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Second Trimester Genetic Amniocentesis at Secondary Center Hospital in Southern Thailand

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ABSTRACT

Objectives: To evaluate the complications and outcomes of second trimester genetic amniocentesis in singleton pregnancy for prenatal diagnosis at secondary center hospital in Southern Thailand.

Materials and Methods: This was a retrospective descriptive study including singleton pregnancy that had been performed second trimester amniocentesis for prenatal diagnosis at Phattalung Hospital between October 2007 and September 2012. The complications after the procedure, results of the diagnosis and outcomes of the pregnancy were reviewed. The data was shown in number and percentage.

Results: A total of 2,626 medical data of genetic amniocentesis in singleton pregnancies were reviewed. The most common indication was advanced maternal age (94.4%), the other indication was couple at risk of severe thalassemia (4.8%). There were chromosome abnormalities (3.3%) and severe thalassemia major (0.9%). The most common chromosome abnormality was trisomy 21 0.8% (22 cases). Other chromosome abnormalities were trisomy 13, 18 and sex chromosome (0.9%). The failure rate of culture was 1.3%. The fetal loss rate was 0.3%, which occurred within 14 days post procedure.

Conclusion: Second trimester genetic amniocentesis performed at secondary center hospital was a safe procedure with minimal complication.

Keywords: second trimester amniocentesis, complications, secondary center hospital

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Introduction

Amniocentesis is the most common invasive procedure for prenatal diagnosis of genetic diseases in pregnant women[1]. As reviewed from the past, it was a safe procedure and usually performed between 15 and 20 weeks of gestation[2,3].

Phattalung Hospital was the first secondary center hospital in Southern Thailand that performed second trimester genetic amniocentesis since year 2000. To perform the procedure at local province hospital were cost benefit and effective, as an increasing number of elderly pregnant women that required

amniocentesis, travelling to the tertiary hospital was costly and time consuming, and finally to decrease the workload of the tertiary hospital. Nowadays, more pregnant women had knowledge and more aware about the prenatal invasive procedure. Therefore this procedure should be a part of routine service in the general obstetric practice.

In Thailand, amniocentesis was commonly performed at the tertiary center hospital. There were many reports of their experiences[3-9]. The purpose of this study was to evaluate the complication and outcome of second trimester amniocentesis which was performed at one of the secondary center hospitals in Southern Thailand.

Materials and Methods

From October 1, 2007 to September 30, 2012 a total of 2,626 cases of genetic amniocentesis were done at Obstetrics and Gynecology Unit, Phattalung Hospital (secondary center hospital), 2,505 cases for fetal karyotype, 127 cases for DNA analysis of thalassemia. Six cases were diagnosed for fetal karyotype and DNA analysis of thalassemia. Most of the cases had an antenatal care in Phattalung province, as some women came from other provinces nearby such as Nakornsrithammarat and Trang province. Before the procedure, genetic counseling had been provided for all pregnant women with their husbands, then the couple signed the inform consent. Every pregnant woman had standard ultrasound examination to confirm gestational age, fetal viability, placenta location, amniotic fluid volume and gross fetal abnormalities.

Amniocentesis was performed by the general obstetricians between 15-22 weeks of gestation under simultaneous free hand ultrasound guidance with a 22-gauge spinal needle. The step of procedure were: first the operators cleaned the site of puncture by povidine solution, then the spinal needle was inserted through uterine wall under the ultrasound guidance. After removing the inner stylet, 1 ml of amniotic fluid was discarded to avoid maternal cell contamination, and then 15-20 ml of amniotic fluid was aspirated in the same syringe and sent for cell culture. The specimens were sealed and packed in the foam box which kept cool by ice. For fetal karyotype, the specimens were sent to Human Genetic Unit, Department of Pathology Rajanukul Hospital in Bangkok by an express bus within 24 hours. For fetal DNA analysis of thalassemia, the specimens were sent to the Human Genetic Unit, Department of Pathology, Songklanagarind Hospital in Songkhla by the hospital car.

All patients'data, complications and outcomes were collected from amniocentesis record forms and medical record forms. The missing data was very low because most of the cases were in Phattalung province. After amniocentesis procedure the authors told every pregnant women if they had complication they must came back or called back to Phattalung Hospital. The data were calculated by number and percentage. This study was approved by the Human Research Ethics Committee of Phattalung Hospital.

Results

A total of 2,626 amniocentesis procedures were performed during the study period. The most common range of maternal age was 35-39 years old (67.3%) (Table 1). The most common range of gestational age performed amniocentesis between 16-18 weeks (90.8%) (Table 2). Every amniocentesis procedure was performed by general obstetricians. The most common indication for amniocentesis was advanced maternal age (94.4%). The other indications were couple at risk of severe thalassemia in fetus (4.8%), previous trisomy child (0.4%) and previous family history of trisomy (0.4%) (Table 3).

The results of abnormal chromosomal were 82 cases (3.3%). The most common abnormality was trisomy 21 (0.9%). The other abnormalities were trisomy 18 (0.2%), trisomy 13 (0.2%), sex chromosome (0.6%) and others (1.3%) as shown in Table 4.

