Prenatal Ultrasonographic Findings in "Trisomy 13"

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Objective: *To evaluate the accuracy of prenatal ultrasonographic diagnosis in fetuses with trisomy 13.*
Material Method: *The present study consisted of all fetuses diagnosed of trisomy 13 and delivered at Ramathibodi Hospital between 1997 and 2006.*
Results: *There were 15 cases of trisomy 13. Twelve cases (80.0%) were detected by prenatal ultrasonographic examination, and 3 cases (20.0%) were missed. Mean maternal age was 31.4 years old. Sixty-six percent were diagnosed in 2nd trimester (mean 19.4 weeks). The earliest gestational age for detection was 12 weeks 6 days. The most common abnormal ultrasonographic findings were holoprosencephaly (46.7%), and facial defects (40.0%).*
Conclusion: *The accuracy of prenatal sonographic diagnosis in trisomy 13 fetuses was 80%. The most sensitive prenatal ultrasonographic findings in trisomy 13 were holoprosencephaly and facial defects.*

Keywords: *Trisomy 13, Prenatal diagnosis, Ultrasonography*

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Trisomy 13 or Patau syndrome is the most severe form of three major autosomal chromosome abnormalities[1]. The trisomy 13 syndrome was first described by Patau in 1960[2]. The frequency of this syndrome is 1:3,000 live births[3]. Most of them are lethal anomalies. Those who survive have severe mental retardation, developmental delay and they fail to thrive[4]. Because the prognosis in this syndrome is extremely poor, early prenatal diagnosis is important/ so that the option of termination can be given to the parents. One definite prenatal diagnosis for this syndrome is chromosome analysis. However, chromosome analysis is not always desirable because it must be done by invasive procedures. Prenatal ultrasonography is a non-invasive screening procedure. Although prenatal ultrasonographic findings are not definite diagnosis, these findings can be an indication for making the definite diagnosis by invasive procedures. There are many features in trisomy 13 that have been reported by prenatal ultrasonographic findings, including central nervous system abnormalities, facial anomalies, cleft lip, cleft palate, urogenital anomalies/echogenic kidneys or pyelectasis, omphalocele, polydactyly of hands/feet or both, rocker bottom feet, cystic hygroma, echogenic intracardiac foci, mild ventriculomegaly, intrauterine growth retardation, single umbilical artery. The most common findings are holoprosencephaly accompanied by various facial defects[5-10].

The objective of the present study was to evaluate the accuracy of prenatal detection of trisomy 13 by using ultrasonography.

Material and Method

The present study was approved by the Ethical Committee, Faculty of Medicine, Ramathibodi Hospital. The present study consisted of all fetuses prenatally diagnosed of trisomy 13 and delivered at the Department of Obstetrics and Gynecology, Ramathibodi Hospital, from 1997 to 2006. All pregnant women were offered one routine ultrasonographic examination at 18-22 weeks' gestation, and additional ultrasonographic examinations were carried out only on clinical indication. However, in high risk pregnant cases or those

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who had selected for first trimester screening for Down syndrome, obtained an ultrasonographic examination in the first trimester. All scans were performed by an obstetrician who was trained as a level one sonographer. In cases of uncertain abnormal findings the women were reviewed by a level two sonographer with repeated scans. The majority of scans were performed on Hitachi (model EUB 415 Tokyo, Japan), Toshiba (model SSA-340 A 'ECCOCEE' Tokyo, Japan) or GE (model Voluson 730, Austria) scanners. The standardized protocol was utilized for all ultrasonographic examinations. Gestational age was based on ultrasonographic measurement of fetal biometry at a routine fetal examination. But in cases when no routine ultrasonographic examination had been done, gestational age was based on the last menstrual period (LMP). In cases with abnormal sonographic findings underwent chorionic villi sampling, amniocentesis or cordocentesis for chromosomal study or a postnatal study was performed. The inclusion criteria were proven trisomy 13 all cases by chromosomal study.

