Interventricular Septal Thickness of Thai Fetuses: at 32 to 35 Weeks' Gestation

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Objective: *To establish the normal value of fetal InterVentricular Septal Thickness (IVST) from 32 to 35 weeks' gestation in Thai fetuses.*

Material and Method: *Thai pregnant women with normal fetuses were recruited for prenatal 2-dimensional M-mode echocardiographic measurements of fetal IVST at 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 IVST was measured from the 4-chamber view during diastole and systole. The 5th, 50th and 95th percentile of the IVST during Diastole (IVSD) and the IVST during Systole (IVSS) were demonstrated. The relationship between the IVSD and IVSS and gestational age were determined.*

Results: *A total of 410 measurements were obtained. The normal values of the IVSD and IVSS according to gestational age were presented as 5th, 50th and 95th percentile ranks. The correlation coefficients (r) between the IVSD and IVSS and gestational age were 0.11 and 0.12, respectively. The IVSD and IVSS were not statistically different with advancing gestation. The 95th percentile of the IVSD was 4.51 millimeters (mm) (range = 4.26 to 4.74 mm) and IVSS was 6.23 mm (range = 5.96 to 6.68 mm). The intraobserver variability was 7.6%.*

Conclusion: *The normal values of fetal IVSD and IVSS in a Thai population from 32 to 35 weeks' gestation were established. This could be used as a baseline data in detecting the asymmetrical septal hypertrophy during fetal life.*

Keywords: *Interventricular septal thickness, Fetal echocardiography*

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Infants of diabetic mothers have an increased risk of cardiac defects and other heart diseases. In particular, cardiomyopathy, characterized by a thick interventricular septum, is often seen in offsprings of women with insulin-dependent diabetes[1,2]. Characteristically, the interventricular septa in these infants are disproportionately thickened for gestational age and are disproportionately large in relation to the left ventricular posterior wall dimension[3]. 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[2,3].

Septal enlargement was not a feature of large for gestational age infants whose mothers do not demonstrate carbohydrate intolerance[4].

Cooper et al[5] 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 in gestation, the fetuses showed a significant increase in the InterVentricular Septal Thickness(IVST) compared to those who were not proved to have asymmetrical septal hypertrophy at birth[6].

Gandhi et al[7] reported that the IVST was greater in the fetuses of insulin-requiring diabetic

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mothers than the normal fetuses of nondiabetic mothers between 32 to 36 weeks' gestation. According to gestational age group studies among the normal fetuses and the fetuses of diabetic mothers, it was shown that the IVST were significantly greater in the group of 32 to 36 weeks' gestation than those in the group of 20 to 24 and 28 to 31 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[2,8,9]. To date, however, only a little information is available on the knowledge about fetal cardiovascular dimensions to permit developmental methods of quantification that can help to describe these changes in Thailand. Thus, the present study focused on the evaluation of fetal IVST based on cross-sectional M-mode echocardiographic measurements among the fetuses of nondiabetic mothers from 32 to 35 weeks' gestation when these measurements may be clinically useful. The aim was to determine the normal value of the IVST during both diastole and systole. These data could provide the threshold values, serving as a means for prenatal evaluation in fetuses of diabetic pregnancies in detecting the asymmetrical septal hypertrophy during fetal life.

Material and Method

The present study was conducted as a descriptive study. After obtaining approval from the hospital ethical committee, the authors recruited normal Thai pregnant women who routinely attended the antenatal clinic at the Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand from November 2004 to November 2005. All had a reliable menstrual history, singletons, uncomplicated pregnancies, 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-g glucose challenge test was less than 130 mg/dL[10]. 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 fetal IVST. The present study was scheduled at 32^{+0} to 35^{+6} weeks $^{+days}$ of gestation.

