The Value of Mid-Trimester Routine Ultrasonographic Screening in Antenatal Detection of Congenital Malformations

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Objective: *To evaluate the detection rate of major fetal anomalies by mid-trimester routine ultrasound screening in a single center with low-risk population.*
Material and Method: *The present study was a cross sectional study. All pregnant women attending the antenatal clinic between January 1996 and December 2002 had routine ultrasound screening between 18-22 weeks'gestation. The ultrasonographic results were compared with the pregnancy outcome in aspects of prediction of major fetal anomalies.*
Results: *Three hundred and sixteen fetuses out of 29,839 (1.06%) had major anomaly. One hundred and forty four fetuses (45.57%) were diagnosed as having major anomaly by routine ultrasound screening. One hundred and seventy two fetuses (54.43%) were undiagnosed. The sensitivity, specificity, positive predictive value, and negative predictive value were 45.57%, 99.97%, 94.74% and 99.42% respectively.*
Conclusion: *Although the rate of the detection of major congenital fetal anomaly was low, almost all lethal and life threatening anomalies could be diagnosed antenatally thus allowing the option of counseling, pregnancy termination, or selective referral.*

Keywords: *Congenital abnormalities, Second trimester pregnancy, Prenatal ultrasonography*

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Major fetal anomalies occur in approximately 2-3% of the general population and these accounts for 20 - 30% of perinatal deaths in developed countries[1-3].

Many clinicians advocate routine ultrasound screening of the fetus during second trimester of pregnancy to detect congenital anomalies, multiple pregnancy, placental abnormalities, and to assess gestational age[4]. The RADIUS (Routine Antenatal Diagnosis Imaging with Ultrasound Study)[4,5] reported that only 17% of anomalous fetuses are detected by ultrasonography performed between 15 and 22 weeks in a low-risk population. Within a subgroup evaluated at tertiary care centers, the detection rate of anomalous fetuses is 35%. Anomaly detection rates in other published series ranges from 21% to 84%[4,6-13].

Ramathibodi Hospital is one of the medical schools in the central part of Thailand where one-stage ultrasonographic screening to pregnant women during 18-22 weeks' gestation has been available since 1993. The authors set up a pilot study in 1994, and concluded that mid-trimester routine ultrasonographic screening in pregnant women seems to be beneficial[14]. Since then, all pregnant women who attended our department before 22 weeks' gestation had routine ultrasound screening.

The specific aim of the present analysis was to evaluate the relative sensitivity, specificity, and positive and negative predictive values for detection of major congenital fetal anomalies by mid-trimester

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routine ultrasound screening in a single center with low-risk population.

Material and Method

The present study population consisted of 29,839 normal pregnant women who underwent second-trimester (18 to 22 weeks' gestation) ultraso-nographic scanning while attending prenatal care, and were delivered (or terminated) at the Department of Obstetrics and Gynecology, Ramathibodi Hospital between January 1, 1996 and December 31, 2002.

All scans were performed by an obstetrician who was trained as a level one ultrasonography. In cases of uncertain abnormal findings, the women were reviewed by a level two obstetrician with repeated scans. The majority of scans were performed on Hitachi (model EUB 415 Tokyo, Japan) or Toshiba (model SSA-340 A 'ECCOCEE' Tokyo, Japan) scanners. The standardized protocol was utilized for all ultrasonographic examinations. Specific components of the examination included assessment of placental location, amniotic fluid volume, uterine and adnexal pathologic conditions, fetal number, presentation, cardiac activity, ultrasonographic biometry (biparietal diameter, head circumference, abdominal circumference, and femur length), and a fetal anatomy survey (including cerebral ventricle, four chamber view of fetal heart, fetal stomach, abdominal wall and cord insertion, fetal renal region and urinary bladder, fetal spine, and extremities). Congenital malformations identified by chart abstraction were divided into major and minor categories. Major malformations are defined as birth defects that require medical or surgical intervention and/or have significant impact from a functional or cosmetic perspective[4,13]. Major anomalies are further subdivided depending on whether they are potentially detectable by obstetric ultrasonography.

Women with suspected fetal anomalies were counseled by a combination of (1) certified genetic counselors, (2) a pediatric geneticist, and (3) maternal fetal medicine specialists.

All cases with major fetal anomaly findings were confirmed by chromosomal study, gross appearance, and autopsy by a pathologist for each anomaly and outcome of pregnancy.

