Chorionic Villus Sampling: Results of 135 High Risk Cases

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OBJECTIVE: To assess the data related to the first-trimester chorionic villus sampling performed in a single tertiary center.
STUDY DESIGN: Transabdominal CVS performed on 135 pregnant women, aged 18 to 38 years, at 11 to 14 weeks' gestation, who sought prenatal diagnosis for various reasons, during the years 2000-2004. Procedure related fetal loss rate, the indications, results of cytogenetic analysis and the clinical outcomes of patients was obtained retrospectively.
RESULTS: The indications for prenatal diagnosis were enzymatic/DNA analysis for single gene defects (31.1%), advanced positive screening test result (22.2%), advanced maternal age (17.8%), and maternal anxiety (11.9%). Karyotyping was totally successful and chromosomal abnormality was detected in 3 women (2.2%). The procedure related fetal loss rate was 0.0%.
CONCLUSION: CVS performed 11-14 weeks of gestation by experienced operators is a quick, reliable, and safe diagnostic method for prenatal diagnosis and the overall incidence of antenatal and neonatal complications is no greater than that expected for a general population.
(Gynecol Obstet Reprod Med 2006; 12:000-000)

Key Words: Prenatal diagnosis, Chorionic villus sampling, Transabdominal, First-trimester, Outcome

Prenatal diagnosis with cytogenetic analysis has been routinely used for more than two decades for couples at increased risk of giving birth to a child with a clinically significant chromosomal abnormality. Although mid-trimester amniocentesis is the most common method for prenatal diagnosis, Chorionic Villus Sampling (CVS) has gained popularity as a means of rapid prenatal diagnosis in early pregnancy. Prenatal diagnosis in the first trimester offers advantages, such as a reduced emotional and physical strain on couples and disadvantages such as higher procedure-related pregnancy loss rate, the incidence of limb deficiency, and false-mosaicism rate. According to the most widely accepted figures, the fetal loss rate is approximately 1% after transabdominal CVS.[1,2]

The expanding demand of first, as well as second, trimester fetal aneuploidy screening prompted us to assess the risks of transabdominal CVS in our institution, which has been performing the invasive diagnostic procedures for more than a decade as a tertiary center. In addition to procedure related fetal loss rate; the indications, results of cytogenetic analysis and the clinical outcomes following transabdominal CVS were also evaluated.

Materials and Methods

This retrospective study was carried out at the Department of Obstetrics and Gynecology, Faculty of Medicine, Gulhane Military Medical Academy, Ankara, Turkey. CVS for chromosomal analysis performed during the period from January 1, 2000 to December 31, 2004 were studied. The routine of our department at 11-14 weeks of gestation during the study period was to offer all pregnant women a nuchal translucency (NT) screening test for aneuploidies (cut off>3 mm) and a CVS to women aged 35 or more.

Women exposed to CVS were identified by records from the department of medical genetics where all chromosomal analyses were performed and registered. Patients picked out for CVS due to twin pregnancies were excluded. A few CVS procedures carried out transvaginally, patients with more than one procedure and patients without delivery record in our department were also excluded. Details from the CVS procedure including the women's age, indication for CVS; procedure related gestational age, number of needle insertion, karyotype of the fetus and pregnancy outcome were obtained from the patient records of our department. The gestational length at which the CVS performed was based on fetal biometry and was recorded as completed weeks. In cases where data were incomplete or found to be incorrectly recorded, the departments were contacted and further information was collected, if available. One-hundred-and-thirty-five (n:135) cases of pregnant women, aged 18 to 38 years at their expected day of delivery, were consisted of the study group. The limit for the advanced maternal age was chosen as 35.

The files of all cases with preterm delivery were reviewed in detail. The fetal losses were classified as spontaneous abortion (loss <24 weeks' gestation) or, when >24 weeks, as either intrauterine death or neonatal death (death of a live-born baby in the first month).[3] Fetal losses were further separated into those in which the fetus was known to have a major or potentially lethal abnormality or condition identified before the procedure or those without

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Submitted for Publication: 19.07.2005

Accepted for Publication: 17.09.2005

such a condition. Finally, the losses were divided into those within two weeks of the procedure or more than two weeks after the procedure. The procedure-related pregnancy loss rate was defined by subtracting the losses in pregnancies with known lethal conditions and those occurring more than two weeks after the procedure from total pregnancy losses. Delivery before 28 and 37 completed weeks were classified as immature and premature, respectively; thereafter as term.

