

Accuracy of Ultrasonography Performed by Thai Maternal Fetal Medicine Fellowship at Songklanagarind Hospital for Fetal Sex Determination during Second Trimester Genetic Amniocentesis

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Objective: To evaluate the accuracy of fetal sex determination using ultrasonography performed by Thai Maternal Fetal Medicine fellowships during second trimester genetic amniocentesis and also identify the possible factors of inaccurate determination.

Material and Method: A prospective non-random study was conducted to evaluate the accuracy of fetal sex determination using ultrasonography performed by Thai Maternal Fetal Medicine fellows at Songklanagarind Hospital during second trimester genetic amniocentesis and also identify the possible factors of inaccurate determination.

Results: Five hundred and sixty singleton pregnant women were enrolled. Eight cases were excluded due to abnormal fetal karyotype. No pregnancy loss or fetal ambiguous genitalia presented. The sex of 11/552 (1.99%) fetuses could not be adequately determined by ultrasonography. Overall, 491 of the 541 diagnoses were correct – an accuracy of 90.8% (CI 88.0-93.1) given an ultrasonographic diagnosis could be made. Among phenotypic females, the accuracy was 226/246, (91.9%; 95% CI 87.7-95.0) and among phenotypic males, the accuracy was 265/295 (89.8%; 95% CI 85.2-92.4). The ultrasonographic diagnosis of female sex was correct in 226/256, (88.3%; 95% CI 84.0-92.0), and the ultrasonographic diagnosis of male sex was correct in 265/285, (93.0%; 95% CI 89.4-95.7). For both sexes combined and for female fetuses, year of fellowship was only significant variable associated with correct sex determination by ultrasonography [2nd year vs. 1st year: overall ORS 2.55, (95% CI 1.44-4.61); female fetuses ORS 6.54, (95% CI 2.48-17.26)].

Conclusion: Fetal sex determination using ultrasonography by Thai Maternal Fetal Medicine Fellows at Songklanagarind Hospital during second trimester genetic amniocentesis is possible. Less experienced physicians should be had increased awareness especially in case of female external genitalia diagnosis.

Keywords: Amniocentesis, Sex determination, Ultrasonography, Advance maternal age

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Fetal sex determination is one interesting part during prenatal ultrasonography. Generally, there are only a small number of medical reasons which indicate the need for antenatal sex determination such as an x-linked inherited risk pregnancy or multiple gestations⁽¹⁾. Family curiosity is the principal reason

for antenatal fetal sex determination. Fetal internal and external genitalia are normally indistinguishable until 8 weeks of gestation and sex determination of fetus is usually carried out only after the 12th week of gestation⁽²⁾ and conducted by an experienced maternal fetal medicine specialist^(3,4).

In Thailand, a developing country, antenatal ultrasonographic examinations, including fetal sex determination, is usually performed by a general obstetrician and radiologist, rather than an experienced specialist. Moreover, there are limited facilities in the country for antenatal ultrasonography especially in rural

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areas. Advanced maternal age pregnancies are generally referred to a tertiary center for genetic amniocentesis, and this is the only chance for many pregnant women to undergo ultrasonography. During genetic amniocentesis, most patients also request sex determination, a request which is usually accommodated if possible. However, the accuracy of sex determination during second trimester genetic amniocentesis in Thailand has never been evaluated. Therefore, we conducted this study with the primary objective of evaluating the accuracy of antenatal fetal sex determination by Thai Maternal Fetal Medicine fellow during second trimester genetic amniocentesis and secondarily to examine factors influencing the accuracy of the procedure.

Material and Method

This prospective non-random study was performed after receiving Institutional Ethics Committee approval. Singleton pregnant woman who were scheduled for second trimester genetic amniocentesis from June 2013 to June 2014 because of advanced maternal age at the Maternal Fetal Medicine Unit, Department of Obstetrics and Gynecology, Songklanagarind Hospital, the major tertiary care facility and referral hospital in southern Thailand, and a university hospital, were enrolled in the study. After routine pre-procedural counseling accompanied, and detailed information about our study was given to all participants, all participants were asked to provide informed consent. Then, ultrasonographic examination was initially done for determine fetal numbering, gestational age determination, structural screening, placental location and needle puncture site. Placenta location means of the location that does or does not obscure for fetal sex determination was determined. Finally, fetal sex was adjunctively documented. The ultrasonographic information about fetal sex diagnosis was given if the participants requested it. All ultrasonographic examinations were performed by our 1st (F1) or 2nd (F2) year Maternal Fetal Medicine fellows. There were two 2nd year and one 1st year fellows in this study. The allocation randomly assigned based on routine schedule. All examinations were performed using transabdominal convex transducer of ultrasonographic machine model E8 GE medical system, Wisconsin, USA). The ultrasonographic determination of fetal sex was based on the fetal external genitalia visualization, which was separated into 3 categories as follows: (1) female: 2 pairs of parallel linear echo folds, the medial fold (labia minora) smaller than lateral fold

