Prenatal Diagnosis : 10-Year Experience

PANNEE SIRIVATANAPA, M.D.*,
CHANANE WANAPIRAK, M.D.*,
PHARUHUS CHANPRAPAPH, M.D.*,
APIRADEE TAKAPIJITRA, B.Sc.*,
THEERA TONGSONG, M.D.*,
SUPATRA SIRICHOTIYAKUL, M.D.*,
ACHARAWAN YAMPOCHAI, B.Sc.*,
RATANAPORN SEKARARITHI, B.A.*

Abstract

To evaluate the indications and results of prenatal diagnosis of the high risk pregnant women attending the antenatal care clinic at Maharaj Nakorn Chiang Mai Hospital, Chiang Mai University during 1988-1998, we analysed 2,315 amniocenteses, 1,000 cordocenteses, and 11,895 obstetric ultrasound examinations. Among the amniocentesis group, 2,017 cases (87%) were done with the indication of advanced maternal age. The prevalence of major abnormal fetal chromosomes among high risk pregnancies was 1:58. Of 1,000 cases with cordocentesis, the most common indication was fetal risk of severe thalassemia (658 cases; 65.8%) and followed by fetal risk of chromosome abnormalities (272 cases; 27.2%). In the group of cordocentesis for diagnosis of thalassemia, 99 and 49 pregnancies were affected with Hb Bart's disease and homozygous β-thalassemia, respectively. Thirty three cases with indication of chromosome analysis had fetuses with abnormal chromosomes. The major indications of ultrasonography included suspicion of intrauterine growth restriction (IUGR), determination of gestational age and screening anomalies, respectively. In conclusion, our extensive experience has enabled us to prenatally detect most fetuses with severe thalassemia, and fetuses with abnormal chromosomes as well as anomalies in a significant number, contributing a great deal to our population. Therefore, we recommend that systematic prenatal diagnosis, either amniocentesis, cordocentesis or ultrasound should be provided to every high risk pregnant woman for a healthy newborn.

Key word : Prenatal Diagnosis, Amniocentesis, Cordocentesis, Ultrasonography, 10-Year Experience, Chiang Mai University

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* Department of Obstetrics and Gynecology, Faculty of Medicine, Chiang Mai University, Chiang Mai 50200, Thailand.

At the present time, each family seems to have no more than two children who are expected to have both good physical and mental health. Prenatal diagnosis is one of the options for couples to have such children, especially those at risk. Currently, there are many prenatal diagnostic procedures such as chorionic villus sampling, amniocentesis, cordocentesis, ultrasonography, fetal skin biopsy, fetal liver biopsy and preimplantation diagnosis. In Maharaj Nakorn Chiang Mai Hospital, a university hospital, only three main prenatal diagnostic procedures, including amniocentesis, cordocentesis and ultrasonography, were well established as routine service from 1988 to 1998. Our annual report of maternal-fetal medicine statistics showed an increased percentage of elderly prenant women (> 35 years) from 8.4 in 1990[1] to 15.7 per cent in 1997[2] and increased numbers of congenital anomalies. Furthermore, the prevalence of severe thalassemia is very high in our population. The objectives of this study were to assess the indications and results of prenatal diagnosis of pregnant women at risk attending the antenatal care clinic at our institute from 1988 to 1998.

MATERIAL AND METHOD

This is a retrospective study based on the obstetric database, prospectively collected in maternal-fetal medicine unit since 1988. High risk pregnant women attending the antenatal clinic at Maharaj Nakorn Chiang Mai Hospital, Department of Obstetrics and Gynecology, Faculty of Medicine, Chiang Mai University, were recruited to the study from June 1988 to May 1998, the period with a total of 62,155 deliveries. The studied pregnant women could be categorized according to prenatal diagnostic procedures into three main groups; firstly, 2,315 pregnant women at risk undergoing amniocentesis; secondly, 1,000 high risk pregnant women undergoing cordocentesis; and finally, 11,895 women with ultrasound examinations. The data concerning indications, results of the tests, and pregnancy outcomes were analyzed, and presented in percentage.

RESULTS

Most pregnant women in the amniocentesis group were confined in the age range of 35-39 years (71.6%), whereas, those in the cordocentesis group were in the age range of 26-35 years (49.9%). Most amninocenteses (80.5%) were done at a gestational age of 16-18 weeks, while most cordocenteses (69.8%) were done at a gestational age of 19-21 weeks. Of 2,315 high risk pregnant women who underwent amniocentesis, most cases (2,017 cases; 87%) had the indication of advanced maternal age (Table 1) and 2,139 cases had successful amniocentesis and culture. There were twenty five cases of failed amniocentesis. Fifty two of the successful procedures were found to have abnormal fetal chromosome but only 38 cases (1.8%) were finally confirmed for abnormality (Table 2). Trisomy 21 and its variants were found in 15 of 38 cases. (Table 3) The prevalence of abnormal fetal chromosome among pregnancy at risk was 1:58. The overall fetal loss rate among the amniocentesis group was 2.4 per cent, including the background loss rate.

