Fetal Structural Anomaly Screening at 11-14 Weeks of Gestation at Maharaj Nakorn Chiang Mai Hospital

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Objective: *To determine the detection rate by ultrasound scanning of fetal anomaly by first trimester (11-14 weeks of gestation).*
Material and Method: *A prospective descriptive study of 597 pregnant women undergoing Nuchal Translucency (NT) measurement at 11-14 weeks of gestation at Maharaj Nakorn Chiang Mai Hospital. The sonographic examinations focused on NT thickness and fetal structural survey. The final diagnoses were based on neonatal outcomes assessed by the pediatricians and abortuses evaluated by the pathologists. The main outcome measure was the detection rate of fetal anomaly using ultrasonographic examination.*
Results: *Of 597 pregnant women recruited into the present study, the mean age was 29.41±5.8 years, the incidence of fetal anomaly was about 4% (24 from 597 cases). The detection rate by first ultrasound scans was 58% (14 from 24 cases) and the most common detected structural anomaly was cystic hygroma and exencephaly. The rate of undetected fetal anomalies was 42% (10 from 24 cases). Abnormal NT was found in 16 from a total of 597 cases (2.7%), most of them, however, had normal karyotype and no gross anomaly at birth.*
Conclusion: *First trimester (11-14 weeks) ultrasound scan is probably a useful method for detection of fetal structural anomalies with a relatively high detection rate, and may be a good adjunct to the conventional examination.*

Keywords: *Fetal anomaly, First trimester ultrasound, Nuchal translucency*

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Currently, ultrasonographic examination is part of the management and planning for obstetric patients and its important role is to detect fetal anomaly. Ultrasound screening for fetal anomalies is conventionally performed at 18 to 20 weeks of gestation. However, recent data suggested that many fetal structural abnormalities could be detected by ultrasound examination at 11-14 weeks of gestation[1-5]. Early diagnosis of these conditions and the appropriate intervention may be beneficial to the mother, both physically and psychologically. This may either allow early reassurance of normality, or enable the woman to make an early decision on the affected pregnancy.

A meta-analysis from the Cochrane library on ultrasound for early pregnancy fetal assessment[6] collected data from 9 good quality trials to assess the use of routine (screening) ultrasound compared with the selective use of ultrasound in early pregnancy (before 24 weeks). According to the meta-analysis, routine ultrasound in early pregnancy appears to enable better gestational age assessment, earlier detection of multiple pregnancies and earlier detection of clinically unsuspected fetal malformation at a time when termination of pregnancy is possible. However, the benefits for other substantive outcomes are not as clear.

It has been well established that Nuchal Translucency (NT) measurement in the first trimester (11-14 weeks of gestation) is one of the best screening tests for Down syndrome. Several institutes have had a policy of routine NT screening for such a purpose[7-11]. In the same setting of first trimester NT scanning, this can be a great opportunity to screen for structural anomaly as well. Therefore, early ultrasonographic

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examination may probably be the important part in fetal anomaly diagnosis and fetal therapy. However, the efficacy and cost-benefit of first trimester screening for fetal anomaly in Thailand has not been evaluated. The purpose of the present study was to determine the detection rate of fetal anomaly by sonographic examination at 11-14 weeks of gestation in the hope that this may be important data to evaluate cost-benefit of routine ultrasound in early pregnancy in the future.

Material and Method

Five hundred and ninety seven pregnant women attending the antenatal care clinic, Maharaj Nakorn Chiang Mai Hospital, between July 2003 and July 2005 were recruited into the present study. The inclusion criteria included 1) regular menstrual cycle with certain last menstrual period, 2) singleton pregnancy with gestational age of 11-14 weeks, based on the last menstrual period and crown-rump length in the first trimester, 3) voluntary participation in the research with informed and written consent. The exclusion criteria included 1) multifetal pregnancy, 2) ultrasound findings of non-viable pregnancy such as anembryonic pregnancy, or molar pregnancy, etc, 3) loss to the follow-up or incomplete data. Each gestational week interval was centered on the week (e.g. 12 weeks interval, 12.5-12.99 weeks).