Table 1. Age Groups of the Study Population

Range	N	%
15-19	6	4.4
20-24	27	20.0
25-29	36	26.7
30-34	42	31.1
35-39	24	17.8
Total	135	100.00

Table 2. Distribution of Procedures per Gestational Age

Range	11	12	13	14	Total
Number	21	36	42	36	135
Percent	15.5	26.7	31.1	26.7	100

Table 3. Indications for Amniocentesis

Primary Indication	n	%
Enzymatic/DNA analysis for single gene defects	42	31.1
Positive screening test	30	22.2
Advanced maternal age	24	17.8
Maternal anxiety	16	11.9
Abnormal sonographic finding	9	6.7
Previous fetus suspected to have chromosomal disorders	6	4.4
Family history of chromosomal disorders	6	4.4
Previous child with trisomy	2	1.5
Total	135	100.0

All the procedures were performed by any of the first three authors, who had performed a minimum of 100 procedures before the study period. Previous to the CVS, an ultrasound examination by means of an high definition ultrasound apparatus (Prosound SSD 5500 Aloka, Tokyo, Japan) equipped with a 2.5-5.0 MHz curved linear transducer, was performed to assess fetal viability and number, gestational age, fetal anatomy and placental location. Next, the abdomen was prepared with an antiseptic solution. Then, A 18 gauge 9-12 cm long spinal needle was inserted through the long axis of the placenta under continuous ultrasound monitoring by a free-hand technique. The stylet was withdrawn from the needle, a syringe containing tissue culture medium was attached to the hub of the needle, and suction was applied until an adequate amount of tissue was obtained. Following the procedure the sample was inspected to ensure that adequate chorionic villi have been obtained. No more than two needle insertions were performed in a single session. A second procedure, if required, was performed 7 days after the first attempt. Local anesthetics, progesterone or antibiotics were not used. Patients with Rh incompatibility were given 300 microgram of anti-D immunoglobulin following the procedure. All women were instructed to report any bleeding, contraction or leakage of amniotic fluid following the procedure.

Fetal karyotyping was carried out in all cases by means of both short and long term methods. Short term incubation was the only method used in cases at risk of Mendelian disease and in which maternal age was below 30 years. When the tissue amount was judged insufficient for setting up both cultures, short term incubation was the method of choice. Prenatal diagnosis was available in 3-10 days.

Results

The study population consisted of 135 women aged 18 to 38 years old. The mean (±SD) age of the women was 28.9±5.2 years with the majority in the range of 30-34 years (Table 1). The mean (±SD) gestational age at chorionic villus sampling was 12.4±1.0 weeks (range 11-14 weeks). The distribution of procedures per gestational week was showed in Table 2. The assigned procedure was performed successfully in all of the patients in the first session.

The most common primary indications for prenatal diagnosis were enzymatic/DNA analysis for single gene defects (31.1%), advanced positive screening test result (22.2%), advanced maternal age (17.8%) and maternal anxiety (11.9%). Details of indications are listed in (Table 3).

A chromosomal abnormality was detected in 3 women representing a prevalence of 2.2%. The karyotypes were consisted of two trisomi 13 and one trisomi 21. All these three women preferred pregnancy termination.

Pregnancy outcome is listed in Table 4. Seven women (5.2%) had an induced abortion, six due to fetal structural abnormalities and one due to chromosomal abnormality. In

the two women terminated due to structural abnormalities the karyotypes were consisted of trisomi 13.

Table 4. Pregnancy Outcomes

	N	%
Abortions (<24 week)	7	5.2
Induced	7	5.2
Major structural abnormalities	4	3.0
Chromosomal disorder	1	0.7
Both	2	1.5
Spontaneous	0	0.0
Deliveries (>24 weeks)	128	94.8
Immature (<28 weeks)	0	0.0
Premature (<37 weeks)	2	1.5
Mature (>37 weeks)	126	93.3
Total	135	100.0

There were no spontaneous miscarriages and stillbirths accounting for a total pregnancy loss of zero. Two cases of preterm delivery were not related to CVS. In one of them, CVS was performed at the 11th week of gestation due to increased nuchal translucency and was resulted in 46XX normal constitutional karyotype. A caesarean was performed at 36th weeks due to intrapartum acute fetal distress. In the remaining fetus, CVS was performed at the 12th week due to cystic higroma and was resulted in 46XY normal constitutional karyotype. An emergency caesarean was performed at 32nd weeks due to complicated placenta praevia.