Of 1,000 women undergoing cordocentesis, 658 cases (65.8%) were performed due to fetal risk of severe thalassemia and the remaining 272 were performed for chromosome study (Table 5). Ninety nine cases and forty nine cases were diagnosed for Hb Bart's disease and homozygous β-thalassemia, respectively (Table 6). In this study, failure of cordocentesis was 3.6 per cent and the fetal loss rate was 2.8 per cent (Table 7).

Ultrasound examinations were performed as indicated, not routinely. Among 12,000 scans (only in the second and third trimester), the main indications included suspicion of fetal growth restriction (FGR), determination of gestational

Table 1. Indications of amniocentesis.

Indications	Cases	%
Advanced maternal age	2,017	87.1
Previous trisomic child	107	4.6
Suspected chromosomal disorders in previous offspring	63	2.7
Family history of chromosomal disorders	42	1.8
Fetal risk of X-linked disorders	18	0.8
Previous child with mental retardation	16	0.7
Abnormal sonographic findings	14	0.6
Maternal or paternal chromosomal translocation	7	0.3
Miscellaneous	31	1.3
Total	2,315	100

Table 2. Summary of the results of genetic amniocentesis.

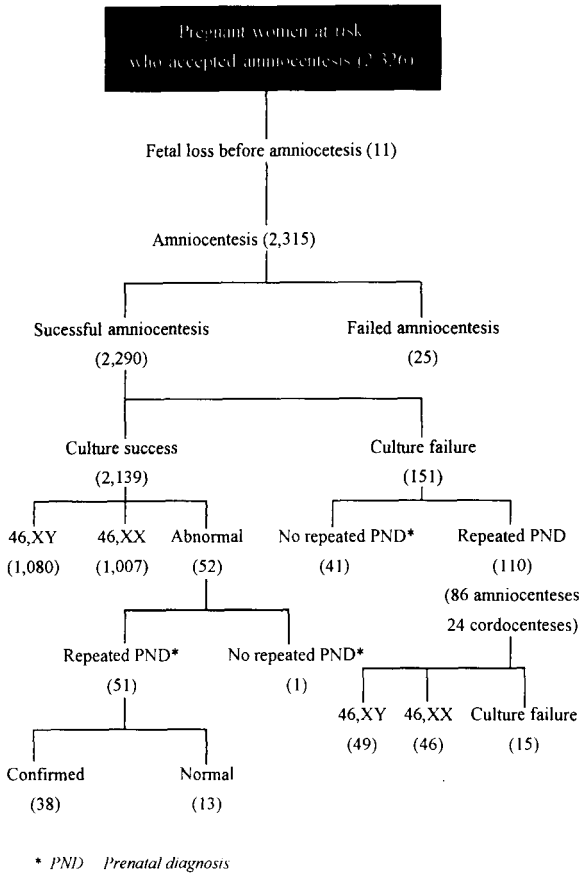

Table 3. Final results of the chromosome studies (from 2,139 culture success).

Results	Cases	%
46,XY	1,080	50.5
46,XX	1,007	47.1
Abnormal chromosomes	52	2.4
Trisomy 21 & variants	15	
Trisomy 18 & variants	5	
Trisomy 13 & variants	3	
47,XXX	3	
47,XXY	2	
Turner syndrome	2	
Other rearrangement	8	
Repeated prenatal diagnosis with normal result	13	
No repeated prenatal diagnosis	1	

Table 4. Pregnancy outcomes (from 2,139 culture success).

Pregnancy outcomes	Cases	%
Termination of affected pregnancies	32	1.5
Continuing pregnancies		
Unknown outcome	262	12.3
Known outcome	1,845	86.2
Fetal loss	52	(2.8)
- Spontaneous abortion	28	
- Dead fetus *in utero*	24	
Live birth	1,793	(97.2)
- Premature delivery	239	
- Term delivery	1,554	
Total	2,139	100

age, screening fetal anomalies due to various risks (Table 8). The three main fetal anomalies and malformations were hydrops fetalis, abnormality of gastrointestinal system, and central nervous system (Table 9). Nearly all frank hydrops fetalis were confined to couples without screening for fetal risk. The other main fetal anomalies included neural tube defects (mostly anencephaly), abdominal wall defects, ventriculomegaly, hydronephrosis, and cystic hygroma. Obviously, abnormalities of the extremities were common but more than half of them were not prenatally detected. However, most significant fetal anomalies were diagnosed prenatally.