All detailed ultrasound examinations were performed by 3 experienced perinatologists with real-time ultrasound equipment using Aloka model Prosound 5000 (Tokyo, Japan) with transabdominal 3.5 MHz curvilinear transducers. Fetal evaluation consisted of NT thickness measured as described by Nicolaides et al[12], and a standard anatomical survey as in the second-trimester anomaly scans, including brain, thorax, heart, stomach, abdominal wall, bladder, kidneys, and limbs. The final diagnoses of fetal anomaly, used as a gold standard, were based on the assessment of the newborns made by the pediatricians or abortuses made by the pathologists. The local ethics committee approved the research protocol. Descriptive statistics, mean $\pm$ SD and frequency table, were presented to describe the results.

Results

During the study period, a total of 597 cases were recruited into the present study. The mean ($\pm$ SD) age of the population was 29.41 $\pm$ 5.8 years, ranging from 19 to 43 years. The mean ($\pm$ SD) of gestational age was 12.29 $\pm$ 1.06 weeks and 3.7% of the cases had a history of fetal anomaly in a previous child.

Among the 597 pregnant women, 24 cases (4%) had abnormal ultrasound findings. There were 14 cases of fetal structural anomalies that could be detected by first trimester ultrasound screening as shown in Table 1. The most common detected structural anomaly was cystic hygroma and exencephaly that could be obviously seen since first trimester of gestation. Of the 573 pregnant women with normal ultrasound finding, 10 (42% of fetuses with anomaly) had structural anomaly, but could not be detected by first trimester scanning as summarized in Table 2. The remaining 563 pregnant women had both normal ultrasound findings and normal neonatal outcomes.

From the 10 cases of fetuses with anomaly that had normal ultrasound finding, five cases (0.8%) were detected in the neonatal period. Each of these cases had anopthalmia, hydrocephalus, skeletal dysplasia, tibial aplasia or multicystic kidney. The remaining five cases were detected as a result of invasive prenatal diagnosis in the second trimester by amniocentesis and cordocentesis, indicated by maternal age and thalassemia risk status. Three of these cases had Hb Bart's disease, one case of trisomy 21 and one case of trisomy18.

Sixteen cases (2.7%) had abnormal nuchal translucency thickness (> 95 percentile of standard

Table 1. Incidence of fetal structural anomalies among 597 cases of first trimester screening anomalies

Cystic hygroma	3
Exencephaly	3
Double outlet of left ventricle	1
Anencephaly	1
Skeletal dysplasia	1
Amniotic band syndrome	1
Hydrops fetalis (trisomy 21)	1
Cystic hygroma with omphalocele	1
Ectopia cordis	1
Limb body wall complex	1

Table 2. Undetected structural anomaly and chromosomal abnormality at first trimester screening

Anophtalmia	1	
Hydrocephalus	1	
Skeletal dysplasia	1	
Tibial aplasia	1	
Multicystic kidney	1	
Trisomy 21	1	} no structural anomaly at the time of amniocentesis
Trisomy 18	1	
HbBart's disease	3	

Table 3. Outcome of cases with abnormal nuchal translucency

Normal outcomes	8	
Abnormal Chromosomes	5	
- Trisomy 21	2	(1 had cystic hygroma with hydrops)
- Trisomy 18	2	(1 had radial ray defects and 1 had cystic hygroma with omphalocele)
- 45,XO	1	(with cystic hygroma)
Cystic hygroma (Normal chromosome)	1	
Arthrogryposis	1	
Spontaneous abortion	1	

value at each gestational age) and outcomes of each case are shown in Table 3. Eight cases (55%) of this group had normal outcomes (normal karyotype and no other gross anomaly at birth). It could be assumed that these cases received unnecessary invasive prenatal diagnosis for karyotype testing. The other five cases with abnormal chromosome, including four cases of trisomy and one case of 45 XO. Some of these cases had abnormal NT and structural anomaly such as cystic hygroma, radial ray defect or omphalocele. However, one case of cystic hygroma was associated with normal karyotype, one case had skeletal abnormality with thickened NT and the other case had no data of karyotype or other anomaly at birth because of spontaneous abortion.

In summary, the total incidence of fetal structural anomaly was 4% (24 from a total of 597 cases). The first trimester ultrasound screening could detect fetal structural anomaly in 58% of cases, thus 42% of structural anomalies were missed.

