Excursion Index of the Septum Primum as a Parameter for Diastolic Function Assessment of Thai Fetuses: at 32 to 35 Weeks' Gestation

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Objective: *To establish the normal value of fetal diastolic function by the measurement of the excursion index of the septum primum (EISP) from 32 to 35 weeks' gestation in Thai fetuses.*
Material and Method: *Fetuses of normal Thai pregnant women were recruited for 2-dimensional echocardiographic measurements of the EISP (the ratio between the linear displacement of the flap valve and the left atrial diameter) from 32 to 35 weeks' gestation. All had a confirmed gestational age, normal structural scanning, and negative diabetic screening at 24 to 28 weeks' gestation. The 5th, 50th and 95th percentile of the EISP were demonstrated. The relationship between the EISP and gestational age were determined.*
Results: *Three hundred twenty-seven measurements were obtained. The normal values of the EISP according to gestational age were presented as 5th, 50th, and 95th percentile ranks. The correlation coefficients (r) between the EISP and gestational age were 0.03. The EISP were not statistically different with advancing gestation. The 5th, 50th, and 95th of the EISP were 0.32, 0.45, and 0.59 respectively. The intra-observer variability was 5.5%.*
Conclusion: *The normal values of fetal EISP in the Thai population from 32 to 35 weeks' gestation were established. This could serve as a baseline data in detection of the alteration of left ventricular diastolic function during fetal life.*

Keywords: *Septum primum mobility, Diastolic function, Normal value, Fetal echocardiography, Excursion index*

J Med Assoc Thai 2007; 90 (6): 1047-52
Full text. e-Journal: *http://www.medassocthai.org/journal*

Conventional echocardiographic assessments of fetal diastolic function are Doppler analysis of mitral and tricuspid inflow waves[1-4]. Recently Firpo and Zielinsky[5] found that the mobility of the septum primum (SP) in the fetuses of diabetic mothers with septal hypertrophy was reduced. In the third trimester, the more hypertrophic the interventricular septum, the worse would be the restriction to ventricular filling and the smaller the excursion of the septum primum flap valve within the left atrium[5]. Possibly the mobility of the SP flap valve in the fetus is a similar parameter which depends on the left atrial diastolic pressure[5]. They also demonstrated that there is a lack of correlation between the linear displacement of the SP and flow velocities through the mitral and tricuspid valves, suggesting that flow analysis of atrioventricular curves may be less suitable for an assessment of diastolic function in fetuses with septal hypertrophy at 32 to 39 weeks' gestation[5]. These findings highlight the need for alternative methods to assess diastolic function in these fetuses. Zielinsky and coworkers[6] proposed the prenatal assessment of left ventricular diastolic function by using analysis of the septum primum mobility, the excursion index of the septum primum (EISP).

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Infants of diabetic mothers have an increased risk of hypertrophic cardiomyopathy, characterized by a thick interventricular septum[7]. These changes were seen in association with impaired fetal diastolic function and it might be one of the leading causes of perinatal morbidity and mortality in pregnancies complicated by type 1 diabetes[7,8]. Cooper et al[9] had documented that for the population of infants found to have asymmetrical septal hypertrophy at birth, the thickened interventricular septum was usually demonstrated at 31 to 34 weeks' gestation. At this point of gestation, the fetuses showed a significant increase in the interventricular septal thickness compared to those who were proved to have normal septal thickness at birth[10]. Gandhi[11] reported that the interventricular septal thickness was greater in the fetuses of insulin-requiring diabetic mothers than the fetuses of nondiabetic mothers between 32 to 36 weeks' gestation. Prenatal detection of the asymmetrical septal hypertrophy in the third trimester might have clinical relevance as persistent pulmonary hypertension of the newborn and idiopathic respiratory distress syndrome have been reported in infants of diabetic mothers with this condition[8,12].

So far, there is only little information available of this alternative parameter used to evaluate fetal left ventricular diastolic function in Thailand. Thus, the present study focused on the evaluation of fetal diastolic function using EISP in the fetuses of non-diabetic mothers from 32 to 35 weeks' gestation when these measurements may be clinically useful. The aim was to determine the normal value of the EISP. These data could provide the threshold values, serving as a baseline data for prenatal evaluation of left ventricular diastolic function during fetal life.

