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Original Article

An overview of a 30-year experience with amniocentesis in a single tertiary medical center in Taiwan

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Abstract

Objective: Amniocentesis is a popular and effective prenatal diagnostic tool for chromosomal disorders. It is well-established that the risk of chromosomal abnormalities increases with maternal age; however, other related indications are seldom reported. Herein, we report our 30-year experience with amniocentesis from a single medical center, focusing on the indications and rates of abnormality.

Material and Methods: A retrospective review of 16,749 pregnant women in the mid-trimester between January 1981 and December 2010 was conducted. The medical records were analyzed.

Results: The indications for amniocentesis were advanced maternal age (≥ 34 years old) ($n = 10{,}970$, 65.5%), increasing-risk maternal triple-marker Down's screening test (≥ 1/270) ($n = 2090$, 12.5%), history of abnormal offspring birth ($n = 792$, 4.7%), abnormal ultrasound findings ($n = 484$, 2.9%), parent with abnormal karyotype ($n = 252$, 1.5%), family history of chromosomal abnormality ($n = 183$, 1.1%), drug and radiation exposure ($n = 165$), abnormal chorionic villus sampling (CVS) results ($n = 25$), intrauterine fetal death ($n = 50$), and other non-specific causes ($n = 1662$, 9.9%). The rate of abnormality for each indication was 16% in the abnormal CVS group, 12% in the intrauterine fetal death group, 11.5% for parental chromosomal abnormality, 8.7% in the abnormal ultrasound finding group, 3.0% in the increasing-risk maternal triple-marker Down's screening test group, 2.5% in the advanced maternal age group, 1.5% for other non-specific causes, 1.4% for history of abnormal offspring birth, and 1.1% for family history of chromosomal abnormality.

Conclusions: Both parents with abnormal karyotype and abnormal ultrasound findings are indications for which consideration of further amniocentesis is highly recommended.

Keywords: amniocentesis; chromosomal abnormality; ultrasound

Introduction

Amniocentesis for genetic diagnosis began in the late 1960s and early 1970s as a tertiary procedure reserved for only the highest-risk patients [1,2]. Although this procedure is familiar in clinical practice, the main role of amniocentesis continues to be the detection of chromosomal abnormalities and well-known clinically evident or hereditary genetic diagnoses [3–8]. Amniocentesis is often used with women of an

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advanced maternal age (AMA) (age ≥ 34 years old) and younger women (≥ 1/270) who have undergone maternal blood Down's syndrome screening [2]. However, not all amniocentesis cases are performed under the above-mentioned indications.

There are very few studies available that discuss indications other than AMA or for other chromosomal disorders. Papers in Canada [9] and Korea [10] have shown that if amniocentesis is performed for couples with a history of abnormal offspring birth or abnormal ultrasound findings, the abnormality rate of amniocentesis is high. Domestic data from Hsieh et al showed that ultrasound and maternal serum α-fetoprotein should be added to the list to increase the efficacy of genetic amniocentesis [11]. In another study, Tseng et al shared their 10-year experience with amniocentesis, suggesting the highest detection rate was found in cases with abnormal ultrasound findings [12]. However, studies addressing the various kinds of indications for amniocentesis are still rare. This study, based on 16,749 amniocentesis cases in a single tertiary medical center from 1981 to 2010, will be of value for those women who need genetic counseling in Taiwan.

Materials and methods

Data were obtained from amniocentesis records of the cytogenetic laboratory at Taipei Veterans General Hospital, a tertiary medical center, between 1981 and 2010. The detailed information of indications for prenatal diagnosis of chromosomal abnormality with cytogenetic analysis included: (1) AMA, that is, if the mother was ≥ 34 years at the expected date of confinement; (2) abnormal chorionic villus sampling (CVS) results; (3) abnormal biochemical markers in maternal serum, such as maternal blood Down's syndrome screening (≥ 1/270); (4) abnormal ultrasound findings; (5) intrauterine fetal death (IUFD); (6) family history of chromosomal abnormalities; (7) parent with abnormal karyotype; (8) history of abnormal offspring birth; (9) radiation or medication exposure during pregnancy; and (10) other non-specific indications, such as anxiety, consanguineous marriage, and so on.

