Prenatal Diagnosis of Cardiovascular Diseases

JARUPIM SOONGSWANG, M.D.*,
PRASERT SUNSANEEVITHAYAKUL, M.D.**,
KRITVIKROM DURONGPISITKUL, M.D.*,
APICHART NANA, M.D.*,
KESAREE PUNLEE, B.Sc.***,
ANUWAT SUTANTHAVIBUL, M.D.**,
WIBOOLPHAN THITADILOK, M.D.**,
DUANGMANEE LAOHAPRASITIPORN, M.D.*,
KANCHANA WANSANIT, B.Sc.***,
CHARUWAN KANGKAKATE, M.Sc.***

Abstract

Fetal echocardiography is a safe means to obtain reliable anatomical and hemodynamic data of the fetal heart. The procedure is essential for prenatal diagnosis of cardiovascular abnormalities. In addition, fetal echocardiography is useful to follow-up the progression, monitoring during treatment and making a plan of treatment especially in life-threatening cardiac conditions. The objective of this study was to find the distribution of indications for fetal echocardiography, fetal cardiac anomalies detected, outcome of the fetuses and to assess the accuracy of the procedure. A retrospective study was done at Siriraj Hospital, Mahidol University, Bangkok, Thailand. Pregnant women whose fetuses had prenatal echocardiographic data and gave birth from January 1999 to December 2001 were included. The total number of pregnant women was 54 cases. The indications for fetal echocardiography were suspicion of fetal cardiovascular disease by the obstetrician 42.6 per cent, family history of congenital heart diseases 14.8 per cent, multiple organ system anomalies 14.8 per cent, chromosomal anomalies 11.1 per cent, hydrops fetalis 9.3 per cent, maternal systemic diseases 5.6 per cent and previous pregnancy with a dead fetus *in utero* 1.9 per cent. The gestational age at the time of the first fetal echocardiography ranged from 17 to 39 weeks (median 28 weeks). The number of fetal echocardiography done in each case ranged from 1 to 10 (median 1.4). Prenatal diagnosis of the abnormal cardiovascular system in fetuses was found in 19 cases (35.2%). There were abnormal cardiac anatomies in 42 per cent, cardiac tumors or abnormal masses in 37 per cent and rhythm disturbances in 21 per cent. When compared with postnatal echocardiography and/or autopsy finding, fetal echocardiography had a sensitivity of 100 per cent, specificity of 96.3 per cent and accuracy of 97.8 per cent.

Conclusion : Fetal echocardiography has good accuracy in the diagnosis of cardiovascular diseases. Obstetrician's suspicion is important in the prenatal diagnosis of heart disease that would have affected the short and long-term outcome of the fetus.

Key word : Fetal Echocardiography, Prenatal Diagnosis

SOONGSWANG J, SUTANTHAVIBUL A, SUNSANEEVITHAYAKUL P, et al
J Med Assoc Thai 2002; 85 (Suppl 2): S640-S647

* Division of Cardiology, Department of Pediatrics,
** Department of Obstetrics & Gynecology,
*** Her Majesty Cardiac Center, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

Prenatal diagnosis of congenital heart disease with fetal echocardiography was introduced in 1972 by Winsberg[1]. With advanced technology, fetal echocardiography has become the most reliable, safe, noninvasive tool to evaluate the cardiovascular system of the fetus[2]. Fetal echocardiography has been used to diagnose anatomical abnormality, functional and rhythmic disturbances. In addition, it is useful for following-up the progression of these abnormalities, assessing the result of management and making plans to deliver in tertiary care especially in ductal dependent lesions[3,4]. Various studies have demonstrated the impact of fetal echocardiogram in reducing the prevalence of congenital heart diseases (CHD), reduced morbidity after delivery and peri-operatively and reduced peri-operative mortality [5,6]. This study intended to find the distribution of indications of the procedure, cardiac abnormalities, outcome of the fetuses and to assess the accuracy of the procedure.

