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Frequencies of Fetal Chromosomal Abnormalities at Prenatal Diagnosis: 10 years experiences in a single institution

We present frequencies of fetal chromosomal abnormalities in 4,907 prenatal cytogenetic examinations at Samsung Cheil Hospital from 1988 to 1997 for 10 yr duration. Prenatal karyotypes were undertaken in 3,913 amniotic fluid samples, 800 chorionic villi samples, and 194 percutaneous umbilical blood samples. The frequency of fetal abnormal karyotypes was 3.1% (150 cases). Numerical chromosome abnormalities were 87 cases (1.8%) and structural aberrations of chromosomes were 63 cases (1.3%). In the numerical chromosomal abnormalities, the frequency of trisomy 21 was by far the highest (36 cases), followed by trisomy 18 in 22 cases and sex chromosome aneuploidies in 19 cases. In the structural chromosomal aberrations, 5 cases had the inversions in chromosome 2, 7, 17, and Y. Chromosomal deletions in 6 cases and additions in 4 cases were analysed. Of the remaining 47 translocation in abnormal fetuses, reciprocal translocation was in 26 cases and Robertsonian translocation in 21 cases. Among them, 41 cases were balanced translocation and 6 were unbalanced. Thirty five cases of translocation were inherited from one of the parents. Four had de novo chromosome rearrangements, and 8 cases were unknown.

Key Words : *Chromosome Abnormalities; Prenatal Diagnosis; Cytogenetics*

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INTRODUCTION

Invasive prenatal diagnosis continues to be the gold standard for pregnancies at increased risk of chromosomal aneuploidy or other genetic diseases. The first fetal karyotype was performed by analysis of cultured cells from the amniotic fluid by Steele and Breg (1). Since amniocentesis was introduced, prenatal diagnosis with cytogenetic analysis had been recognized as a safe and reliable method for couples at high risk of giving birth to a child with a clinically significant chromosomal abnormality (2). Amniocentesis is usually carried out in the second trimester. Afterwards, chorionic villi sampling (CVS) was developed as the means of providing prenatal diagnosis earlier in pregnancy (3). Technical improvements in the late 1980s and early 1990s have made it possible to perform early amniocentesis (4). Recently percutaneous umbilical blood sampling has become the preferred method to access fetal blood at the late second trimester (5). Prenatal cytogenetic analyses using these techniques have been performed in our hospital. Accurate cytogenetic analyses provide an important information on individual cases for genetic counselling (6). Here we report the frequency of fetal chromosomal abnormalities for prenatal cytogenetic diagnosis performed in our laboratory for 10 yr.

MATERIALS AND METHODS

Cytogenetic findings were reviewed retrospectively from 4,907 women who received the prenatal cytogenetic examination for various indications at Samsung Cheil Hospital from 1988 to 1997. Amniocentesis was performed in 3,913 cases, CVS in 800 cases, and cordocentesis in 194 cases. We used the high-resolution banding technique with R-bands by BrdU using Giemsa (RBG banding method), fluorescence in situ hybridization (FISH) and comparative genomic hybridization (CGH) in addition to standard cytogenetic techniques for chromosome analysis.

RESULTS

The indications for prenatal diagnosis with cytogenetic

Table 1. Indications for invasive prenatal diagnosis

Indication	Chorionic villi sampling	Amniocentesis	Cordocentesis
Advanced maternal age	445	2,018	39
Screening positive for maternal serum markers	0	760	22
Abnormal findings on fetal ultrasound	101	372	96
Parental chromosomal abnormality	40	71	0
Previous baby with chromosomal abnormality	63	107	0
Poor obstetrical history	89	196	4
Others	62	389	33
Total	800	3,913	194

Table 2. Results of the prenatal chromosomal diagnosis from 1988 to 1997

Types	Number	Frequency (%)
Normal karyotype	4,757	96.9
Pericentric inversion 9	125	2.5
Abnormal karyotype	150	3.1
Numerical abnormalities	87	1.8
Structural abnormalities	63	1.3

analysis were advanced maternal age, screening positive for maternal serum markers, abnormal findings on fetal ultrasound, parental chromosomal abnormality, previous baby with chromosomal abnormality and poor obstetrical history (Table 1). Main indications for amniocentesis were maternal age being older than 35 yr and screening positive for maternal serum markers (7). Abnormal findings on fetal ultrasound were main indication for cordocentesis (8).

From 4,907 prenatal cytogenetic analyses referred, 4,757 cases showed normal karyotypes (96.9%) which included the familial pericentric inversion of chromosome 9 as a cytogenetic polymorphism in 125 cases (2.5%). Abnormal fetal karyotypes were identified in 150 cases (3.1%) (Table 2).

