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Comparison of adverse perinatal outcomes after single-needle and double-needle CVS techniques

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Abstract

Objective: To determine the impact of the chorion villus sampling (CVS) technique on adverse perinatal outcomes.
Methods: In this case-control study, 412 women who underwent CVS at 11–14 weeks of gestation and 231 women who did not undergo any invasive procedure were retrospectively evaluated. The women in the CVS group were further divided into two groups according to the use of single-needle technique (n=148) vs. double-needle technique (n=264). The adverse outcomes were compared between controls and the two CVS groups, and regression analysis was used to determine the significance of independent contribution.
Results: The rate of preeclampsia for the control group was 2.2%, for the double-needle group was 3% and for the single-needle group was 8.1%. CVS with single-needle technique was found to be an independent and statistically significant risk factor for preeclampsia [odds ratio (OR)=2.1, 95% confidence interval (CI); 1.4–2.7, P=0.008].
Conclusion: The risk of preeclampsia after CVS appears to be increased with single-needle technique compared with double-needle technique.

Keywords: chorion villus sampling; double-needle; preeclampsia; single-needle.

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Introduction

Chorion villus sampling (CVS) is the preferred method of prenatal karyotyping in the first trimester of pregnancy. The demand for CVS is increasing due to the advantage of early antenatal diagnosis and safe pregnancy termination. The sampling procedure can be performed either by single-needle or double-needle technique. In single-needle technique, the needle is inserted into the chorionic villi and moderate suction is applied with a syringe. With double-needle technique, after inserting an outer needle into the chorionic villi, a smaller needle with a syringe is passed through the needle to obtain sample. Although the single-needle technique is accepted as the method of choice for CVS in most centers, both techniques are easy, flexible and have ability to retrieve adequate tissue with minimal trauma in experienced hands.

Placental disruption secondary to CVS during early pregnancy has been suggested to cause abnormal placental development [1]. Additionally, the potential risk of CVS for adverse perinatal outcomes including fetal loss, premature rupture of membranes and hypertensive disorders has been established in several studies [2, 3]. However, previous reports on the predictors of outcomes after CVS have been limited by the use of different definitions of CVS techniques and lack of comparison between techniques. Furthermore, the technique of the procedure is not standardized and variations in the size of the needle, syringe and aspiration technique are present [4]. To our knowledge, there is no solid evidence linking procedure-related factors such as different techniques and needle diameters with CVS complications [5]. Thus, it is essential to take into consideration the type of CVS method as a risk factor for pregnancy complications during counseling before undergoing CVS.

As a result, we hypothesized that the amount of placental disruption in two techniques may show a difference and this may have clinical consequences. The aim of the present study is to evaluate the risk of adverse perinatal outcomes after CVS and to determine whether the type of CVS technique entails a different risk of adverse outcomes.

Methods

This retrospective case-control study included 412 singleton pregnancies who underwent CVS and 231 healthy controls in two prenatal diagnostic centers between January 2010 and February 2015. The study was approved by the Ethics Committee of Tepecik Training and Research Hospital, Izmir, Turkey. Healthy controls were women who were admitted to the antenatal clinic for a routine first-trimester serum screening test at 11–14 weeks' gestation and who did not undergo any invasive procedure. Multiple pregnancies, fetuses with structural or chromosomal abnormalities, syndromes and pregnancies with missing data were excluded. Gestational age was confirmed by the first trimester scan with crown rump length measurement.

The following data regarding clinical characteristics of patients were recorded: maternal age, body mass index, parity, crown rump length measurement, gestational age, smoking habit, levels of free β-human chorionic gonadotropin (hCG) and pregnancy associated plasma protein-A (PAPP-A), type of conception, fetal gender, antenatal bleeding, systemic illnesses history of previous pregnancy (abortus, preeclampsia, gestational diabetes mellitus, preterm birth and intrauterine growth restriction) and indications for CVS. In order to minimize potential impact on fetal loss, CVS indications other than structural anomalies were selected for study. Indications for CVS included advanced maternal age (≥35 years of age), abnormal serum screening test and others (maternal anxiety, parental chromosomal abnormality, previous fetus with chromosomal abnormality, etc.). All patients were counseled by a genetician and written informed consents for CVS were obtained.