MATERIAL AND METHOD

The authors retrospectively studied the data of pregnant women who underwent prenatal fetal echocardiography and later delivered their offsprings at Siriraj Hospital, Mahidol University, Bangkok, Thailand from January 1999 to December 2001. Fetal echocardiography was done by pediatric cardiologists using an echocardiographic machine (Hewlett Packard, Sonos 5500) with a 2.25 MHz transducer. The indications of fetal echocardiography were as follows:

1. Fetal abnormalities: hydrops fetalis, extracardiac anomalies, and chromosomal anomalies.
2. Maternal problems: systemic lupus erythematosus (SLE), diabetes mellitus, environmental exposure e.g. alcohol, warfarin, rubella etc.
3. Family history of CHD.
4. Cardiovascular abnormalities by suspected obstetricians.

Gestational age at the time of the procedure was at least 16 weeks. The echocardiographic study was done as previously described[7] i.e. cardiac position, segmental approach, ventricular function, hemodynamic data and rhythm.

Obstetric data, maternal problems, gestational age, echocardiographic data at the first fetal echocardiography were collected. Follow-up fetal echocardiography was done in some cases i.e., those with abnormal or risk of abnormal cardiovascular system. The parents and obstetricians were informed regarding the results, severity of the cardiac problems, options and possible outcome of management. Then, the appropriate management plan including mode and time of delivery was thoroughly discussed and chosen. The abortion committee was consulted to assist in making the decision in cases of severe forms of cardiovascular diseases, especially

associated with chromosomal or multiple anomalies. Postnatal transthoracic echocardiographic data or autopsy data, outcome and management were also studied.

Statistical analysis

Measured variables were expressed as range and median. Proportions (in percentage) were calculated for categorical data. Accuracy was evaluated using two by two analysis.

RESULTS

Prenatal data

A total of 54 pregnant women and 87 fetal echocardiographies were performed. The median gestational age at the first fetal echocardiography was 28 weeks (17-38 weeks). Forty-one pregnant women had no systemic problems that could affect the fetuses. Maternal problems of the rest (13/54) are shown in Table 1. Median gravida was 2 (ranging from 1 to 6). The distribution of indications for

Table 1. Maternal problems in 13 pregnant women.

	Cases
Adjustment disorder	1
Advanced maternal age	2
Amphetamine ingestion until 10 weeks GA	1
Anemia during early pregnancy	1
Diabetes mellitus	2
Epilepsy (on dilantin & amitryptyline)	1
Myasthenia gravis S/P thymectomy	1
Anti-Ro+, anti-La+, ANA + speckle type >1:2560	1
Papillary carcinoma stage 1 post partial thyroidectomy (on eltroxin)	1
Premature contraction	1
SLE (on steroid 7.5 mg for 3 yrs), anti-Ro+	1

ANA = antinuclear antibody
GA = gestational age
SLE = systemic lupus erythematosus

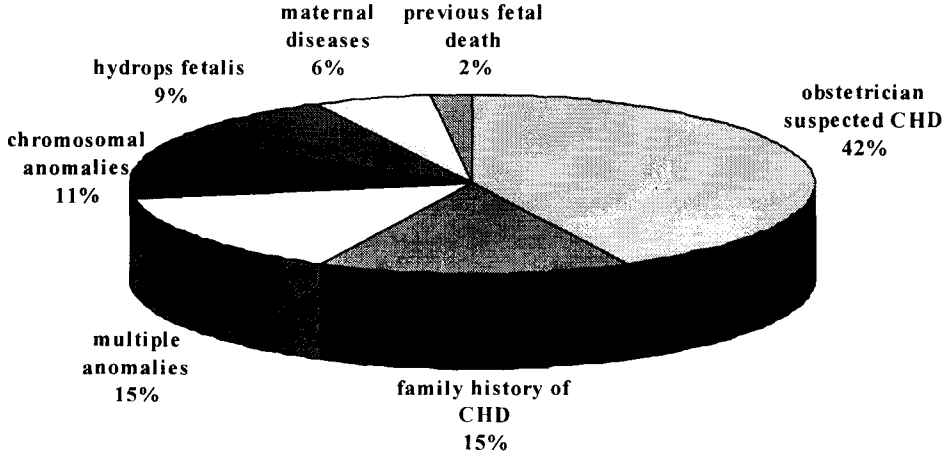

Fig. 1. Percentage of various indications for fetal echocardiography.