Material and Method

The present study was conducted as a descriptive study. After obtaining approval from the Faculty Ethical Committee, the authors recruited normal Thai pregnant women attending the antenatal clinic at the Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand from November 2004 to June 2006. All had a reliable menstrual history, singletons, uncomplicated pregnancies, and ultrasonographic confirmed gestational age before 20 weeks' gestation, normal structural scanning, and negative diabetic screening at 24 to 28 weeks' gestation.

Negative diabetic screening was considered when 50-gram glucose challenge test was less than 130 mg/dL[13]. The only medications taken by these subjects were prenatal vitamins. All of the neonatal data were collected. Written informed consent was obtained from each mother participating in the present study.

Measurements

The parameters studied were the gestational age and the excursion index of the septum primum (EISP). The present study was scheduled at 32^{+0} to 35^{+6} weeks $^{+days}$ of gestation. The ultrasound machine used 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 and patient identification number. The measurements were recorded on VHS for later playback and analysis. The quality of all the pictures and the measurements were checked and reviewed by UB.

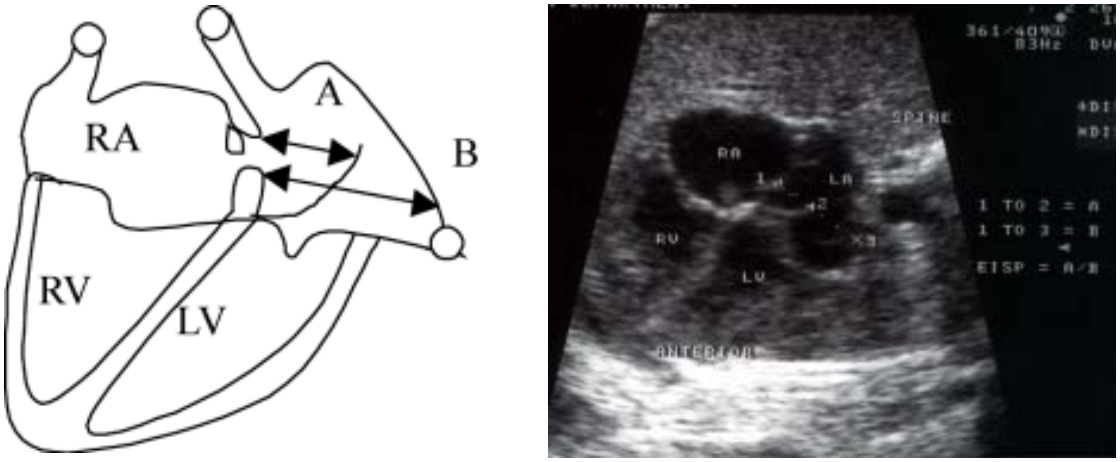
Measurement of the excursion index of the septum primum by two – dimensional echocardiographic evaluation

During the examination, the mother reclined supinely. The measurement was made during fetal apnea. The present study was usually performed in brief, normally lasting about or less than 15 minutes. Fetal heart rate was calculated electronically with M-mode tracing to reassure the normal cardiac rhythm[14]. The values of the interventricular septal thickness during systole and diastole (IVSS and IVSD) and cardiac circumference were obtained in the 4-chamber view[15].

To assess the diastolic 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 a 4 - chamber view[16] (Fig. 1).

The statistical analysis was carried out by using SPSS software package version 11.0 (SPSS Inc., Chicago, IL, USA). Obstetric characteristics are presented as mean $\pm$ standard deviation (SD). The EISP obtained from the fetuses were plotted against gestational age and the correlation coefficients were determined by using Pearson's correlation. The normal values of the EISP were presented as 5^{th}, 50^{th}, and 95^{th} percentile ranks. A p-value < 0.05 was considered statistically significant. The intra-observer variability, comparison of paired readings obtained on two separate occasions was calculated.

Sample size calculation was based on the data from the pilot study. The authors found that the standard deviation of the EISP was approximately 0.15 with an acceptable error of less than 0.05 from each



A B

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 4 - chamber view, and *B* is the maximal left atrialdiameter
(B) The measurement of excursion index of the septum primum by 2 - dimensional echocardiography. *A* is the distance between point 1 to point 2 and *B* is the distance between point 1 to point 3

measurement. The sample size of at least 40 subjects per gestational age was required to obtain the power of the test over 80%.