All women with major fetal anomalies diagnosed before 24 weeks were offered termination of pregnancy in accordance with hospital guidelines.

Pregnancy outcomes were followed and the details were obtained from maternal and neonatal records.

The data was analyzed by two by two table to evaluate the relative sensitivity, specificity, positive, and negative predictive values and accuracy of the ultrasonographic examination.

Results

During the present study period, 29,839 pregnant women were scanned at 18-22 weeks' gestation. Three hundred and sixteen cases (1.06%) of all pregnant women had major fetal anomaly. In these cases, the routine screening ultrasound detected 144 cases of fetal anomaly (45.57%) and 172 cases (54.43%) were not detected by the routine screening ultrasound. All of hydrops fetalis, conjoined twins, and multiple anomalies were detected. Of the 172 (54.43%) fetuses with anomalies that were missed by routine screening ultrasound, they had anomaly such as cleft lip/cleft palate or both, cardiac, skeletal, pulmonary, gastro-intestine, genitourinary, or central nervous system (Table 1).

The validity of second-trimester ultrasonography in detecting the fetal anomaly is shown in Table 2, the sensitivity was 45.57%, the positive predictive value was 94.74%, specificity was 99.97%, negative predictive value was 99.42%, and accuracy was 99.40%. False positive in the present study was 2.53%. Of the 316 anomalous fetuses, 87 cases (27.53%) had termination of pregnancy (28 anencephaly, 14 hydrops fetalis, two renal agenesis, one gastroschisis, three conjoined twins, two multiple anomalies, two cardiac malformation, three holoprosencephaly, eight ventriculomegaly, one sacrococcygeal teratoma, five meningoencephalocele, one exencephaly, seven cystic hygroma, four omphalocele, one diaphragmatic hernia, two bilateral polycystic kidney, one posterior urethral valve obstruction, and two short limb skeletal dysplasia).

Discussion

The present study was designed to determine the accuracy of routine mid-trimester ultrasonography for anomaly detection in a single tertiary care center with approximately 500-600 deliveries per month. The present study included only those pregnant women that received their antenatal care and were delivered or terminated at Ramathibodi Hospital. The authors' analysis was limited to the population who had early booking. This was done to avoid referral bias that would artificially increase both our prevalence and sensitivity.

In the present study of 29,839 pregnant women scanned for fetal anomalies, for a major fetal anomaly,

Table 1. Major fetal anomaly detection by routine ultrasound

	Detected (n = 144)	Undetected (n = 172)
Central nervous system (56 cases)	53 (94.64%)	3 (5.36%)
Anencephaly	28	0
Microcephaly	1	0
Holoprosencephaly	4	0
Ventriculomegaly	13	0
Sacrococygeal mass	1	0
Myelomeningocele	5	3
Excencephaly	1	0
Marked Cystic hygroma* (7 cases)	7 (100%)	0 (0%)
Cardiac (54 cases)	7 (12.96%)	47 (87.04%)
Dextrocardia	1	3
Cardiomegaly (Ebstein's anomaly)	1	0
Congenital heart block	1	0
Cardiac malformation	4	44
Diaphragmatic hernia (4 cases)	2 (50.00%)	2 (50.00%)
Gastrointestinal (23 cases)	14 (60.87%)	9 (39.13%)
Abdominal mass (Hepatic hemangioma)	1	0
Gastroschisis	2	1
Omphalocele	7	2
Tracheoesophageal fistula	0	1
Stomach perforation	0	1
Duodenal atresia	2	2
Jejunal atresia	2	1
Esophageal atresia	0	1
Genitourinary (27 cases)	19 (70.37%)	8 (29.63%)
Hydronephrosis (Obstruction of UPJ 6cases, UVJ 2 cases)**	8	4
Polycystic kidney	7	1
Posterior uretheral valve obstruction	2	0
Renal agenesis	2	0
Hypospadias	0	3
Skeletal (30 cases)	13 (21.67%)	47 (78.33%)
Polydactyly	0	15
Short limb skeletal dysplasia	13	17
Club foot	0	15
Hydrops fetalis (21 cases)	21 (100%)	0 (0%)
Conjoined twins (3 cases)	3 (100%)	0 (0%)
Multiple anomalies (5 cases)	5 (100%)	0 (0%)
Cleft lip / Cleft palate or both	0	56 (100%)