Chromosomal abnormalities detected by amniocentesis were classified into: (1) autosomal chromosome aneuploidies; (2) sex chromosome aneuploidies; (3) structural rearrangements (reciprocal translocation, Robertsonian translocation, balanced translocations, unbalanced translocations, inversions, insertions, deletions, isochromosome, ring chromosome and marker chromosomes); and (4) mosaicism.

The frequency of the different types of abnormalities was calculated according to each indication, and the detection rate for abnormal cytogenetic findings in various indications was estimated.

Results

Analysis was carried out on 16,749 amniocentesis cases dating from 1981 to 2010. Total chromosome aberrations were detected in 455 cases (2.72%), with 2.72% overall positive rates of abnormal cytogenetic findings (455/16,749). The annual amniocentesis numbers and the abnormal numbers are shown in Fig. 1. As shown in Fig. 2, the indications of abnormal biochemical markers, besides AMA, in maternal serum increased dramatically from 1994. The accumulated data for the different indications for amniocentesis are shown from highest to lowest: AMA (65.5%, 10,970/16,749); abnormal biochemical markers in maternal serum (12.5%,

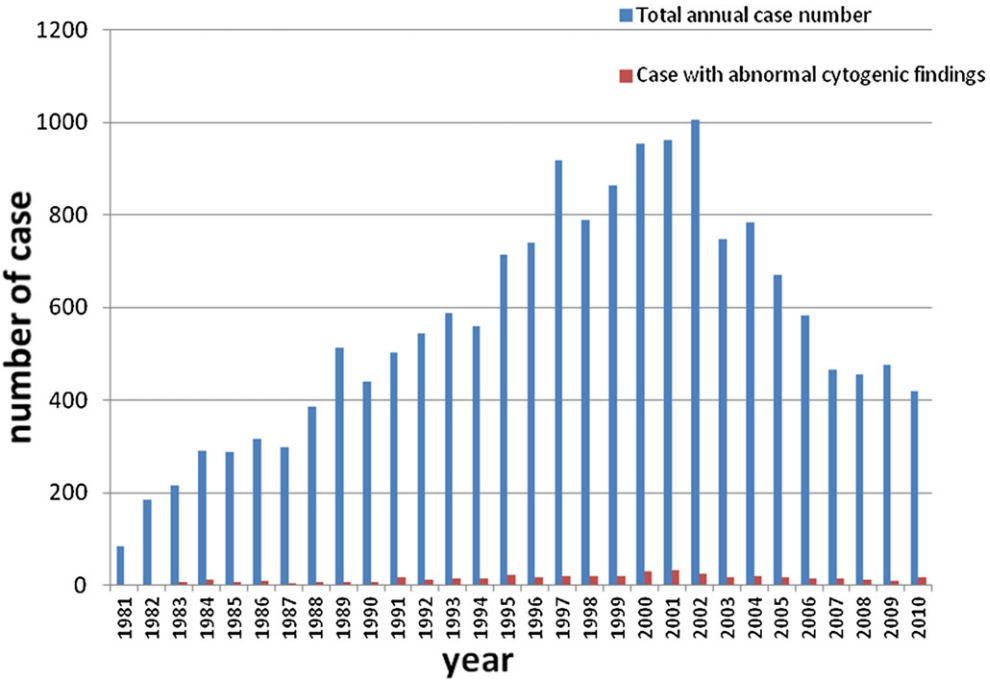

Fig. 1. The annual distribution of total cases of amniocentesis and abnormal cytogenetic findings.