DISCUSSION

Regarding amniocentesis, this study showed that the most common indication was advanced maternal age which accounted for over 80 per cent of cases consistent with previous studies[3-8]. Among successful amniocentesis, culture failure accounted for 6.6 per cent (151 of 2,290 cases) and might be due to early amniocentesis at less than 16 weeks of gestation or improper technique of tissue culture. The rate of fetal loss associated with amniocentesis varies from 0.5-3.5 per cent,[9-11]. In this study, the total fetal loss rate (procedure-related and background loss) was 2.4 per cent. This figure of fetal loss rate seemed to be increased with amniocentesis but was not statistically significantly difference from the control group.[3,12-14] However, one

Table 5. Indications of cordocentesis.

Indications	Cases	%
A. Related to thalassemia (658)		
- Previous Hb Bart's hydrops fetalis	165	16.5
- Previous child of homozygous β-thal. or β-thal/Hb E	159	15.9
- Previous child of Hb H disease	4	0.4
- Pregnancy with Hb H disease	3	0.3
- Couples at risk	290	29.0
- Suspected hydrops fetalis by ultrasonography	37	3.7
B. Chromosome analysis (272)		
- Advanced maternal age and late booking	195	19.5
- Abnormal fetal karyotype from amniocentesis	61	6.1
- Suspected fetal anomaly from ultrasonography	7	0.7
- Others	9	0.9
C. Both	70	7.0
Total	1,000	100

Table 6. Results of cordocentesis.

Results	Cases	%
Normal hemoglobin typing	313	31.3
- and normal karyotype	34	3.4
- and abnormal karyotype	2	0.2
Abnormal hemoglobin typing and normal karyotype	4	0.4
Normal karyotype	216	21.6
Abnormal karyotype	33	3.3
Hb Bart's hydrops fetalis	99	9.9
β-thalassemia homozygote	49	4.9
β-thalassemia/Hb E disease	32	3.2
Hb E homozygote	7	0.7
Hb H disease	4	0.4
α - or β - or Hb E heterozyote	162	16.2
Maternal blood comtamination	5	0.5
Failure to obtain fetal blood	36	3.6
Others	4	0.4
Total	1,000	100

Table 7. Pregnancy outcomes of cordocentesis group.

Pregnancy outcomes	Cases	%
Termination of affected pregnancy	198	19.8
Continuing pregnancies	802	80.2
Unknown outcome	112	11.2
Known outcome	690	69.0
Livebirth	671	(97.2)
Dead fetus in utero or spontaneous abortion	19	(2.8)

Table 8. Indications of obstetric ultrasound (11,895 scans).

Indications	%
Detection of gestational age	27.0
Suspicion of IUGR	24.5
Rule out fetal anomalies	22.2
Surveillance of fetal growth	18.1
Antepartum hemorrhage	3.7
Miscellaneous	4.5

Table 9. Classification of fetal anomalies and malformations (62,155).

Classification	Cases	Cases of PND
Frank hydrops fetalis	208	195
Abnormality of hand and feet	124	41
Abnormality of gastrointestinal system	91	65
Abnormality of cerebral nervous system	62	55
Abnormality of abdominal wall	45	39
Abnormality of lymphatic system	24	20
Abnormality of heart	29	12
Abnormality of bone	18	16
Neural tube defect	40	36
Miscellaneous	108	62
Total	749 (1.2%)	541

study showed that more experienced operators and fewer needle insertions were associated with a lower fetal loss rate[11]. To minimize the fetal loss rate, amniocentesis should be performed by a skilled operator and no more than two insertions. Based on the literature and our own analysis[3], the procedure-related fetal loss was minimal, not more than 0.5-1.0 per cent. Therefore, amniocentesis as indicated is justified for a detection rate of about 2 per cent in this study.

Concerning cordocentesis, in the majority of cases, it was performed for fetal diagnosis of severe thalassemia in couples at risk. Thalassemia is the most common hematologic genetic disorder in Thailand with the high prevalence of α-thal., β-thal. and Hb E gene about 30-40 per cent of the population. Our institute established a heterozygote screening program for prevention and control of thalassemia in 1994. In this program, the pregnancies at risk would be offered cordocentesis for fetal blood analysis with HPLC (High performance liquid chromatography) at 16-24 weeks of gestation. Notably, of pregnancies in the thalassemia carrier screening program, nearly all fetuses with severe thalassemia were prenatally diagnosed early. Currently, severe thalassemia in our hospital is under control. The overall fetal loss rate correlated with cordocentesis in this study was 1.8 per cent consistent with other studies of 1-2 per cent (15-17). Cordocentesis-related fetal loss can be minimized in experienced hands.