Discussion

In the present study, the mean age of the study group was 29.41±5.8 years which is similar to the mean age of low risk pregnancy in the general population. The overall incidence of fetal anomaly was 4% (24 cases from total of 597 cases), comparable to previous studies[13], with the most common fetal abnormalities including cystic hygroma, exencephaly and Hb Bart's disease. The 11-14 week scanning could detect 14 cases (58%) of fetal anomaly, consisting of neural tube defect (exencephaly, anencephaly), lymphatic system abnormality (cystic hygroma), skeletal dysplasia, abdominal wall defect (limb body wall complex), and cardiovascular system anomaly (ectopia cordis and double outlet of left ventricle). Like other previous studies[2,4] major anomalies that can be reliably detected at late first trimester were abnormalities of the central nervous system, anterior abdominal wall, and skeletal system defects.

Based on the present study, 42% of structural fetal anomalies could be missed by first trimester screening. This may be somewhat higher than the missing rate in a previous study[13] where 21% of all structural fetal anomalies were missed by prenatal ultrasound. This can partly be explained by the different pattern of fetal anomaly in the different races. For example, Hb Bart's disease of which our population has the highest incidence, is usually subtle during the first trimester and can be simply missed. Most of the missed cases in the present study had late occurring anomalies, including anopthalmia, hydrocephalus and multicystic kidney. The detection of these abnormalities was limited in the first trimester due to very small structure and quality of ultrasonograhic image, for example heart disease, intracranial structure, eye ball and genitourinary system. In particular, in screening for congenital heart defect, the ability to perform a full cardiac examination increases from 20% at 11 weeks to 92% at 13 weeks[4] therefore, optimal time for successful imaging of the four chambers and great arteries in early gestation appears to be after 13-14 weeks[5,14].

Some anomalies could have been detected in 11-14 weeks scan but the ultrasound scan in the present study missed. Items such as the skeletal dysplasia, tibial aplasia and some aneuploidies were missed. Signs of trisomy 21 might be seen in the first trimester such as the fetal nasal bone but were missed. Sonomarkers of trisomy18 or 13 might also be already visible in the first trimester such as the megacystis, omphalocele, polydactyly and holoprosencephaly[15], but these sonographic signs were missed as well. Although the majority of the fetal anomalies were diagnosed in early pregnancy, a single scan in early pregnancy will not detect all fetal abnormalities, as described above. The detection rate is increased significantly by adding a mid-second-trimester scan to the early pregnancy scan. Therefore, the 18-20-week follow-up examination by conventional second-trimester transabdominal scan should always be performed[16].

In addition to structural screening, the present study found 16 cases (2.7%) to have NT thickness of more than 95 percentile for each gestational age, but half of them (50%) had normal karyotype and had no gross anomaly at birth. However, NT measurement has been proven to be effective in screening for aneuploidy and subsequently obvious structural anomalies, especially congenital heart defects. Although, the efficacy of NT measurement can not be well analyzed in the present study due to a relatively small sample size, the present result suggests that the first trimester scan may not only be beneficial in diagnosis of anomaly at the time of scanning, it can also identify the higher risk group based on NT and warrant obstetricians to follow-up and make diagnosis of anomaly later. Even in the absence of aneuploidy, nuchal thickening is clinically relevant because it is associated with an increase in adverse perinatal outcome caused by a variety of fetal malformations, especially congenital cardiac defects[5,14,17].

In the present study, fetuses that had abnormal NT with abnormal karyotype were likely to have other sonomarkers or structural anomalies such as cystic hygroma or radial ray defect, omphalocele. However there were two cases of abnormal NT with cystic hygroma and normal karyotype.

To the authors' best knowledge, first trimester scanning at 11-14 weeks of gestation does not cause any harm to mothers and fetuses. Furthermore, other disadvantages including psychological effect such as anxiety or depression in mothers have not been established[18].

The present study is just a preliminary report and has some limitations. In particular, the sample size may be too small to represent the pregnant population in Northern Thailand, to determine the efficacy of first trimester screening for such a low incidence of fetal anomalies and to evaluate cost-effectiveness for routine scanning as standard practice. However, the detection rate of fetal anomalies in the present study is quite high (58%), as it was in previous studies[1,7,11,19]. This indicates that the first trimester ultrasound may probably have benefit for anomaly screening either using ultrasound alone or combined with serum biochemical markers. The present results suggest the benefit of first trimester screening but it needs more study to assess the cost-effectiveness. Moreover, the detection rate of fetal anomalies at 11-14 weeks is not as high as mid-pregnancy scan[4], therefore, first trimester scanning cannot substitute mid-pregnancy scan.