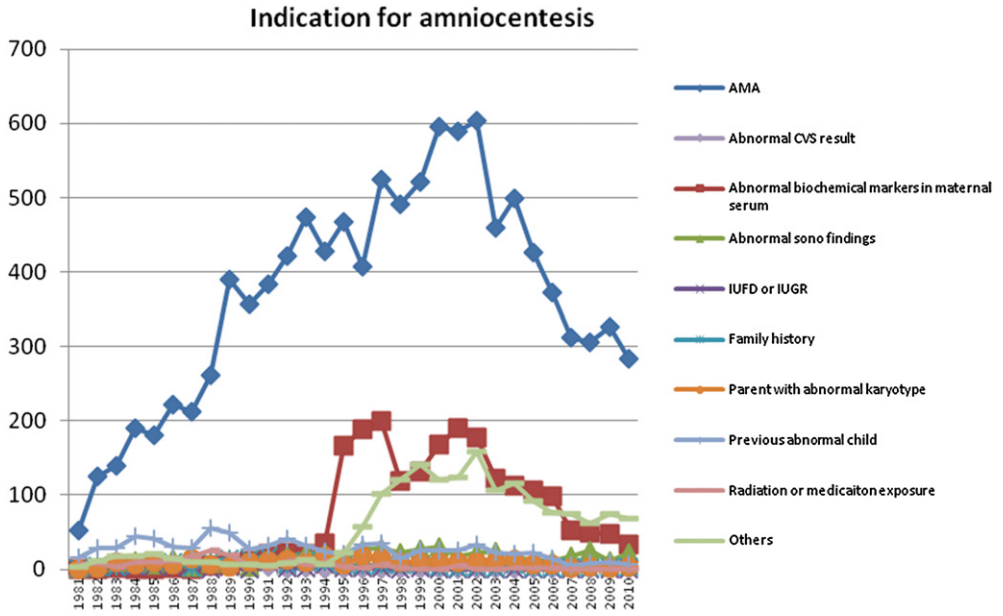

Fig. 2. The annual distribution of all indications for amniocentesis.

2090/16,749); other non-specific indications (9.9%, 1662/16,749); history of abnormal offspring birth (4.7%, 792/16,749); abnormal ultrasound findings (2.9%, 484/16,749); parent with abnormal karyotype (1.5%, 252/16,749); family history of chromosomal abnormalities (1.1%, 183/16,749); radiation or medication exposure during early pregnancy (1.0%, 165/16,749); IUFD (0.3%, 50/16,749); and abnormal CVS results (0.2%, 25/16,749). When the cases with abnormal CVS results (16%, 4/25) and IUFD (12%, 6/50) were excluded, the highest detection rates of chromosomal abnormalities were in cases with the indications of abnormal ultrasound findings (8.7%, 42/484) and parental abnormal karyotypes (11.5%, 29/252). However, the positive predictive values were not so obvious in cases with AMA (2.5%, 271/10,970), abnormal biochemical markers in maternal serum (3.0%, 62/2090), family history of chromosomal abnormality (1.1%, 2/183), history of abnormal offspring birth (1.4%, 11/792), medication or radiation exposure (1.8%, 3/165) and other non-specific indications (1.5%, 25/1662) (Table 1).

Among the cases with chromosomal aberrations, 274 were numerical abnormalities and 181 were structural abnormalities.

For the numerical abnormalities: 2 cases (0.73%) were with triploidy; 112 (40.88%) with trisomy 21; 49 (17.88%) with trisomy 18; 9 (3.28%) with trisomy 13; 22 (8.03%) with mosaic autosomal trisomy; 20 (7.3%) with 45,X; 18 (6.57%) with 47,XXY; 9 (3.28%) with 47,XXX; 6 (2.19%) with 47,XYY; and 29 (10.58%) with a mosaic sex chromosome aberration.