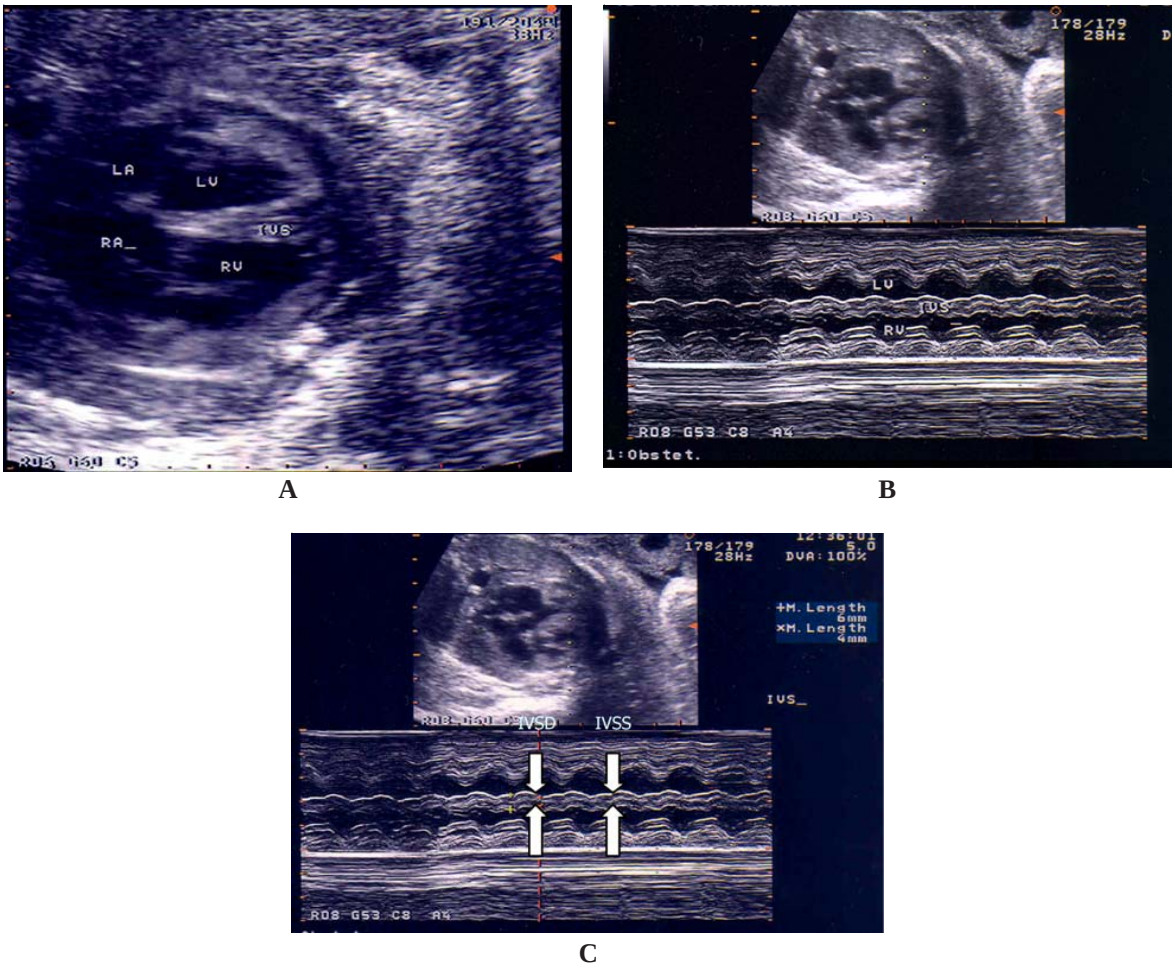
The ultrasound machine used in the present study was Aloka Prosound 5000 (Aloka Co., Ltd., Tokyo, Japan). The system was interfaced with either 3 or 5 MHz abdominal transducers. Each fetus was examined only once by PL blinded to gestational age and patient identification number. The measurements were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

Interventricular septal thickness measurement by M-mode 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[11]. The M-mode cursor was placed perpendicular to the interventricular septum just below the atrioventricular valves at the level of the 4-chamber view according to the standards recommended by the American Society of Echocardiography[12] as shown in Fig. 1A and 1B. A biventricular activity tracing was used to measure the IVST with electronic calipers. The IVST was measured during fetal apnea. It was taken on the distance between the outer edge of each margin and was measured in millimeter (mm)[13] as shown in Fig. 1C. The present study was performed in the usual manner, usually brief, normally lasting about or less than 15 minutes with careful attention given to gain a setting adjusted to produce the best possible image. The magnification of image was always attempted to minimize the error obtained from the caliper system. Fetal heart rate was calculated electronically with M-mode tracing to reassure the normal cardiac rhythm. At least 5 consecutive cardiac cycles, 3 good quality measurements were carried out at adjoining sites in order to calculate the arithmetic mean[4,14].