CHD = congenital heart diseases.

fetal echocardiography are shown in Fig. 1. Nineteen fetuses (35.2%) were found to have an abnormal cardiovascular system: anatomical defect 42 per cent, cardiac mass 37 per cent and rhythm problems 21 per cent. Details of the abnormalities are shown in Table 2. Median individual number of fetal echocardiography was 1.4 (ranging from 1 to 10). Examples of fetal echocardiographic picture are shown in Fig. 2.

Natal and postnatal data

Modes of delivery were normal labor 53.8 per cent, therapeutic abortion 24.1 per cent, Caesarian section 18.5 per cent and dead fetus *in utero* 3.7 per cent. Forty-five cases (83.3%) had postnatal echocardiography or autopsy data to confirm the cardiovascular problems. Five cases were lost to follow-up (9.2%). Four cases (7.5%) underwent therapeutic abortion in rural hospitals without autopsy reports. Comparison of pre and postnatal cardiovascular data are demonstrated in Table 3. The different diagnosis encountered was in a trisomy 21 fetus, the prenatal echocardiogram of which reported suspicion of, partial atrioventricular canal whereas postnatal echocardiogram showed no cardiac lesion. Statistical analysis of prenatal fetal echocardiography compared with postnatal data is demonstrated in Table 4.

There were 2 cases of cardiac rhythm problems with frequent premature atrial contraction (PAC). The fetuses were hemodynamically stable until birth and gradually resolved spontaneously within a month postnatal. One fetus with high-grade atrioventricular block was diagnosed at the gestational age of 36 weeks. The infant developed complete heart block on day 2 of life. This patient also had maternal anti-La and anti-Ro positive. Permanent epicardial pacemaker implantation was done on day 3 and the patient has been clinically fine ever since.

Six women with fetal cardiac anatomy abnormalities underwent therapeutic abortion, mainly due to the associated anomalies. One infant with hypoplastic left heart syndrome underwent Norwood stage 1 operation on day 30 of life and died during the acute post-operative period. One child with hypertrophic cardiomyopathy (HCM) has been fine. The most recent follow-up showed gradual regression in ventricular hypertrophy.

There was one child with a single cardiac mass at the right atrioventricular groove which was detected *in utero* at the gestational age of 20 weeks.

Table 2. Cardiovascular abnormalities found in fetal echocardiography.

	Cases
Rhythm problems	
AV dissociation (heart block)	2
Frequent PAC	2
Anatomic problems	
Common ventricle, common AVV with mild regurgitation, d-TGA	1
Ectopia cordis	1
Hydrops fetalis, myocardial dysfunction, moderate TR, cardiomegaly	2
HCM	1
HLHS	1
Partial AVC	1
Small aortic arch	1
Cardiac mass	
Multiple cardiac mass, moderate TR, massive PE, frequent PAC	1
RV mass, occasional PVC	2
RV mass (19 x 13 mm), LV mass at apex	1
LV mass free wall x 2, RV at apex	1
LV mass 2.3 x 2.7 mm	1
Single mass at RA, right atrioventricular (RAV) groove	1

AV = atrioventricular, PAC = premature atrial conduction AVV = atrioventricular valve, d-TGA = d-transposition of the great arteries, TR = tricuspid regurgitation, HLHS = hypoplastic left heart syndrome, HCM = hypertrophic cardiomyopathy, AVC = atrioventricular canal, PE = pericardial effusion, RV = right ventricle, LV = left ventricle, PVC = premature ventricular conduction, RA = right atrium

