทารกในครรภ์ของมารดาที่ไม่เป็นโรคเบาหวาน

วัสดุและวิธีการ: ผู้ศึกษาได้ตรวจวัด excursion index ของ septum primum ของทารกในครรภ์ 3 กลุ่มจำนวน 53 ราย ด้วยเครื่องตรวจคลื่นเสียงความถี่สูงชนิด 2 มิติ ทุกรายได้รับการตรวจยืนยันอายุครรภ์ด้วยเครื่องตรวจคลื่นเสียงความถี่สูงก่อนอายุครรภ์ 20 สัปดาห์ และทารกในครรภ์ไม่มีความพิการแต่กำเนิด ข้อมูล excursion index ของ septum primum ที่ได้นำมาวิเคราะห์และเปรียบเทียบระหว่าง 3 กลุ่ม

ผลการศึกษา: ข้อมูลในการวัดทั้งหมด 53 ครั้ง ของทารกในครรภ์แยกเป็นรายที่มีภาวะ septal hypertrophy จำนวน 15 ราย ทารกในครรภ์ที่ไม่มีภาวะ septal hypertrophy จำนวน 18 ราย และทารกในครรภ์ที่มารดาไม่เป็นโรคเบาหวานจำนวน 20 ราย ได้นำมาวิเคราะห์ผลลัพธ์พบว่าค่าเฉลี่ยและค่าเบี่ยงเบนมาตรฐาน excursion index ของ septum primum ของทารกในครรภ์ทั้ง 3 กลุ่มเท่ากับ 0.27 ± 0.04 , 0.50 ± 0.04 และ 0.51 ± 0.05 ตามลำดับ ค่า excursion index ของ septum primum ของทารกในครรภ์ที่มีภาวะ septal hypertrophy น้อยกว่าของทารกในครรภ์ที่ไม่มีภาวะ septal hypertrophy และทารกในครรภ์ที่มารดาไม่เป็นโรคเบาหวานอย่างมีนัยสำคัญ ($p < 0.01$) ค่า excursion index ของ septum primum ของทารกในครรภ์ที่ไม่มีภาวะ septal hypertrophy และทารกในครรภ์ที่มารดาไม่เป็นโรคเบาหวานไม่มีความแตกต่างกันอย่างมีนัยสำคัญ ($p = 0.16$)

สรุป: การเคลื่อนไหวของ septum primum ของทารกในครรภ์ที่มีภาวะ septal hypertrophy มีค่าลดลง อาจแสดงว่าการหนาตัวของหัวใจห้องล่างซ้ายที่มากกว่าปกติ เป็นเพราะหัวใจรับภาระการทำงานมากกว่าที่พบในรายทารกที่ไม่มีภาวะ septal hypertrophy ในมารดาที่เป็นและที่ไม่เป็นโรคเบาหวานขณะตั้งครรภ์