For the structural abnormalities: 74 cases (40.9%) were with reciprocal translocation; 39 (21.6%) with Robertsonian translocation; 33 (18.2%) with inversion; 12 (6.6%) with deletion; 2 (1.1%) with duplication; 3 (1.7%) with insertion; 2 (1.1%) with isochromosome; 2 (1.1%) with ring chromosome; and 14 (7.7%) with marker chromosome (Table 2).

Trisomy 21 was found frequently in women with, in order, indications of AMA (27.7%), abnormal maternal serum screening results (30.7%), and a history of abnormal offspring birth (45.5%); trisomy 18 was noted commonly in cases with

Table 1
Case number and detection rate of chromosomal aberrations in different indications for amniocentesis.

Indication	Case number (*N*)	Proportion (%)	Abnormal number (*n*)	Frequency of abnormality (%)
AMA	10,970	65.50	271	2.47
Abnormal CVS results	25	0.15	4	16
Abnormal serum Down's	2090	12.48	62	2.97
Abnormal ultrasound findings	484	2.89	42	8.68
IUFD	50	0.30	6	12
Family history	183	1.09	2	1.09
Parent with abnormal karyotype	252	1.50	29	11.51
History of abnormal offspring birth	792	4.73	11	1.39
Radiation or medication exposure	165	0.99	3	1.82
Others	1662	9.92	25	1.50
Total	16,749	100	455	2.72

Abnormal serum Down's = increased-risk maternal triple-marker Down's screening test (≥ 1/270); AMA = advanced maternal age (≥ 34 years old); CVS = chorionic villus sampling; family history = family history of chromosomal abnormality; IUFD = intrauterine fetal death.

Table 2
Proportion of numerical and structural chromosomal abnormalities.

	Case number (*n*)	Proportion (%)
Numerical abnormality	274	
Triploidy	2	0.73
Trisomy 21	112	40.88
Trisomy 18	49	17.88
Trisomy 13	9	3.28
Mosaic autosomal chromosome abnormalities	22	8.3
45,X	20	7.3
47,XXY	18	6.57
47,XXX	9	3.28
47,XYY	6	2.19
Mosaic sex chromosome abnormalities	29	10.58
Structural abnormality	181	
Reciprocal translocation	74	40.88
Robertsonian translocation	39	21.55
Inversion	33	18.23
Deletion	12	6.63
Duplication	2	1.1
Insertion	3	1.66
Isochromosome	2	1.1
Ring chromosome	2	1.1
Marker chromosome	14	7.73
Total	455	100

the indications of IUFD (33.3%) and abnormal ultrasound findings (26.2%); 45,X in cases with the indication of abnormal ultrasound findings (28.6%); and translocation was frequently noted in cases with the indication of parental abnormal karyotype (69.0%) (Table 3).

Discussion

As the risk prediction for other indications remains controversial, the results from this paper could be used as a reference to estimate the risk of chromosomal abnormality based on the couple's indication for amniocentesis during prenatal genetic consultation. Amniocentesis is not free of complications, even though it has become available for prenatal screening of chromosomal abnormality. Septic abortion might be the most serious complication, although its occurrence is rare. Other complications include rupture of the membrane, infection, hematoma, and preterm labor. Therefore, the necessity of amniocentesis must be considered along with the risk-benefit ratio.

There is no doubt that AMA contributes to the main indication of amniocentesis, and it is also well known that the risk of chromosomal abnormality increases significantly in pregnant women as they age[13]. For mothers older than 34 years, the risk ranged from 0.32% to 0.35% for trisomy 21 and 1.3% for all kinds of chromosomal abnormality [14,15]. In this study, the main indication for amniocentesis from 1981 to 2010 was AMA (65.5%), which was compatible with data from multiple studies

Table 3
Frequencies and types of numerical chromosomal abnormalities according to different indications.