Statistical analysis

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. The IVSD and IVSS 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 IVSD and IVSS were presented as 5^{th}, 50^{th} and 95^{th} percentile ranks. P-value < 0.05 was considered statistically significant. The intraobserver variability, comparison of paired readings obtained by the same author on two separate occasions was calculated.



A B C

Fig. 1 The interventricular septal thickness: (A) 4-chamber view (B) Interventricular septum by M-mode echocardiography (C) The measurement of interventricular septal thickness during diastole and systole: the distance between the outer edge of each margin was measured in millimeter. (IVS: interventricular septum; IVSD: interventricular septal thickness during diastole; IVSS: interventricular septal thickness during systole; LA: left atrium; LV: left ventricle; RA: right atrium; RV: right ventricle)

Sample size calculation was based on the data from the pilot study. The authors found that the standard deviation of fetal IVST was approximately 1.50 mm with an acceptable error of less than 0.50 mm from each measurement. The sample size of at least 50 subjects per gestational age was required to obtain the power of the test over 80%.

Results

During the period of the present study, a total of 420 fetuses from Thai pregnant women who came from many parts of Thailand were enrolled. None of them had any evidence of structural heart diseases. The data could not be obtained from 10 fetuses due to massive maternal obesity and suboptimal fetal position leaving 410 subjects for analysis.

The mean age of the women studied was 27.69 $\pm$ 5.53 years, mean gestational age was 33.24 $\pm$ 0.99 weeks and mean gravidity was 1.83 $\pm$ 0.88. The 5th, 50th and 95th percentiles of the IVSD and IVSS over gestational age are given in Table 1. The scatterplots of the IVSD and IVSS over the gestational age are presented in Fig. 2 and Fig. 3, respectively.

The correlation coefficients (r) of the IVSD and IVSS over gestation age were 0.11 and 0.12, respectively. The IVSD and IVSS were not statistically different with advancing gestation from 32 to 35 weeks' gestation ($p > 0.05$). The 95th percentile of the IVSD

Table 1. Interventricular septal thickness during diastole (IVSD) and interventricular septal thickness during systole (IVSS) based on gestational age (n = 410 cases)

GA (wks^{+days})	N	IVSD (mm)			IVSS (mm)		
		5th percentile	50th percentile	95th percentile	5th percentile	50th percentile	95th percentile
32^{+0}-32^{+6}	106	1.32	2.79	4.26	2.28	4.18	6.09
33^{+0}-33^{+6}	147	1.53	2.99	4.44	2.55	4.25	5.96
34^{+0}-34^{+6}	101	1.24	2.99	4.74	2.55	4.37	6.19
35^{+0}-35^{+6}	56	1.55	3.07	4.59	2.35	4.51	6.68

GA: gestational age; wks: weeks; mm: millimeters

and IVSS were 4.51 mm (range = 4.26 to 4.74 mm) and 6.23 mm (range = 5.96 to 6.68 mm), respectively. Intra-observer variability was 7.6%.

Discussion

Echocardiographic determinations of fetal IVST provides an important quantitative reference point for fetal cardiac assessment. Because of the growth of the fetal heart, one must obtain assessments based on gestational matched normal values[11]. The authors used gestational age as the standard, rather than biparietal diameter of skull or femur length because most standard obstetric programs convert measurement of biparietal skull dimension or femur length to an estimated gestational age. The advantage of measurement from cross-sectional M-mode echocardiography is obvious because the measurements can be obtained with most modern high resolution real-time ultrasound imaging, enabling appropriate selection of the phase of the cardiac cycle in which measurements are to be obtained.