The data consisted of basic characteristics of these pregnant women, ultrasonographic detections, indications for ultrasonographic examination, outcomes of pregnancy, postnatal findings and autopsy reports.

Results

During the study period, there were 57,403 births that were conducted in Ramathibodi Hospital during the study period. There were 15 cases of trisomy 13. Twelve fetuses (80.0%) of trisomy13 were detected anomalies by prenatal ultrasonographic examination. Only 3 cases (20.0%) were missed. All abnormaly fetuses had ultrasonographic examination performed an average of two times in each case.

The demographic information, gestational age of diagnosis and indications for examination are shown in Table 1. The mean maternal age was 31.4 years (range 27-40). Two thirds of cases were multiparous. The prenatal diagnostic gestational age was between 12-24 weeks (mean 19.4 weeks). Ten (66.7%) cases were diagnosed during routine examination. The outcomes of pregnancy were termination of pregnancy in 11 cases (73.3%), 1 case (6.7%) died in utero and 3 cases (20.0%) died shortly after delivery. All were proven diagnosis by chromosome study. The abnormal prenatal ultrasonographic findings in the present study are shown in Table 2.

The most common prenatal sonographic findings in this study were holoprosencephaly (46.7%) and facial defects (40.0%) respectively. Almost all

Table 1. Demographic information

No.	Age	Gravida/ parity	Week of detection	Indication for ultrasound
1	31	2/1	postnatal	Non detected
2	30	3/1	19	Routine u/s
3	40	3/2	18	Routine u/s
4	36	1/0	postnatal	Non detected
5	30	3/2	postnatal	Non detected
6	28	2/1	20	Routine u/s
7	33	2/0	21	Routine u/s
8	34	3/2	21	Routine u/s
9	32	2/1	20	Routine u/s
10	27	1/0	12	1st trimester screening
11	33	1/0	21	Routine u/s
12	31	1/0	24	Suspected anomaly
13	28	2/1	20	Routine u/s
14	30	1/0	19	Routine u/s
15	32	3/2	18	Routine u/s

Routine u/s = routine screening ultrasonography

Table 2. Abnormal sonographic findings

Abnormal findings	n	%
Brain		
Holoprosencephaly (all alobar type)	7	46.7
Microcephaly	1	6.7
Occipital encephalocele	1	6.7
Face		
Facial cleft (4 cleft lip and cleft palate, 2 cleft lip)	6	40.0
Cyclopia	3	20.0
Proboscis	2	13.3
Low set ears	2	13.3
Micrognathia	1	6.7
Hypotelorism	1	6.7
Abnormal form of right ear	1	6.7
Neck		
Nuchal edema	1	6.7
Thorax		
Cardiac defects (3 PDA, 1 ASD)	4	26.7
Chest wall defect	1	6.7
Abdomen		
Abdominal wall defect	1	6.7
Extremities		
Polydactyly (hands/feet)	4	26.7
Others		
Fetal growth retardation	1	6.7
Hydrops fetalis	1	6.7

PDA = patent ductus arteriosus
ASD = atrial septal defect

cases had multiple anomalies. All holoprosencephalic fetuses were alobar type (Fig. 1). Five cases (33.3%) had both holoprosencephaly and facial defects (Fig. 2). The earliest detection in the present study had only abnormal nuchal translucency (3.5 mm) at 12 weeks 6 days by indication for screening of Down syndrome.