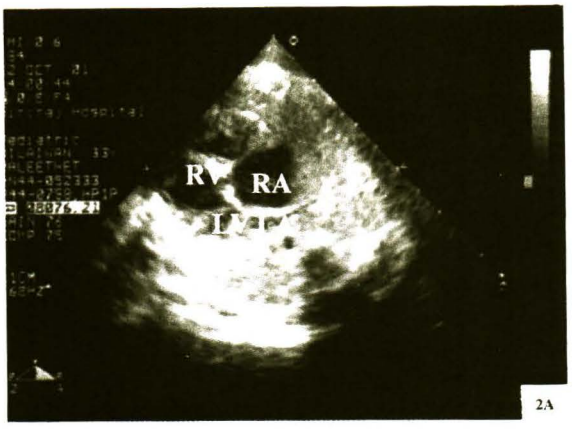

Fig. 2A. Four chambers view of hypoplastic left heart syndrome.

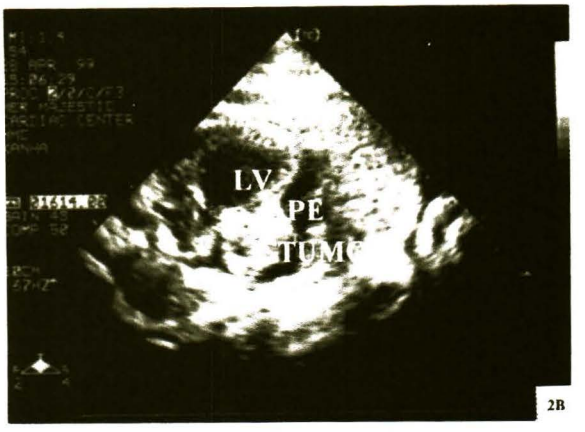

Fig. 2B. Four chambers view of cardiac tumor at right atrioventricular groove.

RA = right atrium, LA = left atrium, RV = right ventricle, LV = left ventricle, PE = pericardial effusion.

Table 3. Comparison of cardiovascular problems, pre and postnatal data.

Cardiovascular data	Frequency	%
Same	40	88.9
Slightly different	4	8.9
Different	1	2.2
Total	45	100

This resulted in hypoplasia of the right ventricle and tricuspid valve and required prostaglandin E1 (PGE1) on day 1 of life. Surgical intervention was done afterward (right modified Blalock Taussig shunt on day 3 of life followed by one and a half ventricular repair at 2 years old). The pathological report revealed a cardiac fibroma that gradually shrunk during the postnatal period. The rest of the children with cardiac masses did not have any hemodynamic effect. In all cases, follow-up demonstrated that the mass gradually decreased in size without treatment. Two cases with multiple cardiac masses developed hypopigmented skin lesions and were diagnosed as tuberous sclerosis.

DISCUSSION

Prenatal period

At present, the focus of congenital heart diseases detection has turned to screening methods and to the impact of prenatal screening and diagnosis of cardiovascular malformations on the perinatal and long-term outcome of the fetus. In Western countries, prenatal diagnosis of cardiac diseases has decreased the incidence of congenital heart diseases especially serious cardiac lesions by termination of pregnancy[8,9]. It has been proved that fetal echocardiography also decreased mortality and morbidity for some ductal dependent cardiac lesions e.g. d-transposed of great arteries (d-TGA)[10].

The rate of prenatal diagnosis of fetal cardiac abnormalities in our institution is low (19 cases). It has been known that the incidence of CHD is 8: 1,000 lives-births. There are about 10,000 to 11,000 live-births per year at Siriraj Hospital, so the total number of CHD is expected to be about 800 cases per year. However, this number includes cardiac lesions that are found normally in the fetus e.g. patent ductus arteriosus (PDA) and atrial septal defect (ASD). The reported detection rate varied from less than 1 per cent to over 70 per cent[11]. This discrepancy was partly due to the difficulty to detect each malformation. At least once during 16-18 weeks gestational age, routine obstetric abdominal ultrasound should include a scan for the four chambers view of the fetal heart which might improve the detection rate. This practice has been recommended by the American Institute of Ultrasound and the American College of Obstetricians and Gynecologists. It has been reported to detect as high as 80

Table 4. Accuracy of fetal echocardiography compared with postnatal data.