During the past decade, ultrasound has become the most common prenatal diagnostic tool in our hospital. As shown in the results, in spite of ultrasound examination as indicated, not routine, it has enabled us to prenatally diagnose major fetal malformations in most cases (more than 70%), markedly different from our ability in the decade before the era of ultrasound. This experience suggests the common problems in our population may be different from those in other developed countries which were mostly due to inadequate amniotic fluid volume visualized by ultrasound. For example, obstetricians in the northern part of Thailand must pay more attention to the possibility of fetal Hb Bart's hydrops fetalis because of its high prevalence as shown in this study. Besides, our perinatal sonographers should keep in mind the possibility of other common malformations in our country, such as neural tube defects, ventriculomegaly, abdominal wall defects, cystic hygroma and hydronephrosis etc.

In conclusion, our extensive experience has enabled us to prenatally detect most fetuses with severe thalassemia, and fetuses with abnormal chromosomes as well as anomalies in a significant number, contributing a great deal to our population. Therefore, we recommend that systematic prenatal diagnosis, either amniocentesis, cordocentesis, or detailed ultrasound should be provided to every high risk pregnant woman for a healthy newborn.

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REFERENCES

1. Maternal-fetal medicince 1990; Annual report. Department of Obstetrics and Gynecology, Faculty of Medicine, Chiang Mai University 1991.
2. Maternal-fetal medicince 1998; Annual report. Department of Obstetrics and Gynecology, Faculty of Medicine, Chiang Mai University 1999.
3. Tongsong T, Wanapirak C, Sirivatanapa P, Piyamongkol W, Sirichotiyakul S, Yampochai A. Amniocentesis-related fetal loss: a cohort study. Obstet Gynecol 1998; 92: 64-7.
4. Wanapirak C, Tongsong T, Sirivatanapa P, et al. Midtrimester amniocentesis: experience of 2040 cases. Thai J Obstet Gynaecol 1997; 9: 269-75.
5. Ajjimakorn S, Tirapinyo M, Thanuntaseth C, Tongyai T, Kangwanpong D. Genetic amniocentesis: five years experience. Thai J Obstet Gynaecol 1990; 2: 87-93.
6. Ajjimakorn S, Kangwanpong D, Tongyai T. Amniocentesis for prenatal diagnosis. J Med Assoc Thailand 1988; 71: 16-20.
7. Suwajanakorn S, Tannirandorn Y, Romayanan O, Phaosavadi S. Midtrimester amniocentesis for antenatal diagnosis of genetic disorders : Chulalongkorn hospital experience. Thai J Obstet Gynaecol 1994; 6: 43-9.
8. Leschot NJ, Verjaal M, Treffers PE. Risk of midtrimester amniocentesis; assessment in 3000 pregnancies. Br J Obstet Gynaecol 1985; 92: 804-7.
9. Lowe CU, Alexander D, Bryla D, Siegel D. The NICHD amniocentesis registry: the safety and accuracy of mid trimester amniocentesis. U.S. Department of Health, Education and Welfare. DHEW Publications No. (NIH) 1978: 78-190.
10. Tabor A, Philp J, Madsen M, Bang J, Obel EB, Norgarrd-Pedersen A. Randomized controlled trial of genetic amniocentesis in 4606 low risk women. Lancet 1986; 1: 1287-93.
11. Marthin T, Liedgren S, Hammar M. Transplacental needle passage and other risk factors associceted with second trimester amniocentesis. Acta Obstet Gynecol Scand 1997; 76: 728-32.
12. Crandall BF, Howard J, Lebherz TB, Rubinstein L, Sample W, Sasti D. Follow-up of 2000 second trimester amniocenteses. Obstet Gynecol 1980; 56: 626-8.
13. Simpson NE, Dallaire L, Miller JR, et al. Prenatal diagnosis of genetic disease in Canada: report of a collaborative study. Can Med Assoc J 1976: 739-46.
14. Golbus SM, Loughman WD, Epstein CJ, Halbasch G, Stephens JD, Hall BD. Prenatal genetic diagnosis in 3000 amniocenteses. N Engl J Med 1979; 300: 157-63.
15. Wanapirak C, Siricholiyakul S, Kunavikatikul C, Piyamonkol W, Sekararithi R. Cordocentesis in Chiang Mai university hospital: 286 cases experience. Thai J Obstet Gynaecol 1996: 79-86.
16. Wilson RD, Farquharson DF, Wittmann BK, Shaw D. Cordocentesis: overall pregnancy loss rate as important as procedure loss rate. Fetal Diagn Ther 1994; 9: 142-8.
17. Duffos, Capella-Pawlvosky M, Forestier F. Fetal blood sampling during pregnancy with use of a needle guided by ultrasound : a study of 606 consecutive cases. Am J Obstet Gynaecol 1985; 153: 655-8.