Total thalassemia major was 18.9% such as β-thalassemia/ Hb E (15.7%), B-thalassemia major (2.4%), and hydrops fetalis (0.8%) as shown in Table 5. The total failure rate of the cell culture was 1.3% which was associated with three problems: maternal blood contamination (15 cases), bacterial contamination (1 case) and logistic problems from flooding in Bangkok (18 cases). Thirty-two cases accepted the second

amniocentesis with two cases denied. True total failure rate 0.6% (16 cases) if there was no flooding.

Table 1. Maternal age (N = 2,626)

Age (years)	Number	Percent
<20	15	0.6
20-24	34	1.3
25-29	41	1.6
30-34	52	1.9
35-39	1,766	67.3
40-44	663	25.2
>44	55	2.1
Total	2,626	100.0
Mean age ± SD	37.6 ± 3.8	

Table 2. Gestational age at time of amniocentesis (N=2,626)

Gestational age (weeks)	Number	Percent
<16	52	1.9
16-18	2,384	90.8
19-21	175	6.7
>21	15	0.6
Total	2,626	100.0
Mean GA ± SD	16.9 ± 2.8	

Table 3. Indications for amniocentesis (N=2,632)

Indication	Number	Percent
Advanced maternal age	2,484	94.4
Previous child trisomy	10	0.4
Family history of trisomy	10	0.4
Couple at risk of severe thalassemia in fetus	127	4.8
Previous child anomaly	1	0.0
Total	2,632	100.0

* Six cases were checked both chromosome and thalassemia (2626+6=2632)

Table 4. Results of the chromosome studies (N = 2,503)

Result	Number	Percent
Normal chromosome	2,421	96.7
Abnormal chromosome	82	3.3
Numerical abnormalities		
trisomy 21	22	0.9
trisomy 18	4	0.2
trisomy 13	4	0.2
Sex Chromosome		
47, XXY	7	0.3
47, XYY	4	0.2
47, XXX	3	0.1
45, X	2	0.1
Structural abnormalities	36	1.3
Total	2,503	100.0

Table 5. Results of genetic amniocentesis for DNA analysis of thalassemia (N = 127)

Results	Number	Percent
Normal	35	27.5
Abnormal	92	72.5
β-thalassemia/Hb E*	20	15.7
β-thalassemia trait	25	19.7
β-thalassemia major*	3	2.4
Hb E trait	30	23.6
Hydrops fetalis*	1	0.8
Alpha- thalassemia trait	2	1.6
β-thalassemia intermedia	2	1.6
HPFHb trait	3	2.3
Hb Malay trait	2	1.6
Hb Constant spring trait	1	0.8
Homozygous Hb E	3	2.4
Total	127	100.0

* Severe fetal thalassemia disease

There were 9 cases (0.34%) aborted within 2 weeks after amniocentesis, one fetal death occurred five day after the procedure, three cases presented with pelvic pain, two cases got fever from chorioamnionitis, and three cases had an amniotic fluid leakage. All of them had normal fetal chromosome results. Two cases with amniotic fluid leakage and two cases with vaginal bleeding which could continue their pregnancy after

supportive treatment with antibiotics. The cases with amniotic fluid leakage continued their pregnancy, 1 case to term and 1 case to 34 weeks. All babies were reported to be normal at birth. (Table 6)

All cases of autosomal trisomy (30 cases), severe thalassemia (24 cases), two of sixteen cases with numerical abnormalities of sex chromosome decided to terminate the pregnancy.

Table 6. Complication within 14 days after procedure. (N = 13)

Complication	Number	Details	Outcome
Fetal death	1	Day 5 after procedure	Abortion
Pelvic pain	1	Day 2 after procedure	Abortion
	1	Day 3 after procedure	Abortion
	1	Day 5 after procedure	Abortion
Fever	1	Chorioamnionitis 2 days after procedure	Abortion
	1	Chorioamnionitis 3 days after procedure	Abortion
Leakage of amniotic fluid	1	Day 1 after procedure	Continue to term
	1	Day 2 after procedure	Continue to 34 wks
	1	Day 2 after procedure	Abortion
	2	Day 3 after procedure	Abortion
Vaginal spotting	2	Day 1 after procedure	Continue to term

Discussion

Amniocentesis for prenatal diagnosis at our hospital was established for more than 10 years. The numbers of amniocentesis for prenatal diagnosis have been increasing every year. The most common indication for prenatal diagnosis was advanced maternal age which was similar to the other studies from tertiary hospitals in Thailand[3-9]. The most common gestational age performed amniocentesis was between 16-18 weeks. The prevalence of all chromosomal abnormalities was 3.3% and the prevalence of trisomy 21 was 0.9%, which was similar to the other studies[3-9]. Pre-procedure counseling before the procedure is very important and can significantly increase the acceptance of this procedure[10,11].