Fetal echocardiogram	Postnatal echocardiography or autopsy (cases)	
	CVS diseases	No CVS diseases
CVS diseases	18	1
No CVS diseases	0	26
	18	27

CVS = cardiovascular system

Sensitivity = 100%, Specificity = 96.3%, Positive predictive value = 94.7%
Negative predictive value = 100%, Accuracy = 97.8%

per cent of fetuses with cardiovascular problems (12). Furthermore, the result in this study emphasized the vigilance of the obstetrician suspicious of fetal CHD (42%).

Despite the rarity of the cardiac mass, it was found in about one third of the cardiovascular abnormalities in the present study. A small but important proportion (2.4%) of irregular heart rhythm, which was hemodynamically significant, has been reported(13). Fetal tachyarrhythmia could be treated adequately in the majority of fetuses with digitalis and flecainide. Emergency delivery might not be indicated(4). There was a high prevalence of fetal bradyarrhythmia detected in mothers with connective tissue diseases between 16-29 weeks of gestation. Irreversible fetal complete heart block in mothers with SLE could be found in up to 1.7 per cent and 5 per cent with anti Ro positive(14), which carried a significant mortality rate (14-22%). Treatment with oral dexamethasone at the stage of second-degree atrioventricular block with close follow-up has been suggested to prevent the progression to complete heart block(15). Premature atrial contraction (PAC) was occasionally found *in utero* and during the neonatal period without hemodynamic effect. In the majority of cases, it was spontaneously resolved(16) as was also found in this study.

Natal and postnatal period

In Thailand, termination of pregnancy due to fetal anomalies is illegal. However, twenty one per cent of fetuses in this study who had multiple congenital anomalies or severe, incompatible with life congenital cardiac lesions were terminated by the consensus of the abortion committee. One study reported more than 50 per cent termination of pregnancies that resulted in a decrease in congenital complex heart diseases(8). Caesarian section was necessary for the delivery of some fetuses especially in hemodynamic compromise lesions and also in some cases that needed immediate specific postnatal care.

The accuracy of fetal echocardiogram is high as proved by many studies(17,18) including the present study. Some minor errors were found particularly in those fetuses whose image quality was poor due to too early (<20 weeks) or too late (>34 weeks) gestational age, or due to maternal obesity. Fetal cardiac tumor has been reported to be benign and the majority are rhabdomyomas(19). This finding was also demonstrated in this study.

SUMMARY

The number of prenatal diagnoses of congenital heart diseases was low in our institution. The accuracy of fetal echocardiography was good. Routine fetal ultrasound at least once in the early second trimester (18-20 weeks) should be done including screening for fetal heart disease by scanning the four chambers view. The practice could increase the rate of prenatal diagnosis of congenital heart disease, decrease the rate of fetal loss and decrease the mortality and morbidity of newborn infants with severe cardiac diseases.

(Received for publication on March 27, 2002)