In order to evaluate the predictive value of the IVST for fetal asymmetrical septal hypertrophy and

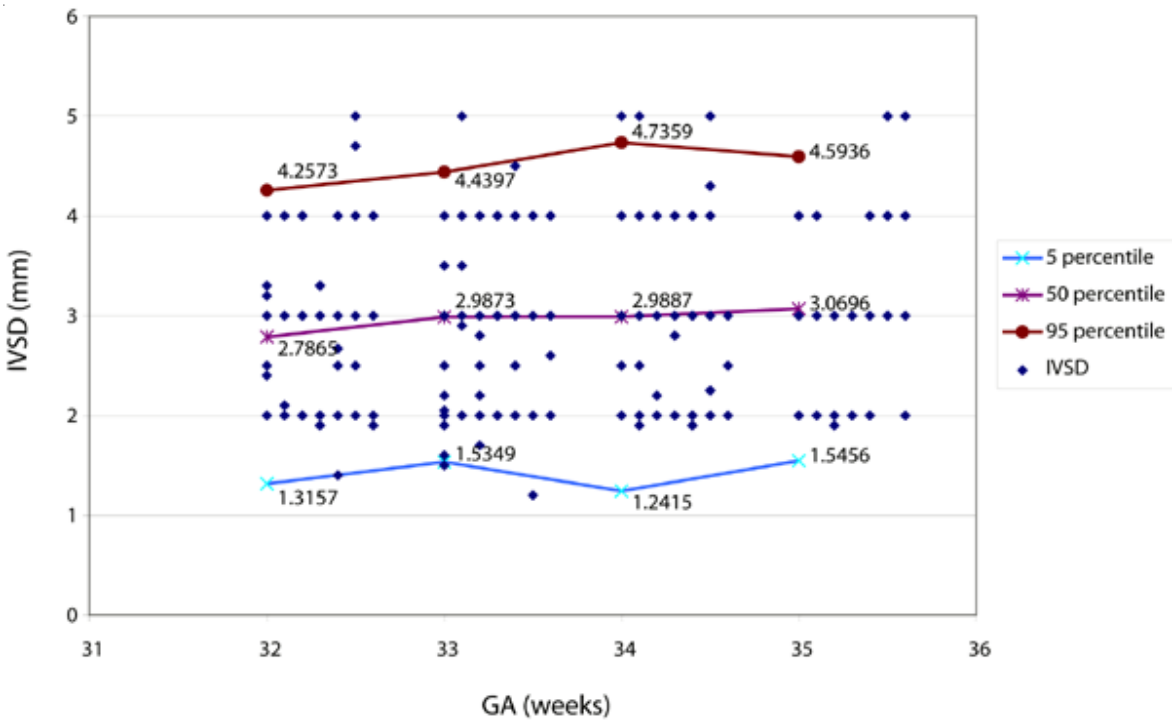


Fig. 2 Normal value of the interventricular septal thickness during diastole (IVSD) according to gestation age. Lines represent the 5th, 50th and 95th percentiles (GA = gestational age)