All CVS procedures were performed transabdominally at 11–14 weeks' gestation using either a single-needle or a double-needle technique by trained perinatologists. The decision about sampling technique was determined by the clinicians based on experience and preferences. A single-needle technique for CVS was performed with an 18-gauge needle under ultrasonic guidance by means of a high-definition ultrasound device, equipped with a 5-MHz curved linear transducer. The needle was flushed with heparin before the procedure. After identifying the location of the chorion, the skin surface was sterilized with povidone-iodine and the transducer was covered with a sheath. The needle was inserted as much as parallel to the chorionic plate without local anesthesia. The stylet was removed, a 10-mL syringe containing 2–3 mL of tissue media was mounted on the needle hub and negative pressure was continuously applied manually. Adequate villi were aspirated by moving the tip of the needle back and forth four or five times inside the placenta. The double-needle technique was carried out with a 17-gauge outer needle and an inner aspiration needle of gauge 19. With this technique, the guide needle is first inserted into the chorionic villi. Thereafter, the stylet was removed and the aspiration needle was passed through this guide needle. Villi were obtained with a syringe containing media while the tip of the aspiration needle was moving forward and backward. No more than two attempts were carried out. The patient was discharged 1 h after the procedure. All women were scheduled to have anomaly and growth scans at 18–22 weeks and 30–32 weeks, respectively. To compare perinatal outcomes, we categorized patients who underwent CVS into two groups according to the techniques used (single-needle or double-needle).

To investigate the association between the CVS technique and the risk of adverse perinatal outcomes, the following perinatal outcomes were collected from the database: sample adequacy (≥15 mg for standard processing), number of needle attempts, culture failure, bleeding after CVS, fetal loss, stillbirth, preterm birth, preterm premature rupture of membranes, placental abruption, intrauterine growth restriction, preeclampsia, gestational diabetes, gestational age at delivery, type of delivery and birthweight. If information regarding pregnancy outcome was not obtained from medical records, patients were called for the lacking data. Preeclampsia was defined as the presence of new onset of hypertension with proteinuria of 300 mg or more in 24 h after 20 weeks of gestation. Intrauterine growth restriction was defined as estimated fetal weight that was less than the 10th percentile for gestational age. Fetal loss was classified as miscarriage within 2 weeks after CVS, within 4 weeks after CVS and before 24 gestational weeks following CVS.

Statistical analysis was performed using SPSS (Statistical Package for the Social Sciences for Windows version 20.0, SPSS Inc., Chicago, IL, USA). Data were expressed as median and interquartile ranges for continuous variables and as number of cases and percentages for categorical variables. The χ^2 test was used to compare categorical variables. Comparisons of continuous variables between groups were performed by the Kruskal-Wallis test. To identify the source of difference among three groups, Bonferroni post hoc test was used. Multiple logistic regression analysis with backward stepwise elimination was used to determine whether CVS technique was a significant predictor for preeclampsia. Odds ratios (ORs) and their 95% confidence intervals (CIs) were calculated. $P<0.05$ was considered statistically significant.

Results

The study population consisted of 846 women who gave birth in two centers during the 5-year period. On the basis of inclusion criteria, 271 women were selected as controls and a total of 575 women were exposed to CVS. One hundred and sixty-three women in the CVS group who did not meet the inclusion criteria were excluded from the study. Of these remaining 412 pregnancies, 264 underwent CVS with the double-needle technique and 148 with the single needle technique. Seventy-three women in the control group, 95 women in the double-needle group and 69 women in the single-needle group developed a pregnancy complication. The maternal and fetal characteristics of the study groups are shown in Table 1. Compared with the control group, pregnancies that underwent CVS had significantly higher maternal age ($P=0.015$), body mass index ($P=0.007$), parity ($P=0.008$) and free β-hCG multiple of the median (MoM) ($P<0.001$) and lower PAPP-A MoM ($P=0.001$). Post hoc analysis demonstrated that maternal age, body mass index and free β-hCG MoM values were significantly lower in the control group than two CVS groups. In addition, post hoc analysis revealed that parity and PAPP-A MoM values were significantly higher in the single-needle group when compared to the control and double-needle groups.

Distribution of perinatal outcomes in the control and CVS groups is shown in Table 2. Between single- and

Table 1: Maternal and fetal characteristics in the study groups.