(labia majora); (2) male: medial pair of folds elongated and fused along midline enclosing the urethra forming the penis, penis and scrotum presented; (3) unable to determine. After finishing of ultrasonographic process, our unit staff who were qualified a Thai Maternal Fetal Medicine subspecialist performed the amniocentesis under continuous real-time ultrasonographic guidance with free-hand technique, using a 23-gauge needle. Approximately 16-20 ml of amniotic fluid was taken from each participant. All participants were checked for fetal heart activity after the needle was withdrawn and were asked to rest for around 30 minutes before discharge from the unit.

The participants' basic demographic characteristics, including maternal age, parity, gestational age, weight and height, were ascertained and recorded. The fetal karyotype and final phenotype were recorded. Hospital neonatal record forms were reviewed in cases which were delivered in our hospital and telephone interviews conducted in cases which were delivered elsewhere. Multifetal gestation, abnormal fetal karyotypes, fetal losses and stillbirths were excluded from analysis. The phenotypes at birth were documented into 3 categories as follows: (1) boy; (2) girl; and (3) ambiguous genitalia.

The required sample size was calculated in order to estimate the percentage accuracy of ultrasonographic sex determination with an acceptable precision. Based on previously published data⁽⁵⁻⁷⁾, it was expected that the accuracy would be around 90%. To obtain a percentage ± 3 percentage points and 5% of unsuccessful determination, an overall sample size of 406 fetuses was required. Assuming approximately equal numbers of male and female fetuses, this would provide a precision within each sex ± 4.2 percentage points. Patients' baseline demographic data were presented as percentage, means and standard deviation. Univariate and multivariate logistic regression analysis were done for present the influence factors association with fetal sex determination accuracy for individual sex. In all statistical tests, *p*-values of <0.05 were considered significant. STATA software version 10 (StataCorp, College Station, TX) was used for all analyses.

Results

Five hundred and sixty singleton pregnant women who underwent a second trimester genetic amniocentesis due to advanced maternal age were recruited into our study. Eight cases were excluded from analysis because of the presence of abnormal fetal

karyotype. Table 1 present the patients' demographic data (maternal age, BMI, nulliparity and gestational age), ultrasonographic findings (placental location and amount of amniotic fluid) and year of fellowship of the operator. There was no pregnancy loss, fetal ambiguous genitalia or abnormal amount of amniotic fluid in the study. Table 2 presents the number of fetuses diagnosed as male and as female and unable to be diagnosed and the phenotype seen at birth. The external genitalia of 11 of the 552 participants (1.99%) could not be adequately visualized to make a diagnosis of the sex. Overall, 491 of the 541 diagnosis were correct – an accuracy of 90.8% (CI 88.0-93.1), given an ultrasonographic diagnosis could be made. Among phenotypic females, the accuracy was 226/246 (91.9%; 95% CI 87.7-95.0), and among phenotypic males, the accuracy was 265/295 (89.8%; 95% CI 85.2-92.4). The

ultrasonographic diagnosis of female sex was correct in 226/256 (88.3%; 95% CI 84.0-92.0), and that of male sex was correct in 265/285 (93.0%; 95% CI 89.4-95.7). Table 3 and 4 present the univariate and multivariate analyses for factors associated with the accuracy of diagnosis of fetal sex. For both sexes combined and for female fetuses, year of fellowship was the only significant variable associated with correct sex determination by ultrasonography [2nd year vs. 1st year: sexes combined ORS 2.55 (95% CI 1.44-4.61); female fetuses ORS 6.54 (95% CI 2.48-17.26)]. There was no evidence that any of the examined variables was associated with correct sex determination by ultrasonography in male fetuses.