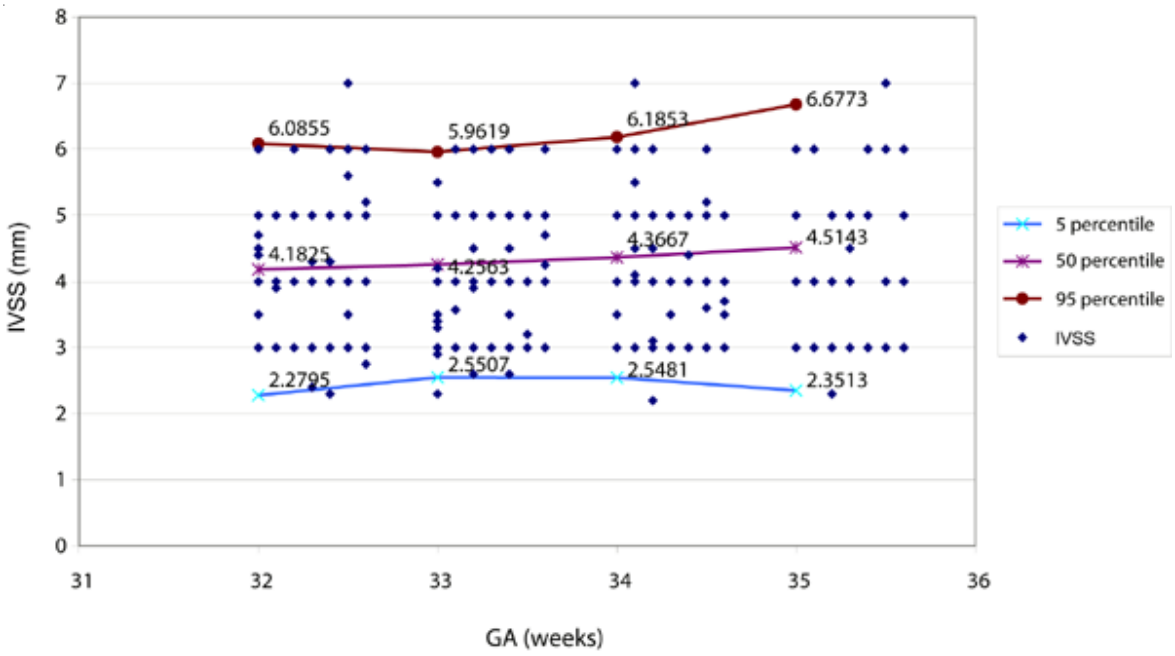


Fig. 3 Normal value of the interventricular septal thickness during systole (IVSS) according to gestational age. Lines represent the 5th, 50th and 95th percentiles (GA= gestational age)

fetal outcome in each population, the threshold value should be established. In the present study, 410 normal Thai fetuses from nondiabetic mothers with reliable gestational age and completed evaluation of neonatal outcomes were enrolled. The technique for measurements was simple and success rate was high. Most of the unsuccessful studies were in the early phase of the present study from maternal habitus and suboptimal fetal position. The authors confined the period of measurements from 32 to 35 weeks' gestation because it included a period of a significant increase in the IVST among the fetuses with asymmetrical septal hypertrophy compared to those who do not have asymmetrical septal hypertrophy at birth[6].

Previous studies have reported that the fetal IVST during both diastole and systole increased significantly in a linear fashion with advancing gestation from 18 weeks to term[4,11,15,16]. Tan et al[11] showed that the 95th percentile of the IVSD among 100 normal fetuses from 32 to 35 weeks' gestation was approximately 4 mm, whereas Veille et al[15] reported that these values of the IVSD and IVSS were approximately 3.0 mm and 4.5 mm, respectively. Zielinsky[17] found that the asymmetrical septal hypertrophy among the fetuses of diabetic mothers had the mean IVST of 7.12 $\pm$ 1.6 mm at the mean gestational age of 32 weeks. In the present study, there was little or no relationship between the fetal IVST and gestational age. The values of fetal IVST were not significantly different with advancing gestation from 32 to 35 weeks. The 95th percentile of the IVSD and IVSS were 4.51 mm and 6.2 mm, respectively. These findings were not similar to the previous studies[4,11,15,16] which reported that the mean septal size during both diastole and systole were increased significantly in a linear fashion with advancing gestation from 18 weeks to term. It may be from a short interval between 32 to 35 weeks' gestation of the observation in the present study.

The authors focused on these gestations since it might have the significant clinical relevance in prenatal detection of the asymmetrical septal hypertrophy among the fetuses of diabetic mothers[2,8,9]. Different cut-off results between various studies can be explained based on the difference in the methods used to measure the IVST, subject selection and the gestational age of the studied population.

Fetuses of diabetic mothers with hypertrophic cardiomyopathy may present as undiagnosed hydrops fetalis or acute fetal distress even in the absence of fetal hydrops which suggests that this condition might be one of the causes of the increased stillbirth rate in pregnancies complicated by type 1 diabetes[18,19]. The authors hope that the establishment of standard measurements and normal value of fetal IVST would

invite a number of clinical applications, including the ability to diagnose asymmetrical septal hypertrophy. This is normally asymptomatic in utero and may only result in congestive heart failure in the immediate postnatal period[20]. 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 present study may represent the normal value of fetal IVST in a Thai population since all of the subjects in the present study were a homogeneous Thai ethnic group.