In conclusion, first trimester (11-14 weeks) ultrasound scanning along with NT measurement and a detailed anatomical survey can play an important role in early detection of fetal structural anomalies. A thorough knowledge of the sonographic features of embryologic development is necessary to avoid potential diagnostic pitfalls. The anatomical ultrasound scan at 18-20 weeks of gestation should also be performed, since a number of anomalies may not be evident at first trimester scanning. Finally, the present study is just a preliminary report with a limited sample size and the cost-effectiveness of such a routine scanning in all pregnant women needs to be evaluated with a larger study.

References

1. Sen C. The use of first trimester ultrasound in routine practice. J Perinat Med 2001; 29: 212-21.
2. Fong KW, Toi A, Hornberger LK, Keating SJ, Johnson JA. Detection of fetal structural abnormalities with US during early pregnancy. Radiographics 2004; 24: 157-74.
3. Eiben B, Glaubitz R. First-trimester screening: an overview. J Histochem Cytochem 2005; 53: 281-3.
4. Weisz B, Pajkrt E, Jauniaux E. Early detection of fetal structural abnormalities. Reprod Biomed Online 2005; 10: 541-53.
5. Carvalho JS. Fetal heart scanning in the first trimester. Prenat Diagn 2004; 24: 1060-7.
6. Neilson JP. Ultrasound for fetal assessment in early pregnancy. Cochrane Database Syst Rev 2000; (2): CD000182.
7. Harris AH. The cost effectiveness of prenatal ultrasound screening for trisomy 21. Int J Technol Assess Health Care 2004; 20: 464-8.
8. Bahado-Singh RO, Cheng CS. First trimester prenatal diagnosis. Curr Opin Obstet Gynecol 2004; 16: 177-81.
9. Wojdemann KR, Shalmi AC, Christiansen M, Larsen SO, Sundberg K, Brocks V, et al. Improved first-trimester Down syndrome screening performance by lowering the false-positive rate: a prospective study of 9941 low-risk women. Ultrasound Obstet Gynecol 2005; 25: 227-33.
10. Nicolaides KH, Spencer K, Avgidou K, Faiola S, Falcon O. Multicenter study of first-trimester screening for trisomy 21 in 75 821 pregnancies: results and estimation of the potential impact of individual risk-orientated two-stage first-trimester screening. Ultrasound Obstet Gynecol 2005; 25: 221-6.

11. Nicolaides KH. First-trimester screening for chromosomal abnormalities. Semin Perinatol 2005; 29: 190-4.
12. Nicolaides KH, Azar G, Byrne D, Mansur C, Marks K. Fetal nuchal translucency: ultrasound screening for chromosomal defects in first trimester of pregnancy. BMJ 1992; 304: 867-9.
13. Markov D, Chernev T, Dimitrova V, Mazneikova V, Leroy Y, Jacquemyn Y, et al. Ultrasound screening and diagnosis of fetal structural abnormalities between 11-14 gestational weeks. Akush Ginekol (Sofiia) 2004; 43: 3-10.
14. Bahado-Singh RO, Wapner R, Thom E, Zachary J, Platt L, Mahoney MJ, et al. Elevated first-trimester nuchal translucency increases the risk of congenital heart defects. Am J Obstet Gynecol 2005; 192: 1357-61.
15. Krampl E. Screening of chromosome anomalies during the first trimester. Gynakol Geburtshilfliche Rundsch 2005; 45: 86-92.
16. Drysdale K, Ridley D, Walker K, Higgins B, Dean T. First-trimester pregnancy scanning as a screening tool for high-risk and abnormal pregnancies in a district general hospital setting. J Obstet Gynaecol 2002; 22: 159-65.
17. Souka AP, Von Kaisenberg CS, Hyett JA, Sonek JD, Nicolaides KH. Increased nuchal translucency with normal karyotype. Am J Obstet Gynecol 2005; 192: 1005-21.
18. Georgsson Ohman S, Saltvedt S, Grunewald C, Waldenstrom U. Does fetal screening affect women's worries about the health of their baby? A randomized controlled trial of ultrasound screening for Down's syndrome versus routine ultrasound screening. Acta Obstet Gynecol Scand 2004; 83: 634-40.
19. Chen M, Lam YH, Lee CP, Tang MH. Ultrasound screening of fetal structural abnormalities at 12 to 14 weeks in Hong Kong. Prenat Diagn 2004; 24: 92-7.