REFERENCES

1. Winsberg F. Echocardiography of the fetal and neonate heart. Invest Radiol 1972; 3: 152.
2. Huhta JC. Uses and abuses of fetal echocardiography: A pediatric cardiologist's view. J Am Coll Cardiol 1986; 8: 451-8.
3. Srinivasan S. Fetal echocardiography. Indian J Pediatr 2000; 67: 515-21.
4. Van Engelen AD, Weijtens O, Brenner JI, et al. Management outcome and follow-up of fetal tachycardia. J Am Coll Cardiol 1994; 24: 1371-5.
5. Kachaner J. The best of pediatric cardiology in 1999. Arch Mal Coeur Vaiss 2000; 93: 63-8.
6. Allan L. Congenital heart disease: Antenatal diagnosis of heart disease. Heart 2000; 83: 367-70.
7. Cordes TM, O'Leary PW, Seward JB, Hagler DJ. Distinguish right from left : A standardized technique for fetal echocardiography. J Am Soc Echocardiogr 1994; 7: 47-53.
8. Hunter S, Heads A, Wyllie J, Robson S. Prenatal diagnosis of congenital heart disease in the northern region of England: Benefits of a training programme for obstetric ultrasonographers. Heart 2000; 84: 294-8.
9. Bull C. Current and potential impact of fetal diagnosis on prevalence and spectrum of serious congenital heart disease at term in the UK. Lancet 1999; 354: 1242-7.
10. Bonnet D, Coltri A, Butera G, et al. Detection of transposition of the great arteries in fetuses reduces neonatal morbidity and mortality. Circulation 1999; 99: 916-8.
11. Todros T. Prenatal diagnosis and management of fetal cardiovascular malformations. Curr Opin Obstet Gynecol 2000; 12: 105-9.
12. Allan LD, Crawford DC, Chita SK, Tynan MJ. Prenatal diagnosis for congenital heart disease. Br Med J 1986; 292: 1717-9.
13. Copel JA, Liang RI, Demasio K, Ozeren S, Kleinman CS. The clinical significance of the irregular fetal heart rhythm. Am J Obstet Gynecol 2000; 182: 813-9.
14. Tseng CE, Buyon JP. Neonatal Lupus Syndromes. Rheum Dis Clin North Am 1997; 23: 31-54.
15. Dorner T, Feist E, Pruss A, Chaoui R, Goldner B, Hiepe F. Significance of autoantibodies in neonatal lupus erythematosus. Int Arch Allergy Immunol 2000; 123: 58-66.
16. Montagne TJ, Taylor PG, Stocktan R, Roy DL, Smith ER. The spectrum of cardiac rate and rhythm in normal newborns. Pediatr Cardiol 1982; 2: 33-8.
17. Allan LD, Sharland GK, Milburn A, et al. Prospective diagnosis of 1006 consecutive cases of congenital heart disease in the fetus. J Am Coll Cardiol 1994; 23: 1452-8.
18. Saxena A, Shrivastana S, Kothari SS. Value of antenatal echocardiography in high risk patients to diagnose congenital cardiac defects in fetus. Indian J Pediatr 1995; 62: 575-82.
19. Holley DG, Martin GR, Brenner BI, et al. Diagnosis and management of fetal cardiac tumors: A multicenter experience and review of published reports. J Am Coll Cardiol 1995; 26: 516-20.

การตรวจความผิดปกติของหัวใจและหลอดเลือดของทารกในครรภ์

จารุพิมพ์ สูงสว่าง, พ.บ., อนุวัตน์ สุตัณฑวิบูลย์, พ.บ.**,*
*ประเสริฐ ศันสนีย์วิทยกุล, พ.บ.**, วิบูลพรรณ ฐิตะดิลก, พ.บ.**,*
กฤตย์วิกรม ดุรงค์พิศิษฏ์กุล, พ.บ., ดวงมณี เลาหประสิทธิพร, พ.บ.*, อภิชาติ นานา, พ.บ.*,*
*กาญจนา หวานสนิท, วท.บ.***, เกศรี ปั้นลี้, วท.บ.***, จารุวรรณ คังคะเกตุ, วท.ม.****