The fetal loss within 14 days after the procedure was 0.3%. Compared to other studies, the rate of fetal loss was lower than previous studies in the past 10 years[7, 8,12]. However, the studies performed by Odibo, et al in 2008, and Hamprasertpong, et al in 2011, showed the fetal loss rate after the procedure is much lower than our study by only 0.12-0.13%[13,14].

Probably, these tertiary centers had more experiences from subspecialty doctors, with more practices over a longer period of time. This study also showed that the incidence of fetal loss and other complications were in an average rate, even with the procedure performed by general obstetricians. There are many advantages to perform this procedure at the secondary center hospital such as, cost saving, reduce time from transferring decreased work load at tertiary center hospitals, and finally it strengthens the capability of the health care team in the secondary center hospital. The culture failure rate in our study was low only 16 cases (0.6%). The rate was low when compared with the other studies in Thailand[3-7,9]. This is due to high quality of the cytogenetic laboratory in Bangkok. All of the culture failures were due to contamination from maternal blood or from bacteria which can be improved by effective training and adherence to the standard technique of the procedure. The main problem in the provincial hospital is lack of genetic laboratory nearby. Culture failure rate in this study also had a problem from transferring specimen. Every single hospital

should have a good collaboration with the laboratory with a good logistic system for transferring the specimen on time. However, as all of us knew, shortage of genetic laboratory in the public section will be a major problem in the near future.

The implications of this study showed that genetic amniocentesis is a safe procedure and can be performed by general obstetricians at the secondary hospital center if strictly adheres to the standard technique. All of abnormal diagnosed cases were terminated at our hospital. Moreover, not all of the obstetricians are cooperative and willing to perform the termination.

This study was the first report from single secondary center hospital in southern Thailand. The results from the present study could be useful to motivate many secondary centers to perform second trimester amniocentesis. The limitation of the study was that it was a retrospective study, which may lack some important data especially fetal loss and other complications.

In conclusion, second trimester amniocentesis can be set up as a routine general obstetric service at the secondary center hospital. The procedure is safe with minimal complication. Setting up this system in the province hospital has many advantages especially for pregnant women, as they can easily access to the necessary health care system nearby their home.

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การเจาะถุงน้ำคร่ำเพื่อวินิจฉัยโรคทางพันธุกรรมในไตรมาสที่สองเพื่อการวินิจฉัยก่อนคลอดที่โรงพยาบาลระดับทุติยภูมิในภาคใต้ของประเทศไทย

เสริมศรี ปฐมพาณิชรัตน์, พวงพกา ชูช่วย, นวลใย วรรณเวช

วัตถุประสงค์ *: เพื่อประเมินภาวะแทรกซ้อน และผลของการเจาะถุงน้ำคร่ำในไตรมาสที่สอง เพื่อการวินิจฉัยก่อนคลอดที่โรงพยาบาลระดับทุติยภูมิ ในภาคใต้ของประเทศไทย*

วัสดุและวิธีการ *: เป็นการศึกษาแบบย้อนหลังเชิงพรรณนาในหญิงตั้งครรภ์เดี่ยว ที่เข้ารับการเจาะถุงน้ำคร่ำในไตรมาสที่สอง เพื่อการวินิจฉัยก่อนคลอด ระหว่างเดือนตุลาคม พ.ศ.2550 ถึงเดือนกันยายน พ.ศ.2555 ที่โรงพยาบาลพัทลุง เพื่อประเมินภาวะแทรกซ้อนจากการเจาะถุงน้ำคร่ำ ผลของการวินิจฉัย และผลของการตั้งครรภ์*

ผลการศึกษา *: หญิงตั้งครรภ์เดี่ยว 2,626 คน ได้รับการเจาะถุงน้ำคร่ำเพื่อการวินิจฉัยก่อนคลอด ข้อบ่งชี้ส่วนใหญ่คือ อายุมากร้อยละ 94.4 รองลงมาคือคู่สมรสที่มีความเสี่ยงที่จะมีบุตรเป็นโรคธาลัสซีเมียชนิดรุนแรงร้อยละ 4.8 จำนวนโครโมโซมผิดปรกติพบร้อยละ 3.3 เป็นโรคธาลัสซีเมียชนิดรุนแรงร้อยละ 0.9 ความผิดปรกติของจำนวนโครโมโซมที่พบบ่อยที่สุดคือโครโมโซมเกินคู่ที่ 21 ร้อยละ 0.9 จำนวนโครโมโซมที่เกินคู่อื่นๆ คือโครโมโซมคู่ที่ 13,18 และโครโมโซมเพศพบร้อยละ 0.9 ความล้มเหลวในการเพาะเลี้ยงเซลล์จากน้ำคร่ำพบร้อยละ 1.3 อัตราการสูญเสียทารกในครรภ์หลังการเจาะน้ำคร่ำภายใน 2 สัปดาห์พบร้อยละ 0.3*

สรุป *: การเจาะถุงน้ำคร่ำเพื่อการวินิจฉัยโรคทางพันธุกรรมในไตรมาสที่สองที่โรงพยาบาลระดับทุติยภูมิเป็นหัตถการที่สามารถทำได้อย่างปลอดภัย โดยมีภาวะแทรกซ้อนน้อย*