INCIDENCE OF CHROMOSOMAL ABNORMALITIES IN 153 PREGNANCIES WITH ULTRASOUND DETECTED FETAL ABNORMALIES

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ABSTRACT

One hundred and fifty-three patients with fetal abnormalities diagnosed on ultrasound were karyotyped between January 1992 and December 1993. There were 19 (12.4%) fetuses with chromosomal abnormalities. The risk of chromosomal aberrations in the malformed fetuses were increased in the presence of intrauterine growth retardation (15.4%), oligohydramnios (20%) and polyhydramnios (25%). Fetal karyotyping is thus essential in the management of such pregnancies.

Keywords: ultrasonically abnormal fetus, cytogenetic abnormality

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INTRODUCTION

With the advent of modern sonography, fetuses with structural malformations can now be identified by detailed ultrasonographic examinations. A strong association between fetal structural malformations and chromosomal abnormalities has been reported by several workers [1-3]. Fetal karyotyping, often in the form of fetal blood sampling, is mandatory in the management of such pregnancies. Our aim was to conduct a retrospective study to provide an overview of the frequency of chromosomal aberrations in fetuses with ultrasound detected anomalies.

MATERIALS AND METHODS

The study population consisted of 153 patients with fetal abnormalities diagnosed on ultrasound and who had fetal blood sampling performed in the Antenatal Diagnostic Centre at the National University Hospital, Singapore from January 1992 to December 1993. Ultrasonographic examinations were performed by skilled operators using the Acuson 128XP.

Fetuses with malformations in two or more systems were categorised as 'multiple malformations'.

Asymmetrical intrauterine growth retardation was diagnosed when the ratio of the head circumference (HC) to the abdominal circumference (AC) was above the 95% percentile for gestational age.

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Amniotic fluid volume was assessed by measuring the amniotic fluid index (AFI) as described by Phelan et al [4]. A diagnosis of polydramnios was made when the deepest vertical pocket was ≥ 8 cm or when an AFI was above the 95th centile for gestational age [5]. Oligohydramnios was diagnosed in the presence of the deepest vertical pool devoid of cord or fetal limbs measuring less than 5 cm. Fetal blood sampling was performed under aseptic conditions using a 22-gauge needle. An injection of tubocurare 0.1 mg/kg was administered intraperitoneally to all fetuses to facilitate the procedure. Under ultrasound guidance, 2 to 6 mL of fetal blood was withdrawn from the intrahepatic portion of the umbilical vein and sent in heparinized tubes for karyotyping.

RESULTS

Of the 153 cases, 90 (58.8%) had a single structural defect, 31 (20.3%) had multiple malformations and 32 (20.9%) had features of hydrops fetalis without any structural defects. A summary of the abnormal karyotypes of the fetuses with ultrasonically recognized abnormalities is shown in Table I. There were 19 (12.4%) fetuses with chromosomal abnormalities. Trisomy 18 and 21 were the most common types of fetal aneuploidy in our study. In addition to the cases with Trisomies and Turners' syndrome, there were 5 fetuses with other chromosomal abnormalities. They included one with 46, XY, inv (9) (p11q12), one with 46,XY,t (9q; 17p) and another with 46,XY,11p$^-$. There were also two earlier cases in which chromosomal banding was not performed and these included a 46,XY with a translocation between 2 D-group chromosomes and another 46,XY with one member of the D group showing extra chromosomal material on the p arm. Thirty-two (20.9%) fetuses had cardiovascular defects with a 15.6% incidence of chromosomal abnormalities. This incidence of fetal aneuploidy is surpassed only by the group of fetuses with multiple malformations (35.4%). There were 31 cases with multiple malformations and 27 (87%) had cardiovascular defects. Of the eleven chromosomally abnormal fetuses with multiple malformations, all these were associated with cardiovascular defects. Other structural defects seen in these eleven chromosomally abnormal fetuses with multiple malformations include holoprosencephaly (n=3), clefting of vermis (n=1), diaphragmatic hernia (n=2), short limbs (n=1), thick nuchal fold (n=2) and cervical hygroma (n=2).

The mean gestational age of the fetuses at the time of karyotyping was 26.2 ± 5.0 weeks (range 20 to 33). The mean maternal age was 29.5 ± 4.4 years (range 19 to 40).

Table II describes the age of the patients in relation to fetal

structural and chromosomal abnormalities. The cases with Turners' syndrome were omitted as it has been established that this syndrome does not increase with advancing maternal age. There were 132 (86.3%) cases of fetal malformations in the absence of amniotic fluid volume abnormalities and intrauterine growth retardation. There were 5 cases with oligohydramnios and 4 cases with polyhydramnios which were associated with other fetal structural defects. The incidence of fetal aneuploidy in the group with oligohydramnios and polyhydramnios was 20% and 25% respectively. There were 13 growth retarded fetuses with structural defects and 2 (15.4%) of them were chromosomally abnormal.