	Control group (n=231)	CVS group		P-value
		Double needle (n=264)	Single needle (n=148)	
Maternal age (years)	27 (22–33)	30 (22–35)	30 (22–35)	0.007
BMI (kg/m^2)	25 (24–28)	26.5 (25–30)	27 (25–30)	0.002
Parity	1 (0–2)	1 (0–2)	1 (0–3)	0.004
CRL (mm)	62 (52–72)	63 (53.2–73)	64 (55–74)	0.257
Gestational age (days)	85 (81–96)	88 (81–96)	86 (81–96)	0.201
Smoking	6 (2.6)	8 (3)	6 (4)	0.722
Free β-hCG MoM	1.01 (0.8–1.19)	1.03 (0.86–1.29)	1.05 (0.89–1.38)	0.007
PAPP-A MoM	1.11 (0.71–1.3)	0.91 (0.61–1.2)	0.91 (0.58–1.24)	0.002
Conception				
Spontaneous	216 (93.5)	247 (93.6)	137 (92.6)	0.917
Ovulation induction drugs	11 (4.8)	13 (4.9)	8 (5.4)	0.96
In-vitro fertilization	4 (1.7)	4 (1.5)	3 (2)	0.928
Female gender	108 (46.7)	145 (54.9)	80 (5.4)	0.158
Bleeding prior to CVS	9 (3.9)	11 (4.2)	9 (6.1)	0.57
Chronic hypertension	5 (2.2)	8 (3)	7 (4.7)	0.371
Gestational DM	7 (3)	9 (3.4)	6 (4)	0.867
History of				
Abortus	16 (6.9)	20 (7.6)	15 (10)	0.509
Preeclampsia	7 (3)	10 (3.8)	7 (4.7)	0.694
Gestational DM	9 (3.9)	8 (3)	6 (4)	0.82
Preterm birth	15 (6.5)	17 (6.4)	12 (8.1)	0.785
IUGR	12 (5.2)	11 (4.2)	8 (5.4)	0.807
CVS indications				
Advanced maternal age	NA	105 (39.8)	52 (35.1)	0.352
Abnormal serum screening	NA	140 (53)	81 (54.7)	0.74
Others	NA	19 (8.2)	15 (10.2)	0.298

Data are presented as median (interquartile ranges) or n (%) unless otherwise specified.
BMI=Body mass index, CRL=crown rump length, CVS=chorion villus sampling, DM=diabetes mellitus, hCG=human chorionic gonadotropin, PAPP-A=pregnancy associated plasma protein-A, IUGR=intrauterine growth restriction.

double-needle techniques, the rate of preeclampsia occurrence was significantly higher in the group with single-needle technique compared with the control group. Additionally, we constructed a multivariate regression analysis to assess whether the single-needle technique was an independent risk factor for perinatal outcomes (Table 3). Body mass index, chronic hypertension, PAPP-A MoM, history of preeclampsia and CVS with single-needle technique (OR=2.1, 95% CI; 1.4–2.7, P=0.008) were found to be an independent and statistically significant risk factor for preeclampsia.

Discussion

In this study, to our knowledge, the impact of the CVS technique on the subsequent risk of perinatal outcomes was evaluated for the first time. We found that women who underwent CVS with the single-needle technique had a significantly greater risk of preeclampsia than those underwent CVS with the double-needle technique. This finding leads us to speculate whether single- and double-needle techniques are equally safe or not.

The possible association between CVS and preeclampsia was highlighted by previous reports. Grobman et al. found a more than 4-fold increased risk of developing preeclampsia in nulliparous women having CVS [6]. Adusumalli et al. [7] noted this relationship in only severe hypertensive disorders including severe preeclampsia, eclampsia and HELLP syndrome. In contrast, Odibo et al. [8] indicated a decreased incidence of preeclampsia in women after CVS. However, the authors concluded that they could not completely exclude the possibility of residual confounding factors in their study population. In addition, Lindgren et al. [9] and Khalil et al. [10] did not confirm any association between CVS and preeclampsia. Although these two studies were conducted on women who underwent CVS with a single-needle, details of the procedure technique were not fully described.

Table 2: Distribution of perinatal outcomes in the control and CVS groups.

	Control group (n=231)	CVS group		P-value
		Double needle (n=264)	Single needle (n=148)	
Number of attempts				
1	NA	261 (98.9)	146 (98.6)	0.848
2	NA	3 (1.1)	2 (1.3)	
Inadequate sample	NA	2 (0.8)	2 (1.3)	0.555
Culture failure	NA	1 (0.4)	0	0.455
Bleeding<14 days	NA	5 (1.9)	6 (4)	0.324
Fetal loss<14 days	NA	2 (0.8)	3 (2)	0.259
Fetal loss<4 weeks	NA	1 (0.4)	1 (0.7)	0.677
Fetal loss<24 weeks	1 (0.4)	3 (1.1)	4 (2.7)	0.148
Stillbirth	0	0	0	1
Preterm birth	21 (9.1)	23 (8.7)	10 (6.8)	0.706
PPROM	13 (5.6)	18 (6.8)	14 (9.5)	0.357
Placental abruption	6 (2.6)	9 (3.4)	7 (4.7)	0.538
IUGR	17 (7.4)	21 (7.9)	13 (8.8)	0.882
Preeclampsia	5 (2.2)	8 (3)	12 (8.1)[a]	0.009
Gestational DM	10 (4.3)	13 (4.9)	9 (6.1)	0.745
Gestation at delivery	39 (38–40)	39 (38–40)	39 (38–40)	0.540
Cesarean delivery	65 (28.1)	78 (29.5)	44 (29.7)	0.924
Birthweight	3350 (3100–3710)	3325 (3025–3710)	3200 (3020–3710)	0.268

Data are presented as median (interquartile ranges) or n (%) unless otherwise specified.
[a]P<0.05 compared with controls and double-needle technique.