Results

During the period of the present study, 333 fetuses from Thai pregnant women who came from various parts of Thailand were enrolled. None of them had any evidence of structural heart diseases. The data could not be obtained from six fetuses due to sub-optimal fetal position leaving 327 subjects for analysis. The mean age of the women studied was 27.67 $\pm$ 5.23 years, mean gestational age was 33.31 $\pm$ 1.00 weeks and mean gravidity was 1.81 $\pm$ 0.93. The fetal parameters: the mean and standard deviation of heart rate, cardiac circumference, and ultrasonic estimated weight by Hadlock formula were 142.75 $\pm$ 9.63 beat per minute, 121.72 $\pm$ 7.00 mm, and 2023.70 $\pm$ 255.64 grams, respectively. The mean and standard deviation of the fetal IVSS and IVSD were 4.45 $\pm$ 0.99 mm and 3.03 $\pm$ 0.81 mm, respectively. The 5th, 50th, and 95th percentiles of EISP over gestational age are demonstrated in Table 1. The scatterplots of the EISP over the gestational age are presented in Fig 2.

The correlation coefficient (r) of the EISP over gestation age was 0.03. The EISP were not statistically different with advancing gestation from 32 to 35 weeks' gestation ($p > 0.05$). The 5th percentile of the EISP was 0.32 (range = 0.31 to 0.33). The intra-observer variability was 5.5%.

Table 1. The excursion index of the septum primum (EISP) based on gestational age (n = 327 cases)

GA (weeks)	N	EISP		
		5th percentile	50th percentile	95th percentile
32^{+0}-32^{+6}	78	0.330	0.456	0.582
33^{+0}-33^{+6}	116	0.306	0.453	0.600
34^{+0}-34^{+6}	90	0.311	0.442	0.575
35^{+0}-35^{+6}	43	0.307	0.450	0.593

GA: gestational age

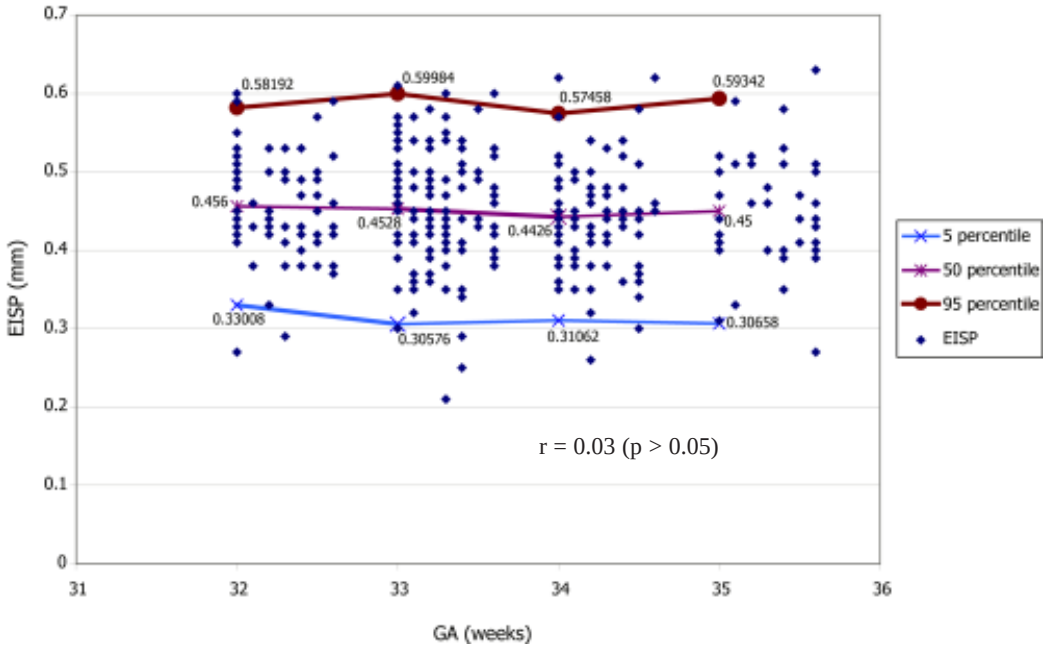


Fig. 2 Normal value of the excursion index of the septum primum (EISP) according to gestational age (GA). Lines represent the 5th, 50th and 95th percentiles (mm = millimeter)

Discussion

In order to evaluate the predictive value of fetal diastolic function using the EISP and fetal outcome in each population, the threshold value should be established. In the present study, 327 normal fetuses from non-diabetic mothers with reliable gestational age and completed evaluation of neonatal outcomes were enrolled. The authors confined the period of measurements from 32 to 35 weeks' gestation because it included a period of a significantly clinical relevance in prenatal detection of the asymmetrical septal hypertrophy among the fetuses of diabetic mothers[8,12].