การตรวจกรองความพิการของทารกในครรภ์ช่วงอายุครรภ์ 11-14 สัปดาห์ ของสตรีตั้งครรภ์ในโรงพยาบาลมหาราชนครเชียงใหม่

เกษมศรี ศรีสุพรรณดิฐ, ธีระ ทองสง, สุพัตรา ศิริโชติยะกุล, พฤหัส จันทร์ประภาพ

วัตถุประสงค์: *เพื่อศึกษาหาอัตราการตรวจพบความพิการโดยกำเนิดชนิดต่าง ๆ ในปลายไตรมาสแรก (11-14 สัปดาห์) ด้วยการตรวจคลื่นเสียงความถี่สูง*

รูปแบบการศึกษา: *การศึกษาเชิงพรรณนา*

วัสดุและวิธีการ: *ทบทวนผลการตรวจคลื่นเสียงความถี่สูงของสตรีตั้งครรภ์จำนวน 597 รายที่ได้รับการตรวจคลื่นเสียงความถี่สูงในช่วงอายุครรภ์ 11-14 สัปดาห์ ที่โรงพยาบาลมหาราชนครเชียงใหม่ ซึ่งได้ทำการตรวจเพื่อวัดค่าความหนาของถุงน้ำสะสมใต้ต้นคอทารก รวมถึงความพิการทางโครงสร้างต่าง ๆ ของทารก และนำมาเปรียบเทียบกับผลลัพธ์สุดท้ายของการตั้งครรภ์ โดยใช้ความพิการแต่กำเนิดที่ตรวจพบเมื่อแรกคลอดโดยกุมารแพทย์ หรือ ผลการตรวจทางพยาธิวิทยาโดยพยาธิแพทย์ในกรณีที่แท้งเป็นเกณฑ์มาตรฐาน ซึ่งผลการศึกษาหลักที่ต้องการวัดเป็นอัตราของการตรวจพบความพิการโดยกำเนิดจากการตรวจด้วยคลื่นเสียงความถี่สูง*

ผลการศึกษา: *จากสตรีตั้งครรภ์ทั้งหมด 597 รายที่มีอายุเฉลี่ย 29.41 $\pm$ 5.8 ปี พบว่ามีอุบัติการณ์ของความพิการแต่กำเนิดทั้งหมดร้อยละ 4 (24 ราย จาก 597 ราย) และอัตราการตรวจพบความพิการโดยการตรวจคลื่นเสียงความถี่สูงในช่วง 11-14 สัปดาห์เป็นร้อยละ 58 (14 ราย จาก 24 ราย) โดยความพิการที่ตรวจพบได้มากที่สุดคือความผิดปกติของถุงน้ำบริเวณต้นคอและภาวะไม่มีกะโหลกศีรษะ ความพิการแต่กำเนิดที่มาพบภายหลังแต่ไม่สามารถตรวจพบได้จากการตรวจคลื่นเสียงความถี่สูงในช่วงปลายไตรมาสแรกคิดเป็นร้อยละ 42 (จำนวน 10 ราย จาก 24 ราย) นอกจากนี้ผลตรวจคลื่นเสียงความถี่สูงของสตรีตั้งครรภ์ทั้งหมด 597 ราย พบว่ามีทารกที่มีถุงน้ำสะสมบริเวณคอหนาผิดปกติจำนวน 16 ราย จาก 597 ราย (ร้อยละ 2.7) แต่ส่วนมากทารกมักมีผลการตรวจโครโมโซมเป็นปกติและไม่มีความพิการแต่กำเนิดหรือความผิดปกติใด ๆ*

สรุป: *การตรวจคลื่นเสียงความถี่สูงของสตรีตั้งครรภ์ในช่วงอายุครรภ์ 11-14 สัปดาห์น่าจะมีประโยชน์ในการค้นหาความพิการแต่กำเนิดของทารกในครรภ์ได้ ซึ่งอัตราของการตรวจพบความพิการค่อนข้างสูง และอาจนำมาใช้ร่วมกับการตรวจที่มีอยู่เดิมในปัจจุบันได้ต่อไป*