Table 3: Multiple logistic regression analysis predicting preeclampsia in pregnancies underwent CVS.

Variable	OR	95% CI	P-value
Maternal age	0.96	0.91–1.05	0.126
BMI	1.26	1.08–1.55	0.034
Parity	1.12	0.94–1.46	0.413
Smoking	0.925	0.61–1.56	0.521
Chronic HT	3.77	2.48–6.25	<0.001
Free β-hCG MoM	1.51	0.96–2.24	0.093
PAPP-A MoM	0.71	0.58–0.93	0.001
History of preeclampsia	3.3	1.8–6.4	<0.001
History of gestational DM	1.4	0.92–2.28	0.238
Single-needle technique	2.1	1.4–2.7	0.008

BMI=Body mass index, CVS=chorion villus sampling, DM=diabetes mellitus, hCG=human chorionic gonadotropin, HT=hypertension, PAPP-A=pregnancy associated plasma protein-A.

Presence of placenta is a necessity for preeclampsia and abnormal placentation in the first trimester is hypothesized to play a major role in the pathophysiology [9]. Placental disruption by invasive procedures has been suggested to cause reduced placental perfusion and subsequent oxidative stress leading to endothelial cell dysfunction [11]. Perforation of the placenta during amniocentesis was associated with an increased risk of spontaneous abortion [12]. Reid et al. [13] reported higher but not statistically significant poor pregnancy outcomes when the amniocentesis was performed transplacentally. As chorionic villi are actually removed in CVS, placental disruption is assumed to be greater for CVS than transplacental amniocentesis [9]. Therefore, it appears that impairment of further trophoblastic invasion may probably arise from placental disruption induced by CVS. Furthermore, maternal immune response to paternally derived fetal antigens may cause endothelial dysfunction and alteration in the balance of vasoactive agents, such as vascular endothelial growth factor, placental growth factor and soluble fms-like tyrosine kinase-1 [7, 14, 15].

Another finding of our study is the difference in the rate of fetal loss prior to 24 weeks after a CVS procedure. Fetal loss rate before 24 weeks for all women who underwent CVS (single and double-needle techniques) was found to be 1.7%, which is concordant with the rate (2.18%, 95% CI: 1.61–2.82) reported in a meta-analysis conducted with 42,716 women [16]. However, the fetal loss rate prior to 24 weeks after CVS with single-needle technique (2.7%) was more than two times higher than the rate observed after CVS with the double-needle technique (1.1%). Although the difference was not statistically significant, this finding could be another indicator for the increased placental disruption after single-needle technique.

As the needle size used in the double-needle technique (17 gauge) is large compared with the one used in the single-needle technique (18 gauge), one might think

that the double-needle technique would be associated with more disruption of placental tissue and complication rates. However, our study demonstrated that the degree of trauma caused by needle movement is higher and more important than the trauma caused by needle size. In the double-needle system, the outer trocar passes the uterine wall and remains fixed; therefore, friction between the needle and uterine wall is limited. In the single-needle system, however, besides lateral dislodgment of the needle, there is continuous friction during the entire sampling period. This movement may mimic the effect of multiple punctures and disturb the uterine integrity. Maximum depth of the needle tip, lateral dislodgement of the needle and operator control may also differ between the two techniques. Therefore, the amount of placental disruption may not be the same in the two CVS techniques.

Our study is limited the retrospective nature as most of the studies are on the association of CVS and related complications. Therefore, unidentified confounding factors such as antiphospholipid antibody syndrome and autoimmune diseases could have contributed to a higher rate of preeclampsia in the single-needle technique group. Our study may be subject to some degree of selection bias due to smaller control group. Therefore, increasing the ratio of controls to cases can increase the statistical power of this investigation. In addition, the small sample size may preclude achieving a statistically significant association between CVS techniques and adverse perinatal outcomes, particularly fetal loss rate. Despite these limitations, our study is the first one revealing the difference between CVS techniques in terms of pregnancy outcomes. Prospective studies with higher numbers of patients and those designed to investigate the effect of CVS on risk of adverse perinatal outcomes may reveal additional associations. The strength of our study is that all of the procedures were performed by clinicians experienced in maternal fetal medicine. As procedure-related complications may be related to operator experience, this study is unrestricted by this limitation.