DISCUSSION

In our series of 153 pregnancies with various fetal abnormalities diagnosed by antenatal ultrasonography, 12.4% (19 cases) were found to have abnormal karyotypes. Other authors have variously reported the incidence of chromosomal abnormalities in pregnancies with ultrasonically diagnosed fetal anomalies to range from 13% to 35%[1,3,6,8,9]. Eydoux et al[6] reported a 13.03% incidence of chromosomal abnormalities in a study population with a mean maternal age of 27.6 years. In our study, the mean maternal age was 29.5 years and the incidence of chromosomal abnormalities in the presence of fetal anomalies was 12.4%. Furthermore, in women younger than 35 years of age, the incidence of chromosomal abnormalities (excluding Turner's syndrome) in the presence of fetal defects was 8%, compared to 30% in the women aged 35 years and above. This is probably not surprising as even in the absence of fetal anomalies, rates of fetal chromosomal aneuploidy, especially the non-dysfunctional types, will increase with advancing maternal age. However, it should be mentioned that some authors have reported bimodal maternal age distributions for Trisomy 18 with two peaks at 25-30 years and 40-45 years[7].

Our data also showed that the incidence of chromosomal abnormalities was higher in fetuses with multiple malformations (35.4%) compared to fetuses with a single defect (6.6%) (Table I). Eydoux et al[6] also reported a high rate (29.2%) of chromosomal aberrations in fetuses with polymalformations. They also found that among the abnormal karyotypes in fetuses with multiple defects, Trisomy 18 was the most common. This finding was similar in our series (Table I).

There were 32 (20.9%) fetuses with cardiac defects alone and these were associated with a 15.6% incidence of abnormal karyotypes. Furthermore, in the group of 11 chromosomally abnormal fetuses with multiple malformations, all had cardiovascular defects. This seems to emphasise the need to properly evaluate the heart, which is probably the most challenging aspect of antenatal diagnostic ultrasonography.

There have been only a few reports on the relationship between fetal malformations, amniotic fluid volume abnormalities and chromosomal defects. Our data (Table III) showed that the incidence of chromosomal abnormalities was higher in fetuses with fetal malformations and polyhydramnios (25%) or oligohydramnios (20%) compared to those with structural malformations alone (11.6%). Gagnon et al[3] reported data on 56 fetuses with malformations and polyhydramnios or oligohydramnios. They found that chromosomal abnormalities were not more frequent in the presence of an amniotic fluid volume abnormality than in its absence (14.3 versus 16.4%). Eydoux et al[6] in a large series found that 15.8% of fetuses with malformations alone were chromosomally abnormal. However, in fetuses with both malformations and amniotic fluid disorders (n=121), the incidence of chromosomal abnormalities was not very different (14.9%).

Our data (Table III) also showed that the incidence of chromosomal abnormalities was higher in fetuses with malformations and intrauterine growth retardation (15.4%), compared to those with structural malformations alone (11.6%). These findings are similar to reports by other authors[6,10]. Eydoux et al[6] described 180 pregnancies with isolated fetal growth retardation and found 12 (6.7%) chromosomal aberrations. They also found that the risk of chromosomal abnormalities was higher if the growth retardation was associated with fetal malformations (31%), polyhydramnios (27%) or both (47%). Snijders et al[10] reported on 458 patients with growth retarded pregnancies at 17 to 40 weeks gestation. They also found that the incidence of chromosomal defects was higher in the group with growth retardation and malformations (40%), than in those fetuses with growth retardation alone (3%).

In summary, our study revealed that there was an increased risk of chromosomal abnormalities (12.4%) in the presence of a malformed fetus. This risk appears to be increased in the presence of multiple malformations (35.4%), when the maternal age exceeds 35 years (30%), in the presence of intrauterine growth retardation (15.4%), oligohydramnios (20%) and polyhydramnios (25%). Fetal karyotyping is thus essential when such fetal malformations are detected on ultrasonographic

Table I – Fetal abnormalities and chromosomal defects

Fetal abnormalities	No. of cases	Chromosomal defects					Total	%
		Trisomy 18	Trisomy 21	Trisomy 13	45,XO	Others		
Cardiovascular	32		2			3	5	15.6
Central nervous system	9	1					1	11.1
Genitourinary	12						—	—
Gastrointestinal	8						—	—
Musculo skeletal	10						—	—
Respiratory	4						—	—
Fetal hydrops with no structural defects	32		1		1	0	2	6.25
Thick Nuchal Fold > 5 mm (11)	9						—	—
Facial	6						—	—
Multiple malformations	31	4	2	1	2	2	11	35.4

examination.

Table II – Maternal age in relation to structural and chromosomal abnormalities (excluding 3 cases with Turner's syndrome)

Maternal age	No. of structurally abnormal fetuses	No. of fetuses with chromosomal abnormalities
18 to 25 years	18	2 (11.1%)
26 to 34 years	112	8 (7%)
35 to 41 years	20	6 (30%)

Table III – Chromosomal abnormalities in fetuses with structural defects, oligohydramnios, polyhydramnios or intrauterine growth retardation (IUGR)

	No. of cases	Trisomy 18	Trisomy 13	Trisomy 21	45,XO	Others	Total No.
Malformation without oligohydramnios, polyhydramnios or IUGR	132	4	1	4	1	5	15 (11.6%)
Malformation with IUGR	13*			1	1		2 (15.4%)
Malformation with polyhydramnios	4	1					1 (25%)
Malformation with oligohydramnios	5*				1		1 (20%)

* One case had IUGR and oligohydramnios

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