* Turner's syndrome 6 cases and 1 case of Trisomy 18
** UPJ = Uretero-pelvic junction, UVJ = Uretero-vesical junction

Table 2. Validity of routine screening ultrasonography

Ultrasonographic diagnosis	Neonatal diagnosis		Total
	Anomaly (%)	Normal (%)	
Anomaly	144 (45.57%)	8 (2.53%)	152
Normal	172 (54.43%)	29,515	29,687
Total	316 (1.06%)	29,523	29,839

Sensitivity = 45.57%, Specificity = 99.97%, Positive predictive value = 94.74%, Negative predictive value = 99.42%, False positive = 2.53%

Table 3. Comparison of studies evaluating second-trimester ultrasonography for fetal anomaly detection

	Our study	RADIUS[3]	Helsinki Trial[5]	Levi et al[6]	Chitty et al[7]	Shirley et al[9]	Luck[9]	Anderson et al[10]	MUSC[11]	Eurofetus[12]
	1996-2002	1987-1991	1986-1987	1984-1989	1989-1990	1989-1990	1988-1991	1991-1993	1993-1996	1990-1993
No. of fetuses and neonates	29,839	7,685	4,691	16,353	8,432	6,183	8,523	7,880	2,031	61 centers.
Prevalence (%)	1.06	2.4	0.43	2.3	1.5	1.4	1.95	1.98	3.0	
Sensitivity (%)	45.57	16.6	40.9	21	74.4	60.7	84.3	60	75.0	61.4
Specificity (%)	99.97	99.9	99.8	99.9	99.98	99.98	99.9		99.9	84
PPV (%)	94.74	83.8	64.3	100	97.9	98.1	98.6		95.7	
NPV (%)	99.42	99.9	99	98.7	99.6	99.5	99.7		99.2	
False positives	8 (2.53%)	6 (0.07%)		8 (0.05%)	2 (0.02%)	1 (0.02%)	2 (0.02%)		2 (0.10%)	305 (9.9%)
Timing of scan (week)	18-22	15-22	16-20	18-20	18-20	19	19	16-20	15-22	18-22
Termination of pregnancy rate	0.29% (87)	0.11% (9)	0.23% (11)		0.61% (52)	0.47% (29)	0.22% (19)	0.53% (42)	0.54% (11)	27%

PPV: positive predictive value; NPV: negative predictive value
RADIUS: Routine Antenatal Diagnostic Imaging with Ultrasound Study
MUSC: Medical University of South Carolina
Euroferus: Eurofetus study group

the prevalence was 1.06% (n = 316). One hundred forty four cases (45.57%) of these fetuses were diagnosed but 172 cases (54.43%) of newborns with major anomalies were not detected antenatally. The sensitivity, specificity, and accuracy were 45.57%, 99.97%, and 99.40% respectively.

The present study probably had the largest sample size in any single centre but the diagnostic value was not different from the previous reported studies[4,6-13] (Table 3). Low sensitivity in the present study could possibly be explained by the wide range of anomaly detection reported here and the following considerations.

(1) differences in neonatal ascertainment, for example cleft lip, cleft palate,

(2) differences in what is considered a major anomaly,

(3) differences in what is considered to be a major ultrasonographically detectable,

(4) the risk status of the population

(5) operator's experience and

(6) time allocated per scan

It is important to note that the highest detection rate was in the central nervous system, while lower detection rate were in in cardiac, skeletal, and cleft lip/cleft palate. These results reflected the conditions previously mentioned.

Careful consideration of the 172 missed anomalies in the present study suggested that the nature of these anomalies might also be responsible for this lower rate of detection. This is because there were a disproportionate number of difficulties to diagnose anomalies and late appearing anomalies in this group. Fifty fetuses had anomalies that could be not detected due to ultrasonographic operator's experience (one with lumbosacral meningocele, two with spina bifida, and forty-seven cases with cardiac anomalies). Fifty-six cases of missed cleft lip/cleft palate could have been easily diagnosed by ultrasonography, especially cleft lip. It is possible that there were many women to be scanned at each time by a level one operator or the definition that the authors' regard as minor anomalies, for example cleft lip/cleft palate have contributed to this. The diagnosis would not have changed the management and therefore the authors did not spend too much time scanning for this type of anomaly. The authors concentrated only on lethal major anomaly and paid little attention on such as cleft lip/cleft palate, hypospadias, polydactyly, or club foot.