In conclusion, our study indicates that type of CVS technique may actually have a beneficial effect on reducing CVS-related adverse outcome rates. It is likely that mechanical disruption caused by single-needle technique may not be fully compensated by the developing placenta. Therefore, when counseling women regarding the risk of adverse perinatal outcomes after CVS, it may be appropriate to consider procedure-specific risks.

References

[1] Basaran A, Basaran M, Topatan B. Chorionic villus sampling and the risk of preeclampsia: a systematic review and meta-analysis. Arch Gynecol Obstet. 2011;283:1175–81.
[2] Kollmann M, Haeusler M, Haas J, Csapo B, Lang U, Klaritsch P. Procedure-related complications after genetic amniocentesis and chorionic villus sampling. Ultraschall Med. 2013;34:345–8.
[3] Farina A. Nonabortal pregnancy complications of chorionic villous sampling. Curr Opin Obstet Gynecol. 2011;23:129–34.
[4] Alfirevic Z, Sundberg K, Brigham S. Amniocentesis and chorionic villus sampling for prenatal diagnosis. Cochrane Database Syst Rev. 2003;3:CD003252.
[5] Young C, von Dadelszen P, Alfirevic Z. Instruments for chorionic villus sampling for prenatal diagnosis. Cochrane Database Syst Rev. 2013;1:CD000114.
[6] Grobman WA, Auger M, Shulman LP, Elias S. The association between chorionic villus sampling and preeclampsia. Prenat Diagn. 2009;29:800–3.
[7] Adusumalli J, Han CS, Beckham S, Bartholomew ML, Williams J III. Chorionic villus sampling and risk for hypertensive disorders of pregnancy. Am J Obstet Gynecol. 2007;196:591.e1–7.
[8] Odibo AO, Singla A, Gray DL, Dicke JM, Oberle B, Crane J. Is chorionic villus sampling associated with hypertensive disorders of pregnancy? Prenat Diagn. 2010;30:9–13.
[9] Lindgren P1, Cederholm M, Haglund B, Axelsson O. Invasive procedures for fetal karyotyping: no cause of subsequent gestational hypertension or pre-eclampsia. Br J Obstet Gynaecol. 2010;117:1422–5.
[10] Khalil A, Akolekar R, Syngelaki A, Penco JM, Nicolaides KH. Effect of chorionic villus sampling on uterine artery Doppler. Fetal Diagn Ther. 2010;28:9–13.
[11] Wilson ML, Goodwin TM, Pan VL, Ingles SA. Molecular epidemiology of preeclampsia. Obstet Gynecol Surv. 2003;58:39–66.
[12] Tabor A, Alfirevic Z. Update on procedure-related risks for prenatal diagnosis techniques. Fetal Diagn Ther. 2010;27:1–7.
[13] Reid KP, Gurrin LC, Dickinson Newnham JP, Phillips JM. Pregnancy loss rates following second trimester genetic amniocentesis. Aust N Z J Obstet Gynaecol. 1999;39:281–5.
[14] Silver RK, Wilson RD, Philip J, Thom EA, Zachary JM, Mohide P, et al. NICHD EATA Trial Group. Late first-trimester placental disruption and subsequent gestational hypertension/preeclampsia. Obstet Gynecol. 2005;105:587–92.
[15] McKeeman GC, Ardill JE, Caldwell CM, Hunter AJ, McClure N. Soluble vascular endothelial growth factor receptor-1 (sFlt-1) is increased throughout gestation in patients who have preeclampsia develop. Am J Obstet Gynecol. 2004;191:1240–6.
[16] Akolekar R, Beta J, Picciarelli G, Ogilvie C, D'Antonio F. Procedure-related risk of miscarriage following amniocentesis and chorionic villus sampling: a systematic review and meta-analysis. Ultrasound Obstet Gynecol. 2015;45:16–26.

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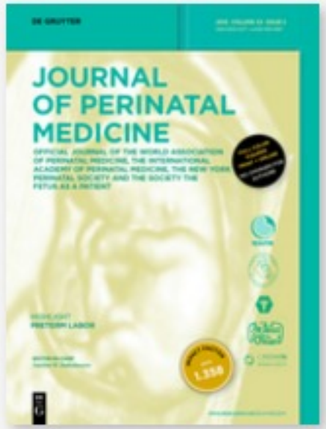

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