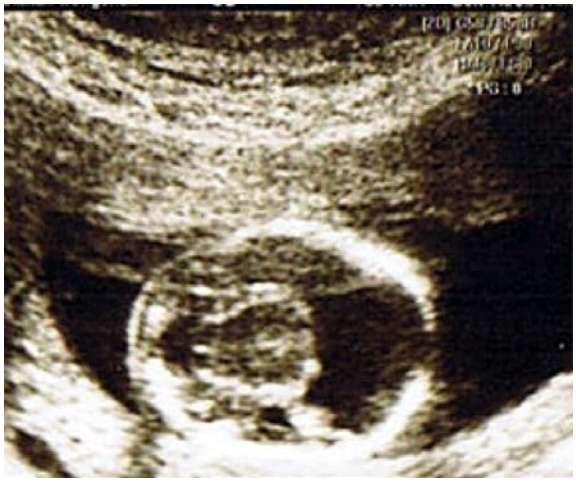
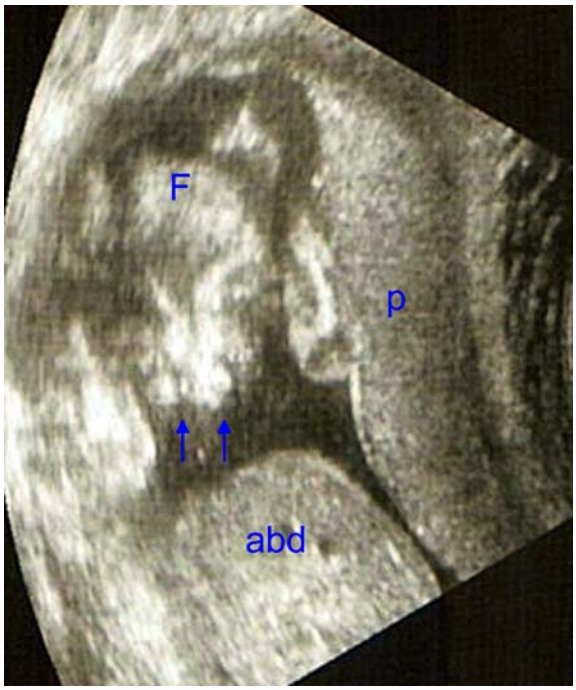


Fig. 1 Alobar holoprocencephaly



F = forehead, p = placenta, abd = abdomen

Fig. 2 Bilateral cleft lip (arrow)

In the 3 cases that were missed in routine ultrasonographic examination diagnosis were delivered at 38, 38 and 39 weeks gestation with the last case presented with severe preeclampsia. All had cardiac anomalies and neonatal death shortly after birth.

Discussion

During the last two decades, ultrasonography has been widely used for prenatal diagnosis, providing a non-invasive and non-harmful method for both mother and fetus. The prevalence of trisomy 13 in the present study was 3 in 10,000 births which is less than previously reported[3]. Prenatal ultrasonographic findings can be identified in 80.0% of these fetuses that are lower than previously reported[6]. The most common ultrasonographic features of trisomy 13 in the present study were holoprosencephaly associated with facial defect which was similar to other publications[3,4]. In the present study, all pregnant women were offered one routine ultrasonographic examination at 18-22 weeks' gestation; therefore most of the anomaly fetuses were detected at 20-21 weeks' gestation.

Holoprosencephaly is an intracranial abnormality that is categorized according to the severity of brain anomaly as alobar, semi-lobar, and lobar, for which the etiology is still not completely known. Several chromosomal abnormalities are associated with this condition with the most frequent being trisomy13[6,7,11]. The present study found holoprosencephaly in 46.7% of the cases, which was the same finding as in previously report[9]. In this, 71% of holoprosencephalic cases presented with facial anomalies, which was the same as in a previous study[12].

Even though holoprosencephaly is an extremely rare condition, it can be identified early through prenatal ultrasonographic findings of congenital anomalies. Because the primitive brain completes to divide at seven weeks gestation[11]. Thus, if all the pregnant women started to have an early prenatal ultrasongraphic, the prenatal sonographic finding of holoprosencephaly in 1st trimester such as holosphere or no butterfly sign were reported[8,13]. In the present study, there was an earliest detection (12 weeks 6 days' gestation) with only abnormal nuchal translucency thickness. That agrees with the Snijders et al study[14] who reported that 70% of fetuses with trisomy 13 had increased nuchal translucency. The 1st trimester screening program would be helpful and should be provided as a routine examination.