การวินิจฉัยก่อนคลอด : ประสบการณ์ 10 ปี

พรรณี ศิริวรรธนาภา, พ.บ., ธีระ ทองสง, พ.บ.*,*
ชเนนทร์ วนาภิรักษ์, พ.บ., สุพัตรา ศิริโชติยะกุล, พ.บ.*,*
พฤหัส จันทร์ประภาพ, พ.บ., อัจฉราวรรณ แย้มโพธิ์ใช้, วท.บ.*,*
อภิรดี ตรรกไพจิตร, วท.บ., รัตนาภรณ์ เศขรฤทธิ์, ศศ.บ.พยาบาล**

การศึกษาย้อนหลังเพื่อประเมินผลการวินิจฉัยก่อนคลอดในโรงพยาบาลมหาราชนครเชียงใหม่ในแง่ข้อบ่งชี้ ผลการตรวจสอบและผลการตั้งครรภ์ โดยศึกษาในช่วงปี พ.ศ. 2531-2540 การวินิจฉัยก่อนคลอดที่ให้บริการประจำแก่สตรีตั้งครรภ์ที่มีความเสี่ยงได้แก่ การเจาะน้ำคร่ำตรวจโครโมโซม (2,315 ครั้ง) เจาะเลือดสายสะดือทารก (1,000 ครั้ง) และการตรวจคลื่นเสียงความถี่สูง (11,895 ครั้ง) ส่วนใหญ่ของการเจาะน้ำคร่ำ (ร้อยละ 87) มีข้อบ่งชี้เนื่องจากมารดาอายุมาก ประสบความสำเร็จในการเจาะและเลี้ยงเซลล์ 2,139 ราย มีความชุกของโครโมโซมผิดปกติที่สำคัญ 1:58 ข้อบ่งชี้หลักของการตรวจเลือดสายสะดือคือทารกมีความเสี่ยงต่อโรคธาลัสซีเมียชนิดรุนแรง (ร้อยละ 65.8) และตรวจโครโมโซม (ร้อยละ 27.2) ในกลุ่มเจาะเพื่อวินิจฉัยธาลัสซีเมียพบทารกเป็นโรคฮีโมโกลบินบาร์ท 99 ราย โรคเบต้า-ธาลัสซีเมีย 49 ราย ในกลุ่มตรวจโครโมโซมพบว่าทารกมีความผิดปกติของโครโมโซม 33 ราย สำหรับการตรวจคลื่นเสียงความถี่สูงตรวจตามข้อบ่งชี้ (ไม่ได้ตรวจเป็นกิจวัตร) ข้อบ่งชี้หลักคือเพื่อกำหนดอายุครรภ์ สงสัยทารกโตช้า และคัดกรองความพิการโดยกำเนิด ทำให้สามารถคัดกรองความพิการโดยกำเนิดสำคัญได้กว่าร้อยละ 72 โดยสรุป: ประสบการณ์กว้างขวางนี้ช่วยให้สามารถป้องกันโรคธาลัสซีเมียในทารกได้เกือบหมด ความพิการโดยกำเนิดสามารถวินิจฉัยได้ก่อนคลอดเป็นส่วนมาก และค้นหาความผิดปกติทางโครโมโซมได้จำนวนมาก การวินิจฉัยก่อนคลอดด้วยวิธีทั้งสามน่าจะเหมาะสมที่จะให้บริการแก่ครรภ์เสี่ยงสูงอย่างเป็นระบบ

คำสำคัญ : การวินิจฉัยก่อนคลอด, การเจาะน้ำคร่ำ, การเจาะเลือดสายสะดือทารก, คลื่นเสียงความถี่สูง, ประสบการณ์สิบปี, มหาวิทยาลัยเชียงใหม่

พรรณี ศิริวรรธนาภา, ธีระ ทองสง, ชเนนทร์ วนาภิรักษ์ และคณะ
จดหมายเหตุทางแพทย์ ฯ 2543; 83: 1502-1508

* ภาควิชาสูติศาสตร์และนรีเวชวิทยา, คณะแพทยศาสตร์ มหาวิทยาลัยเชียงใหม่, เชียงใหม่ 50200