Discussion

Our study is the first study in Thailand to evaluate the probabilities of correct fetal sex determination during the second trimester genetic amniocentesis. A few reports have reported the feasibility of fetal sex determination during second trimester amniocentesis using ultrasonography^(5,6). Reece et al studied 115 patients in 1987 and found the overall accuracy rate of prediction to be around 92.7%. Meagher et al in 1996 reported that sex determination could be done in 93.3% of fetuses with 99.3% accuracy during second trimester amniocentesis. Both studies found higher accuracy than in our present study. We postulate that with the operators in both earlier studies were highly experienced maternal fetal medicine specialists unlike in our study which the operators were 1st and 2nd year of fellows. Indeed, the influence of operator experience was presented in our study. More experienced doctors (2nd year fellowship) archived higher accuracy than less experienced doctors (1st year fellowship). Thus, we suggest that the accuracy in our study may represent the expected accuracy of fetal sex determination using ultrasound during second trimester when conducted by Thai general obstetricians. The assessment of ultrasonographic sex determination during second trimester by fellowship training physicians is an important advantage of our study.

Our study found that more error occurred with

Table 1. Patient demographic and ultrasonographic characteristics

Characteristic	Number (%) or mean (SD) (n = 552)
Age (years), mean (SD)	37.4 (2.69)
BMI (kg/m ²), n (%)	
<18.5	16 (2.9)
18.5-25	325 (58.9)
>25	211 (38.2)
Nulliparous, n (%)	
Yes	184 (33.3)
No	368 (66.7)
Placental location, n (%)	
Anterior	257 (46.6)
Posterior	295 (53.4)
Gestational age (days), n (%)	
112-118	148 (26.8)
119-126	300 (54.3)
127-144	104 (18.8)
Year of fellowship, n (%)	
1 st year	149 (27.0)
2 nd year	403 (73.0)

Table 2. Accuracy of sex determination

	Girl baby at delivery	Boy baby at delivery	Total
Ultrasonography diagnosed as female fetus	226	30	256
Ultrasonography diagnosed as male fetus	20	265	285
Unable to diagnosed by ultrasonography	6	5	11
Total	252	300	552

Table 3. Univariate analysis for factor associated with correct sex determination by ultrasonography according to baby's sex

Variable	Boy		p-value	Girl		p-value
	Total	Correct n (%)		Total	Correct n (%)	
Maternal age (years)			0.05			0.83
35-36	119	108 (90.8)		121	112 (92.6)	
36-40	139	128 (92.1)		87	80 (92.0)	
>40	37	29 (78.4)		38	34 (89.5)	
BMI (kg/m ²)			0.49			0.80
<18.5	9	8 (88.9)		7	6 (85.7)	
18.5-24.99	177	162 (91.5)		143	131 (91.6)	
≥25	109	95 (87.2)		96	89 (92.7)	
Parity			0.48			0.25
Nulliparous	101	89 (88.1)		82	73 (89.0)	
Multiparous	194	176 (90.7)		164	153 (93.3)	
Gestational age (days)			0.12			0.51
112-118	73	61 (83.6)		67	61 (91.0)	
119-126	167	154 (92.2)		130	118 (90.8)	
127-144	55	50 (90.9)		49	47 (95.9)	
Placental location			0.15			0.58
Anterior	135	125 (92.6)		113	105 (92.9)	
Posterior	160	140 (87.5)		133	121 (91.0)	
Year of fellowship			0.50			<0.01
1 st year	83	73 (88.0)		63	50 (79.4)	
2 nd year	212	192 (90.6)		183	176 (96.2)	

Table 4. Multivariate analysis of factors associated with correct sex determination by ultrasonography according to baby's sex

Baby sex	Variable	Level	ORS	95% CI	p-value
Girl	Year of fellowship	1 st year	1	-	<0.01
		2 nd year	6.54	2.48, 17.26	
Both sex	Year of fellowship	1 st year	1	-	<0.01
		2 nd year	2.55	1.41, 4.61	

ultrasonographic diagnosis as female with that as male. We postulate that obscuring of the prominent penis character by fetal position may mislead the operator. So, we suggest that less experienced physician should have increased awareness for fetal sex diagnosis when the fetus is suspected to be female by ultrasonographic examination. Moreover, an influence of gestational age, maternal age, maternal body mass index, parity and placental location on fetal sex determination accuracy was not found in our study. By contrast, gestational age appeared to be a significant factor in correct fetal sex determination in previous studies^(7,8).

In conclusion, fetal sex determination using ultrasonography during second trimester genetic amniocentesis is feasible. However, the less experienced physician should have increased awareness, especially in the case of suspected female external genitalia. Counselling about the accuracy should be provided to all pregnant women because an incorrect determination can affect the psychological and mental health of the family⁽⁹⁾.