การทำ Fetal echocardiography ถือเป็นวิธีที่ปลอดภัยและได้ผลที่เชื่อถือได้ในการบอกถึงความผิดปกติของหัวใจและหลอดเลือดของทารกในครรภ์ นอกจากนี้ยังใช้ติดตามการเปลี่ยนแปลงและติดตามผลของการรักษา ตลอดจนวางแนวทางการรักษา โดยเฉพาะในภาวะที่รุนแรงที่อาจมีผลต่อชีวิตได้ จุดประสงค์ของการศึกษานี้ เพื่อศึกษาถึงข้อบ่งชี้ของการตรวจ fetal echocardiography ของโรงพยาบาลศิริราช, ความผิดปกติของระบบหัวใจและหลอดเลือดที่พบ และผลของการดูแลรักษาตลอดจนประเมินความแม่นยำของการตรวจ fetal echocardiogram เมื่อเปรียบเทียบกับการตรวจหลังคลอดด้วย Transthoracic echocardiogram และ/หรือการตรวจทางพยาธิวิทยา

การศึกษาย้อนหลังในโรงพยาบาลศิริราช คณะแพทยศาสตร์ศิริราชพยาบาล มหาวิทยาลัยมหิดล ในหญิงตั้งครรภ์ที่ได้รับการตรวจ fetal echocardiogram ทุกราย และให้กำเนิดบุตรหรือแท้งในช่วงเวลาตั้งแต่ มกราคม 2542 ถึง ธันวาคม 2544 พบว่า มีทั้งหมด 54 ราย โดยมีข้อบ่งชี้ในการทำคือ สูติแพทย์สงสัยทารกมีความผิดปกติของหัวใจและหลอดเลือด 42.6%, มีประวัติครอบครัวเป็นโรคหัวใจพิการแต่กำเนิด 14.8%, มีความผิดปกติของระบบอวัยวะอื่น ๆ หลายระบบ 14.8%, มีโครโมโซมผิดปกติ 11.1%, มีภาวะบวมน้ำ (hydrops fetalis) 9.3%, มารดามีปัญหาสุขภาพ 5.6% และมารดามีประวัติทารกเสียชีวิตในครรภ์ 1.9% อายุครรภ์ขณะทำ fetal echocardiogram ครั้งแรกคือ 17–39 สัปดาห์ (ค่ามัธยฐาน 28 สัปดาห์) จำนวนครั้งที่ทำมีตั้งแต่ 1–10 ครั้ง (ค่ามัธยฐาน 1.4 ครั้ง) ตรวจพบมีความผิดปกติของหัวใจและหลอดเลือด 19 ราย (35.2%) โดยพบว่าเป็นความผิดปกติของหัวใจ 42%, มีก้อนในหัวใจ 37%, หัวใจเต้นผิดจังหวะ 21% เมื่อเปรียบเทียบกับการตรวจหลังคลอดและ/หรือการตรวจทางพยาธิวิทยาพบว่า มี sensitivity 100%, specificity 96.3% และ accuracy 97.8%

สรุปการตรวจ fetal echocardiography เป็นการตรวจที่ให้ความแม่นยำสูงในการตรวจภาวะผิดปกติของระบบหัวใจและหลอดเลือดของทารกในครรภ์ สูติแพทย์จะเป็นด่านที่สำคัญมากในการสงสัยภาวะนี้ ซึ่งจะมีผลต่อการดูแลทารกหลังคลอดทั้งระยะสั้นและระยะยาว

คำสำคัญ : การตรวจหัวใจของทารกในครรภ์ด้วยคลื่นเสียงสะท้อน, การตรวจความผิดปกติของทารกในครรภ์

จารุพิมพ์ สูงสว่าง, อนุวัตน์ สุตัณฑวิบูลย์, ประเสริฐ ศันสนีย์วิทยกุล, และคณะ
จดหมายเหตุทางแพทย์ ฯ 2545; 85 (ฉบับพิเศษ 2): S640–S647

* สาขาวิชาหัวใจและหลอดเลือด, ภาควิชากุมารเวชศาสตร์,
** ภาควิชาสูติศาสตร์-นรีเวชวิทยา,
*** ศูนย์โรคหัวใจสมเด็จพระบรมราชินีนาถ, คณะแพทยศาสตร์ศิริราชพยาบาล, มหาวิทยาลัยมหิดล, กรุงเทพ ฯ 10700