Fetuses of diabetic mothers with hypertrophic cardiomyopathy may present as undiagnosed hydrops fetalis or acute fetal distress even in the absence of fetal hydrops. It suggests that this condition might be one of the causes of the increased stillbirth rate in pregnancies complicated by type 1 diabetes[17,18].

The authors believe that the establishment of standard measurements and normal value of fetal EISP invites a number of clinical applications, including the ability to diagnose the alteration of left ventricular diastolic function in the fetus at risk of asymmetrical septal hypertrophy. This is usually asymptomatic *in utero* and may only result in congestive heart failure in the immediate postnatal period[18]. Since early medical or surgical treatment might alter the prognosis, the gravid patient should be promptly transferred to a center where cardiovascular services are available.

The limitation of the present study was the lack of neonatal echocardiograms. Further study should include longitudinal neonatal follow-up and postnatal echocardiographic examination to relate changes in the diastolic function that occur as fetuses adapt to the postnatal periods.

Conclusion

The authors established a normal value of a fetal excursion index of the septum primum (EISP) from 32 to 35 weeks' gestation in a normal Thai population. The present study could be used as baseline data for the evaluation of left ventricular diastolic function in the fetus of diabetic mothers at risk for hypertrophic cardiomyopathy.

Acknowledgement

The authors wish to thank Professor Sompop Limpongsanurak, Chairman of the Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University for his permission to conduct and report this study.

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Excursion index ของ *septum primum* เพื่อประเมินการทำงานของหัวใจห้องล่างข้างซ้ายของเด็กไทยในครรภ์ที่มีอายุครรภ์ 32 ถึง 35 สัปดาห์

ลาวัลย์ ปัจจักขภัติ, บุญชัย เอื้อไพโรจน์กิจ, ธีระ วัชรปรีชานนท์, สมชาย ธนวัฒนาเจริญ, ศักนัน มะโนทัย, ธีระพงศ์ เจริญวิทย์

วัตถุประสงค์: เพื่อหาค่าปกติของ excursion index ของ septum primum ของเด็กไทยในครรภ์ที่มีอายุครรภ์ 32 ถึง 35 สัปดาห์

วัสดุและวิธีการ: ผู้ศึกษาได้ตรวจวัด excursion index ของ septum primum ของเด็กไทยในครรภ์ที่มีอายุครรภ์ 32 ถึง 35 สัปดาห์ ด้วยเครื่องตรวจคลื่นเสียงความถี่สูง ทุกรายได้รับการตรวจยืนยันอายุครรภ์ด้วยเครื่องตรวจคลื่นเสียงความถี่สูงก่อนอายุครรภ์ 20 สัปดาห์ ผลการตรวจกรองภาวะเบาหวานเมื่ออายุครรภ์ 24 ถึง 28 สัปดาห์อยู่ในเกณฑ์ปกติและเด็กในครรภ์ไม่มีความพิการแต่กำเนิด ข้อมูลที่ได้นำมาวิเคราะห์หาค่าปกติและความสัมพันธ์ระหว่าง excursion index ของ septum primum กับอายุครรภ์

ผลการศึกษา: ข้อมูลจากสตรีตั้งครรภ์จำนวน 327 ราย ได้นำมาวิเคราะห์ ผลลัพธ์พบว่าค่า excursion index ของ septum primum ของเด็กในครรภ์ที่ระดับ 5, 50 และ 95 เปอร์เซ็นไทล์ไม่มีความแตกต่างกันอย่างมีนัยสำคัญเมื่ออายุครรภ์เพิ่มขึ้น สัมประสิทธิ์ความสัมพันธ์ระหว่าง excursion index ของ septum primum กับอายุครรภ์ มีค่าเท่ากับ 0.03 excursion index ของ septum primum ที่ระดับ 5, 50 และ 95 เปอร์เซ็นไทล์เท่ากับ 0.32, 0.45 และ 0.59 ตามลำดับ

สรุป: การศึกษานี้ทำให้ทราบค่าปกติของ excursion index ของ septum primum ของเด็กไทยในครรภ์ที่มีอายุครรภ์ 32 ถึง 35 สัปดาห์ ข้อมูลนี้มีประโยชน์สำหรับนำมาใช้เป็นพื้นฐานในการวินิจฉัยการทำงานที่ผิดปกติของหัวใจห้องล่างข้างซ้ายของเด็กไทยในครรภ์ที่มารดาเป็นโรคเบาหวาน