What is already known on this topic?

Family curiosity is the principal reason for

antenatal fetal sex determination.

Fetal internal and external genitalia are normally indistinguishable until 8 weeks of gestation.

Sex determination of fetus is usually carried out only after the 12th week of gestation.

What this study adds?

It is possible to determine fetal sex determination using ultrasonography by Thai Maternal Fetal Medicine Fellows during second trimester genetic amniocentesis.

Less experienced physicians should be had increased awareness especially in case of female external genitalia diagnosis.

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Potential conflicts of interest

None.

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ความแม่นยำในการวินิจฉัยเพศทารกในครรภ์โดยแพทย์ประจำบ้านต่อยอดเวชศาสตร์มารดาและทารกในครรภ์
โรงพยาบาลสงขลานครินทร์ขณะตรวจ คลื่นเสียงความถี่สูงก่อนการเจาะตรวจเยื่อถุงน้ำคร่ำช่วงไตรมาสที่สอง

ธารารัตน์ หาญประเสริฐพงษ์, อุ่นใจ กอนันตกุล, อลัน กีเตอร์, จิตเกษม สุวรรณรัฐ, สุรัชย์ พงศ์หล่อพิศิษฎ์, ชุขณา เพชรพิเชฐเชียร,
มนภัทร สุกใส

วัตถุประสงค์: เพื่อศึกษาความถูกต้องในการวินิจฉัยเพศของทารกในครรภ์ด้วยการตรวจคลื่นเสียงความถี่สูงโดยแพทย์ประจำบ้านต่อยอดเวชศาสตร์มารดา
และทารกในครรภ์โรงพยาบาลสงขลานครินทร์ก่อนการเจาะตรวจเยื่อถุงน้ำคร่ำช่วงไตรมาสที่สองของการตั้งครรภ์

วัสดุและวิธีการ: เป็นการศึกษาแบบไปข้างหน้าเพื่อประเมินความถูกต้องในการวินิจฉัยเพศของทารกในครรภ์ด้วยการตรวจคลื่นเสียงความถี่สูงโดย
แพทย์ประจำบ้านต่อยอดเวชศาสตร์มารดาและทารกในครรภ์โรงพยาบาลสงขลานครินทร์ก่อนการเจาะตรวจเยื่อถุงน้ำคร่ำช่วงไตรมาสที่สองของการตั้งครรภ์
และแสดงปัจจัยที่สัมพันธ์กับการวินิจฉัยคลาดเคลื่อน

ผลการศึกษา: มีหญิงตั้งครรภ์ที่เข้าร่วมการศึกษา 560 คน โดยคัดออกภายหลัง 8 คนเนื่องจากตรวจพบว่าทารกในครรภ์มีความผิดปกติของแท่งพันธุกรรม
ไม่พบการสูญเสียการตั้งครรภ์หรือทารกอวัยวะเพศกำกวมร้อยละ 1.99 ไม่สามารถให้การวินิจฉัยเพศได้ร้อยละ 90.8 การวินิจฉัยถูกต้อง จำแนกตามเพศ
เมื่อคลอดความถูกต้องในการวินิจฉัยร้อยละ 91.9 และ 89.8 สำหรับทารกเพศหญิงและชายตามลำดับ การวินิจฉัยด้วยการตรวจคลื่นเสียงความถี่สูง
มีความถูกต้องร้อยละ 88.3 และ 93 สำหรับทารกหญิงและชายตามลำดับ แพทย์ประจำบ้านต่อยอดชั้นปีที่ 2 เป็นปัจจัยที่มีนัยสำคัญต่อการวินิจฉัย
ทารกเพศหญิงได้ถูกต้อง

สรุป: การวินิจฉัยเพศของทารกในครรภ์ด้วยการตรวจคลื่นเสียงความถี่สูงโดยแพทย์ประจำบ้านต่อยอด เวชศาสตร์มารดาและทารกในครรภ์
โรงพยาบาลสงขลานครินทร์ก่อนการเจาะตรวจเยื่อถุงน้ำคร่ำช่วงไตรมาสที่สองของการตั้งครรภ์มีความเป็นไปได้ แพทย์ประจำบ้านต่อยอด
ที่มีประสบการณ์น้อยควรมีความระมัดระวังเป็นพิเศษเมื่อจะวินิจฉัยทารกว่าเป็นหญิง