Anomaly	Amniocentesis in the different indications [Number (*n*) / Frequency (%)]									
	AMA	Abnormal CVS result	Abnormal serum Down's	Abnormal ultrasound findings	IUFD	Family history	Parent with abnormal karyotype	Abnormal offspring birth	Radiation or medication exposure	Others
Triploidy	1 (0.4%)	0	0	0	1 (16.7%)	0	0	0	0	0
Autosomal trisomy										
Trisomy 21	75 (27.7%)	0	19 (30.7%)	6 (14.3%)	1 (16.7%)	0	1 (3.5%)	5 (45.5%)	1 (33.3%)	4 (16%)
Trisomy 18	31 (11.4%)	0	3 (4.8%)	11 (26.2%)	2 (33.3%)	0	0	0	0	2 (8%)
Trisomy 13	7 (2.6%)	0	0	2 (4.8%)	0	0	0	0	0	0
Mosaic	16 (5.9%)	0	1 (1.6%)	0	0	0	1 (3.5%)	0	0	4 (16%)
Sex Chromosome										
45,X	6 (2.2%)	0	1 (1.6%)	12 (28.6%)	1 (16.7%)	0	0	0		0
47,XXY	14 (5.17%)	1 (25%)	2 (3.2%)	0	0	0	0	1 (9.1%)	0	0
47,XXX	5 (1.9%)	1 (25%)	2 (3.2%)	0	0	0	0	0	0	1 (4%)
47,XYY	6 (2.2%)	0	0	0	0	0	0	0	0	0
Mosaic	19 (7.0%)	0	6 (9.7%)	0	0	0	1 (3.5%)	0	0	3 (12%)
Translocation										
Reciprocal	39 (14.4%)	1 (25%)	9 (14.5%)	3 (7.1%)	1 (16.7%)	1 (50%)	13 (44.8%)	2 (18.2%)	2 (66.7%)	3 (12%)
Robertsonian	16 (5.9%)	0	4 (6.5%)	4 (9.5%)	0	1 (50%)	7 (24.1%)	2 (18.2%)	0	5 (20%)
Inversion	20 (7.4%)	0	7 (11.3%)	0	0	0	3 (10.3%)	1 (9.1%)	0	2 (8%)
Deletion	6 (2.2%)	0	1 (1.6%)	2 (4.8%)	0	0	3 (10.3%)	0	0	0
Duplication	2 (0.7%)	0	0	0	0	0		0	0	0
Insertion	1 (0.4%)	0	0	1 (2.4%)	0	0	0	0	0	1 (4%)
Isochromosome	1 (0.4%)	0	0	1 (2.4%)	0	0	0	0	0	0
Ring chromosome	1 (0.4%)	0	1 (1.6%)	0	0	0	0	0	0	0
Marker chromosome	8 (3.0%)	1 (25%)	3 (4.8%)	0	0	0	0	0	0	2 (8%)
Total	271	4	62	42	6	2	29	11	3	25

Abnormal offspring birth = history of abnormal offspring birth; abnormal serum Down's = increased-risk maternal triple-marker Down's screening test (≥1/270); AMA = advanced maternal age (≥ 34 years old); CVS = chorionic villus sampling; family history = family history of chromosomal abnormality; IUFD = intrauterine fetal death.

[12,14–16]. However, we found that the indications for amniocentesis changed significantly in 1994, because maternal blood Down's syndrome screening became popular at that time. Popularity of prenatal screening methods increased the number of amniocentesis cases, and also changed the distribution of various kinds of indications for amniocentesis [10].