The procedure related fetal loss rate was 0.0% in our study and this rate was the result of having no spontaneous miscarriages within two weeks following CVS.

Discussion

Although it is essential for women to know the risk of fetal and maternal complications associated with CVS before the procedure, its assessment is not at all obvious. The total pregnancy loss rate is thought to be influenced by many factors such as maternal age, fetal number, gestational age, the indications for the procedure, the operator skill, and the certain technical risk factors.[4-8] And so, it is a combination of the procedure related loss and the background loss rates Thus, pregnancy outcomes following CVS depend on the unique characteristics of each prenatal diagnosis center and figures, naturally, may vary among the centers.

Second-trimester amniocentesis, as an accurate and reliable method, is used as a reference in the evaluation of every kind of prenatal diagnostic method. Transabdominal CVS was also subjected to such a comparison in two randomized studies. A study performed in Denmark randomly assigned 3.079 low-risk women less than 35 years old to transabdominal CVS, transcervical CVS, or second-trimester amniocentesis.[9] The total fetal loss rates for transabdominal CVS (6.3%) and amniocentesis (6.4%) were not significantly different. The European MRC Working Party on the Evaluation of Chorionic Villus Sampling performed an international trial in which 3.248 women from 31 centers were randomized to CVS or amniocentesis.[10] On average, there were only 52 cases per center in the European trial. There was a 4.6% increase in the pregnancy loss rate in the CVS group. The rate of fetal death before 28 weeks and the rate of elective abortion were, respectively, 2.9% and 1% greater in the CVS group. However, the CVS approach was not transabdominal in all cases and was determined by the obstetrician performing the procedure. Our CVS loss rate in high risk pregnancies was so low when the losses due to lethal conditions were excluded. The fetal loss rate of our study was 0 in 135 (0.0%) within two weeks following amniocentesis or until 24 weeks, until 37 weeks, and until term of gestation. Any one of these figures is lower than the previous studies mentioned above. Although, it is generally accepted that invasive procedure-related complications are, to a certain extent, dependent upon the training and clinical experience of the operator,[11-14] small number of the patients in the present study makes it necessary to monitor these figures to show whether this low loss rate is a transitory or a real feature.

It should be mentioned that the real surprise for us was not these low figures; but the lacking of an agreed classification method for reporting of them. In order to support a defined method to compare results from different units as well as pre-procedural counseling of patients, the procedure-related pregnancy loss rate of our study was reported according to the method suggested by Nanal et al (loss within two weeks with no known lethal abnormality).[3] We do acknowledge that some of later losses could still be procedure-related and should not be ignored, and also that some of losses soon after any procedure may have happened anyway. It seems also to be important to use cumulative fetal loss rate in order to determine the weeks after the procedure that still carries an increased risk.

Although the evidence concerning limb deficiency and CVS is conflicting, the debate over this issue has contributed to the deeper understanding of the technical details of the procedure, and has shed light on some of the physiological processes occurring during CVS. In a detailed review of the topic, Firth[15] concluded that the earlier in gestation the procedure is carried out, the stronger is the association, and the greater the likelihood of more severe defects. The technical aspects of the procedure may have a bearing on the amount of placental trauma associated with the sampling. The trauma resulting from CVS is most likely to be influenced by the external size of the needle or catheter, the extent of traverse through the chorion to the sampling site, the number of insertions, the size of the sample, and the amount of intraplacental movements of the needle/catheter. Bearing in mind these technical aspects and performing CVS after the completed tenth week (by the time the development

of the extremities has already been completed) we avoided the limb deficiencies that are possibly caused by the procedure.

Cederholm et al[16] recently investigated the effect of amniocentesis and CVS on the risk of bleeding, placental abruption, complications related to amniotic cavity and membranes, abnormal labour, operative deliveries and the impact of gestational length at the time of the procedure in the women, 35 to 49 years old, with single births exposed to CVS (n: 1984) or not exposed (n: 47854). An association between chorionic villus sampling and maternal complications could neither be excluded nor confirmed due to the relatively small number of chorionic villus sampling procedures.

In conclusion, although it is possible that some minor findings would probably be under-diagnosed or was not recorded, our present findings suggest that transabdominal CVS performed 11-14 weeks of gestation by experienced operators are not associated with higher procedure-related pregnancy loss and the overall incidence of antenal and neonatal complications is no greater than that expected for a general population.

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