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 IVST which occur as fetuses adapt to the postnatal periods.

Conclusion

The authors established a normal value of fetal IVST in a normal Thai population from 32 to 35 weeks' gestation. The present study could be used as a baseline data for evaluation of the fetus at risk for hypertrophic cardiomyopathy, especially in the light of recent epidemiologic data linking increased incidence of diabetes in the general population.

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ความหนาของผนังกั้นระหว่างหัวใจห้องล่างของเด็กไทยในครรภ์ที่มีอายุครรภ์ 32 ถึง 35 สัปดาห์

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

วัตถุประสงค์*: เพื่อหาค่าปกติของความหนาของผนังกั้นระหว่างหัวใจห้องล่างของเด็กไทยในครรภ์ที่มีอายุครรภ์ 32 ถึง 35 สัปดาห์*

วัสดุและวิธีการ*: ผู้ศึกษาได้ตรวจวัดความหนาของผนังกั้นระหว่างหัวใจห้องล่างในช่วงหัวใจคลายตัว(diastole) และช่วงหัวใจบีบตัว (systole) ของเด็กไทยในครรภ์ ด้วยเครื่องตรวจคลื่นเสียงความถี่สูง ในสตรีตั้งครรภ์ปกติ อายุครรภ์ 32 ถึง 35 สัปดาห์ ได้รับการตรวจยืนยันอายุครรภ์ด้วยเครื่องตรวจคลื่นเสียงความถี่สูงก่อนอายุครรภ์ 20 สัปดาห์ ผลการตรวจกรองภาวะเบาหวานเมื่ออายุครรภ์ 24 ถึง 28 สัปดาห์ อยู่ในเกณฑ์ปกติ และเด็กในครรภ์ไม่มีความพิการแต่กำเนิด ข้อมูลที่ได้นำมาวิเคราะห์หาค่าปกติ และความสัมพันธ์ระหว่างความหนาของผนังกั้นระหว่างหัวใจห้องล่างในช่วงหัวใจคลายตัวและช่วงหัวใจบีบตัวกับอายุครรภ์*

ผลการศึกษา*: ข้อมูลจากสตรีตั้งครรภ์จำนวน 410 ราย ได้นำมาวิเคราะห์ ผลลัพธ์พบว่าค่าความหนาของผนังกั้นระหว่างหัวใจห้องล่างของเด็กในครรภ์ในช่วงหัวใจคลายตัวและช่วงหัวใจบีบตัว ที่ระดับ 5, 50 , และ 95 เปอร์เซ็นต์ไทล์ ไม่มีความแตกต่างกันอย่างมีนัยสำคัญเมื่ออายุครรภ์เพิ่มขึ้น สัมประสิทธิ์ความสัมพันธ์ระหว่างความหนาของผนังกั้นระหว่างหัวใจห้องล่างในช่วงหัวใจคลายตัว และช่วงหัวใจบีบตัวกับอายุครรภ์มีค่าเท่ากับ 0.11 และ 0.12 ตามลำดับ ความหนาของผนังกั้นระหว่างหัวใจห้องล่างในช่วงหัวใจคลายตัวและช่วงหัวใจบีบตัว ที่ระดับ 95 เปอร์เซ็นต์ไทล์เท่ากับ 4.51 และ 6.23 มิลลิเมตรตามลำดับ*

สรุป*: การศึกษานี้ทำให้ทราบค่าปกติของความหนาของผนังกั้นระหว่างหัวใจห้องล่างในช่วงหัวใจคลายตัวและช่วงหัวใจบีบตัวของเด็กไทยในครรภ์ที่มีอายุครรภ์ 32 ถึง 35 สัปดาห์ ข้อมูลนี้มีประโยชน์สำหรับนำมาใช้เป็นพื้นฐานในการวินิจฉัยทารกในครรภ์ที่มีความหนาของผนังกั้นระหว่างหัวใจห้องล่างผิดปกติ*