False-positive diagnosis was rare and slightly higher than in other previous studies (Table 3), thus, it might cause anxiety for the concerned parents. To date, there is no study specifically designed to evaluate the psychological impact of such diagnosis. The false-positive in the present study was debatable because three cases of unexplained nonimmune hydrops could be considered positives that resolved before delivery; the others false-positive might be from the sonologist's experience (1 microcephaly, 2 cardiac malformations, and 2 ventriculomegaly). Fortunately, neither of these fetuses was terminated.

Routine anomaly screening improves perinatal outcome most directly through termination of pregnancy for certain anomalies. Fetuses with conditions that require immediate postnatal pediatric surgery can be referred to an appropriate center[15-18]. In the present study, a special group requiring surgery encompassed those with urinary tract anomalies, the same as in a previous report[15]. Although some parents who are confronted with the diagnosis of a lethal or severely impairing fetal disease frequently choose termination of pregnancy, many parents will not necessarily opt initially to termination, but are grateful for the opportunity to prepare them for an adverse pregnancy outcome. Some parents will choose to terminate pregnancy when a non-life-threatening condition is diagnosed in their fetuses, but this is a very personal decision that, in pre-viable fetuses, is in the hands of the patient, not the caregivers.

In conclusion, with these diagnostic capabilities the advantages of mid-trimester routine ultrasonographic screening for major fetal anomalies was useful in the presented population although the rate of the detection was low. Almost all lethal and life-threatening anomalies could be diagnosed antenatally to allow the options of counseling, pregnancy termination, or selective referral. However, the sensitivity in the present study is not much different from the others. The importance of additional factors for successful scanning is emphasized, such as education, equipment quality, and fetal ultrasound examination at different gestational ages, for a better understanding of natural history of fetal morphology[19].

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การตรวจหาความผิดปกติของทารกในครรภ์ด้วยคลื่นเสียงความถี่สูงที่ระยะกลางไตรมาสของการตั้งครรภ์

สมศรี พิทักษ์กิจรณกร, อภิชาติ จิตต์เจริญ, ธวัช เจตน์สว่างศรี, พัญญู พันธ์บูรณะ, อดิเทพ เชาว์วิศิษฐ, รสิก รังสิปราการ, นพดล สโรบล, ยงยุทธ เหราบัติ

วัตถุประสงค์: *เพื่อประเมินอัตราการตรวจพบความผิดปกติของทารกในครรภ์ด้วยคลื่นเสียงความถี่สูงที่ระยะกลางไตรมาสของการตั้งครรภ์*

วัสดุและวิธีการ: *ศึกษาในสตรีตั้งครรภ์ทุกรายที่มาฝากครรภ์ตั้งแต่มกราคม พ.ศ. 2539 ถึงธันวาคม พ.ศ. 2545 ที่ได้รับการตรวจด้วยคลื่นเสียงความถี่สูงที่ช่วงอายุครรภ์ 18-22 สัปดาห์ โดยศึกษาเปรียบเทียบผลการตรวจพบความผิดปกติของทารกในครรภ์ด้วยคลื่นเสียงความถี่สูงที่ระยะกลางไตรมาสของการตั้งครรภ์กับผลการตั้งครรภ์*

ผลการศึกษา: *จากการศึกษาสตรีตั้งครรภ์จำนวน 29,839 ราย พบความพิการแต่กำเนิด 316 ราย (ร้อยละ 1.06) โดยสามารถให้การวินิจฉัยได้ด้วยคลื่นเสียงความถี่สูงที่ระยะกลางไตรมาสของการตั้งครรภ์ 144 ราย (ร้อยละ 45.57) และไม่สามารถให้การวินิจฉัยได้ 172 ราย (ร้อยละ 54.43) ค่า sensitivity, specificity, positive predictive value, negative predictive value เท่ากับร้อยละ 45.47, 99.97, 94.74และ 99.42 ตามลำดับ*

สรุป: *แม้ว่าอัตราการตรวจพบความผิดปกติของทารกในครรภ์ด้วยคลื่นเสียงความถี่สูงที่ระยะกลางไตรมาสของการตั้งครรภ์จะไม่สูง แต่ก็สามารถวินิจฉัยภาวะความผิดปกติที่รุนแรงก่อนคลอดได้ ซึ่งจะช่วยในการแนะนำการดูแลครรภ์ การยุติการตั้งครรภ์ต่อไป*