The overall rate of chromosome aberration (2.72%), including the rates of abnormality in groups with AMA, abnormal maternal serum screening results, and abnormal ultrasound findings, were very similar to those of previous studies [10–12,14,17,18]. Table 4 gives a summary of similar studies. Ultrasound findings might be one of the best indicators for arranging further amniocentesis, since our study showed a high positive rate of abnormality when the indication for amniocentesis was abnormal ultrasound findings (8.7%). This rate was consistent with the study of Tseng et al (8.9%) [12], and higher than those from Yang et al (6.5%) [15] and Karaoguz et al (5.3%) [18], but far lower than that from Hsieh et al (20.3%) [11]. The possible reasons for the significantly high abnormal amniocentesis findings in the abnormal ultrasound group in Hsieh et al's laboratory study might be caused by selection bias (Hsieh was a pioneer in ultrasound and high-risk pregnancy), and the other might be the relatively limited number of cases in their study ($n = 2975$), compared with 16,749 in our study, and 7028 in Tseng et al's study [12]. In our study, cases with the indication of IUFD had the highest rate of abnormality, but the real reason for this is unknown. The majority of the abnormalities were aneuploidies, which means that these babies might have a critical genetic abnormality, resulting in a lethal situation. Of course, this may be an incidental finding, related to the extremely small number of cases.

In this study, we confirmed the value of maternal blood Down's syndrome screening in younger women, as up to 3.0% of those with abnormal maternal serum marker indications for amniocentesis had positive amniocentesis results, compared with 2.5% of those whose indications were AMA.

Parental abnormal karyotypes were also a good indicator for arranging amniocentesis, as confirmed in our study, as up to 11.5% of those whose indication for amniocentesis was parental abnormal karyotypes had positive amniocentesis results.

From our data given in this study, patients with the indications of family history, previous birth of an abnormal child, radiation or medication exposure, and others, did not have a greater risk of chromosomal abnormality than the general population.

AMA is the indication with the highest prediction rate for numerical abnormality [16], and this was also confirmed in our study. However, although AMA did not increase the incidence of structural abnormality [16], our study showed a 0.86% rate for women with AMA, compared with 0.4% in all amniocentesis cases, and 0.33% in Caron et al's study [9].

In our analysis, cases with the indications of AMA and abnormal maternal serum screening results had a higher prevalence of trisomy 21. Cases with abnormal ultrasound findings showed a higher risk for trisomy 18 and 45,X, and

Table 4
Amniocentesis of different studies, including the indications and their detection rates for chromosomal aberration.[a]

Study [reference]	Case number/ abnormality	AMA	Abnormal CVS results	Abnormal serum Down's	Abnormal ultrasound findings	IUFD	Family history	Parent with abnormal karyotype	Abnormal offspring birth	Radiation or medication exposure	Others
1987, Bell et al [17]	1000 (2.1%)	750					100				
1989, Kim et al [14]	126 (3.2%)	74	2	7		3		2	21		3
1992, Hsieh et al [11]	2975 (3.0%)	1629 (2.0%)			148 (20.3%)				143 (11.8%)	157 (5.3%)	
2006, Tseng et al [12]	7028 (2.9%)	4026 (2.31%)		1500 (2.6%)	553 (8.9%)	949 (2.7%)					
2006, Karaoguz et al [18]	6041 (3%)	3197		2011	492 (5.3%)			14	173		
2008, Han et al [10]	31,615 (3.1%)	5817		21972	1802		253	32	1138		
This study	16,749 (2.7%)	10970 (2.5%)	25 (16%)	2090 (3.0%)	484 (8.7%)	50 (12%)	183 (1.1%)	252 (11.5%)	792 (1.4%)	165 (1.8%)	1662 (1.5%)

Abnormal offspring birth = history of abnormal offspring birth; abnormal serum Down's = increased-risk maternal triple-marker Down's screening test (≥1/270); AMA = advanced maternal age (≥ 34 years old); CVS = chorionic villus sampling; family history = family history of chromosomal abnormality; IUFD = intrauterine fetal death.

[a] Data presented as *n* (number) and % (percentage).

cases with a parental abnormal karyotype demonstrated a higher risk for translocation.

In conclusion, this paper has presented the largest series of amniocentesis cases in Taiwan, and might be useful in estimating positive amniocentesis results before genetic counseling.

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