The other findings of trisomy 13 in this present study, apart from holoprosencephaly and

facial defects, were polydactyly and cardiac anomalies; these findings corresponded with the report of Tongsong, et al[5] However, another feature detection in the present study included nuchal edema, low set ears, intrauterine growth retardation, hydrops fetalis, abdominal and chest wall defect which can extend beyond with those of other syndromes, such as trisomy 18, trisomy 21 and Meckel-Gruber syndrome[5-8]. For this reason, all of these ultrasonographic features, except for holoprosencephaly and facial defects, may be of limited assistance in the screening for trisomy 13. The result of the present study agrees with many other published studies that holoprosencephaly with facial defects was the most sensitive marker for ultrasonographic screening of trisomy 13[5-9]. In the three missed cases in the present study, all of them presented cardiac anomalies with polydactyly, which might be difficult in only one routine scan at 18-22 weeks' gestation by a level one sonographer.

The degree of ultrasonographic findings depends on a variety of factors including the type of chromosomal abnormlities, gestational age at the time of examination, criteria for a positive finding, experience of sonographer and the quality of the ultrasound machine[6,9,10].

Conclusion

The accuracy of prenatal sonographic diagnosis in fetuses with trisomy 13 was 80%. The common abnormal prenatal sonographic findings were holoprosencephaly and facial defect. Early ultrasound scanning should be useful for detection.

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สิ่งตรวจพบก่อนคลอดในภาวะ Trisomy 13 ด้วยคลื่นเสียงความถี่สูง

สมศรี พิทักษ์กิจรณกร, ปัทมา พรหมสนธิ, พัญญู พันธ์บูรณะ, รสิก รังสิปราการ, อภิชาติ จิตต์เจริญ

วัตถุประสงค์: *เพื่อประเมินความแม่นยำของการใช้คลื่นเสียงความถี่สูงในการช่วยวินิจฉัยภาวะ Trisomy 13 ก่อนคลอด*

วัสดุและวิธีการ: *ศึกษาทารกทุกรายที่คลอดหรือแท้งในโรงพยาบาลรามาธิบดีที่ได้รับการวินิจฉัยเป็น Trisomy 13 ระหว่างปี พ.ศ. 2540-2549*

ผลการศึกษา: *พบทารก 15 ราย ที่ได้รับการวินิจฉัยเป็น Trisomy 13 และมีความชุก 3 รายใน การคลอด 10,000 ราย ในจำนวนนี้สามารถตรวจพบก่อนคลอดด้วยคลื่นเสียงความถี่สูง 12 ราย (ร้อยละ 80) และไม่สามารถตรวจพบก่อนคลอด 3 ราย (ร้อยละ 20) ค่าเฉลี่ยของอายุมารดาขณะตั้งครรภ์เท่ากับ 31.4 ปี สองในสามของมารดากลุ่มนี้เป็นการตั้งครรภ์หลังเป็นส่วนใหญ่ (ร้อยละ 66.7) โดยได้รับการวินิจฉัยก่อนคลอดในไตรมาสที่สองของการตั้งครรภ์ (ค่าเฉลี่ย 19.4 สัปดาห์) สามารถตรวจพบความผิดปกติได้เร็วที่สุดที่อายุครรภ์ 12 สัปดาห์ ความผิดปกติที่พบบ่อยจากการตรวจด้วยคลื่นเสียงความถี่สูงก่อนคลอดคือมีความผิดปกติของเนื้อสมองแบบ holoprocencephaly ร้อยละ 46.7 และมีความผิดปกติของใบหน้าทารกร้อยละ 40 ตามลำดับ*

สรุป: *ความแม่นยำของการใช้คลื่นเสียงความถี่สูงในการช่วยวินิจฉัยภาวะ Trisomy 13 ก่อนคลอดพบได้ร้อยละ 80 ความผิดปกติที่สามารถตรวจพบด้วยคลื่นเสียงความถี่สูงก่อนคลอดที่ช่วยคัดกรองภาวะ Trisomy 13 ได้แม่นยำมากขึ้น คือความผิดปกติของเนื้อสมองแบบ holoprocencephaly และความผิดปกติของใบหน้าทารก*