Of the abnormal karyotypes, numerical abnormalities were 87 cases (1.8%) and structural aberrations were 63 cases (1.3%) (Table 3). Numerical abnormalities were classified as autosomal abnormalities, sex chromosome abnormalities and triploidy. The majority of numerical chromosomal abnormalities were autosomal trisomies. Of note, the frequency of trisomy 21 (36 cases, 0.7%) was by far the highest and 22 cases (0.4%) had trisomy 18. Sex chromosome aneuploidies were found in 19 cases, of which 9 cases were Turner syndrome fetus (45,X).

In the structural chromosomal aberrations, inversions were observed in chromosomes 2, 7, 17, and Y in 5 cases. All were pericentric inversions and inherited from one of the parents except in one case which parents' karyotyping could not be tested. Chromosomal additions were found in 4 cases, deletions in 6 cases, reciprocal translocations in 26 cases and Robertsonian translocations

Table 3. Types and frequency of chromosomal anomalies detected in prenatal diagnosis

Types	Number	Abnormal frequency (%)
Numerical anomalies	87	58.0
Autosomal anomalies		
Trisomy 21	36	24.0
Trisomy 18	22	14.7
Trisomy 13	5	3.3
Trisomy 9	2	1.3
Trisomy 8	1	0.7
Sex chromosome anomalies		
45,X	9	6.0
47,XXX	3	2.0
47,XXY	4	2.7
47,XYY	2	1.3
48,XXXX	1	0.7
Triploidy (69,XXX)	2	1.3
Structural anomalies	63	42.0
Translocation		
Reciprocal	26	17.3
Robertsonian	21	14.0
Deletion	6	4.0
Inversion	5	3.3
Addition	4	2.7
Marker (47,XY,+mar)	1	0.7

in 21 cases. Chromosome analysis of both parents showed normal karyotypes in one addition case and four deletion instances. Among 47 cases with translocations, 41 cases had balanced translocations and 6 cases had unbalanced translocations. Out of six cases with unbalanced translocations consisted of two familial Robertsonian translocations involving the chromosome 21 and four unbalanced reciprocal translocations of which two were derived from the parental reciprocal translocations and two were not known the parental origin. Thirty five fetuses with translocation were found to be inherited from one of the parents and four cases appeared de novo chromosome rearrangements. Cytogenetic test of the parents could not be done in 8 cases.

DISCUSSION

Prenatal diagnosis has become the major focus of genetic counselling and for this, several important areas of technology have evolved (5). Especially, cytogenetic prenatal diagnosis using analysis of cultured cells from the amniotic fluid at mid-trimester was introduced in 1966 by Steele and Breg (1). Although mid-trimester amniocentesis remains the most common and the safest practice for prenatal diagnosis, CVS has gained growing popularity as a successful and safe first trimester prenatal diagnostic technique in early pregnancy since its inception (9-11). Recently, chorionic villus sampling has been increasing with routine ultrasound evaluation of nuchal translucency at 10-12 weeks of gestation (12). As an alternative to mid-trimester amniocentesis, early amniocentesis is a reasonably safe procedure and has the advantage of earlier results (13, 14). Cordocentesis is a procedure used to obtain a sample of fetal blood directly from the umbilical cord with ultrasonographic guidance and is used to give a quick result when ultrasonographic examination has shown some fetal abnormality and culture of amniotic fluid cells has failed (15-17).

Prenatal cytogenetic diagnoses using these above are well established in several countries (18, 19). It has been performed for more than 10 yr in our hospital. Accurate analysis for the frequency of chromosomal abnormalities give an important information for the physician or obstetrician who would make referrals to a prenatal genetic center (2). And the results of prenatal cytogenetic analysis provide the useful information for pregnant women with higher risk than in the general population. There have already been many studies on the risk of various chromosomal abnormalities through prenatal cytogenetic diagnosis (20-22).

The results of fetal cytogenetic abnormalities in our study are similar to those of previous reports (2, 23). Several studies have shown that Down syndrome is the most common and clinically significant cytogenetic abnormalities detected in prenatal cytogenetic diagnosis (24, 25). In our study, Down syndrome was also the most frequent abnormality and the next was the Edwards syndrome with trisomy 18 (26, 27). It has been known that most of the apparently balanced chromosome rearrangements identified by prenatal diagnosis are familial (28, 29). We tested the parents of 39 fetuses with translocations. Thirty five fetuses were confirmed to be inherited from a parental translocation and four were found to be rearranged de novo. The frequency of chromosomal abnormalities in the general population is estimated to be 0.5% of live births, but the frequency of chromosomal abnormality within the high-risk population was higher than that of the general population (24). The frequency of chromosomal abnormalities in our study was 3.1%. It was also higher than that of in the general population. In comparison with the results of chromosomal analysis in amniocentesis reported by Kwak et al. (30) and Bae et al. (31), numerical aberration rate was very similar but structural aberration rate was lower than our study.

This report suggests that the prenatal cytogenetic analysis should be performed in high-risk groups and the studies with a large number of cases including follow up data be essential for the improved genetic counselling.

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