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Original Article

Contemporary Outcomes of Chorionic Villus Sampling from the First Trimester to Neonatal Follow-Up

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ABSTRACT

Objective: To evaluate contemporary indications, diagnostic yield, diagnostic limitations, and pregnancy–neonatal outcomes of chorionic villus sampling (CVS) in a tertiary referral population in the era of widespread non-invasive prenatal testing.

Methods: This retrospective cohort study included 70 singleton pregnancies that underwent CVS at a tertiary referral center between October 2023 and June 2025. Maternal characteristics, indications for CVS, genetic testing results, and procedure-related outcomes were recorded. Pregnancy loss, the need for repeat invasive testing, termination decisions, and delivery and neonatal outcomes were assessed.

Results: Major fetal structural anomalies were the leading indication (40%). Pathological genetic findings were identified in 21.4% of cases. Despite multimodal testing, 5.7% remained without a result, and 17.1% required repeat invasive sampling. No immediate complications occurred. Four pregnancy losses before 24 weeks' gestation (5.7%) were observed. Three occurred in pregnancies with major structural or chromosomal abnormalities, while one occurred in a structurally normal fetus with inconclusive cytogenetic results. When anomaly-associated cases were excluded, the observed loss rate among structurally normal pregnancies was 1.4%. No membrane rupture or chorioamnionitis occurred. Among live births, 97.2% were delivered at term. Neonatal outcomes were reassuring, and stillbirths (3.1%) were attributable to severe fetal or maternal pathology rather than the CVS procedure.

Conclusion: Structural fetal anomalies are now the leading indication for CVS. Post-procedure complications were rare, and most adverse outcomes were observed in pregnancies with underlying fetal or maternal pathology. These findings support the continued role of CVS as a diagnostic option in selected high-risk pregnancies.

Keywords: Chorionic villus sampling, prenatal diagnosis, genetic testing, chromosomal abnormalities, pregnancy outcomes, diagnostic yield, non-invasive prenatal testing, structural anomalies

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INTRODUCTION

Prenatal identification of genetic and chromosomal abnormalities has become a central component of contemporary obstetric and perinatal care. The detection of numerical and structural chromosomal anomalies, as well as of single-gene disorders, plays a critical role in risk assessment, counseling, and early pregnancy management.[1] Invasive diagnostic procedures such as chorionic villus sampling (CVS) and amniocentesis (AC) remain essential tools in this process and are supported by current professional guidelines, including those of the American College of Obstetricians and Gynecologists (ACOG), the Royal College of Obstetricians and Gynaecologists, and the International Society of Ultrasound in Obstetrics and Gynecology (ISUOG).[2-4]

CVS is typically performed between 10 and 14 weeks of gestation and enables retrieval of fetal genetic material several weeks earlier than AC, which is generally not recommended before 15 weeks because of an increased risk of complications.[1,5] Achieving a diagnosis in the first trimester provides several important advantages, including reduced parental anxiety, earlier clinical decision-making, and the opportunity to perform pregnancy termination at a safer gestational age (GA) when indicated.[1,6,7] Additional procedural benefits include the absence of direct fetal manipulation and of disruption to the fetal membranes. For these reasons, CVS has long been regarded as a reliable and effective first-trimester diagnostic option in experienced centers.[8]

Despite these strengths, several technical limitations may influence diagnostic accuracy. Maternal cell contamination (MCC), confined placental mosaicism, and culture failure can complicate the interpretation of CVS results and may necessitate further invasive testing in a subset of patients.[9,10] Reported culture failure rates following CVS range from approximately 2.2% to 34%, while MCC rates range from 1.06% and 24.6%, reflecting substantial variability across centers and laboratory methodologies.

Although recent advances in prenatal screening, particularly non-invasive prenatal testing (NIPT), have reduced the number of invasive procedures, accurate counseling remains essential when offering CVS.[11,12] Reported procedure-related pregnancy loss rates range from 0.7% to 3.2%.[1,9,12,13] This variability may reflect differences in loss definitions, GA thresholds, and the inclusion of structurally or chromosomally abnormal pregnancies. Accordingly, counseling should incorporate accurate center-specific outcome data.[12]

The aim of this study was to evaluate the indications, diagnostic efficiency, procedural outcomes, and short-term pregnancy and neonatal outcomes of CVS performed in a tertiary referral center. By examining genetic testing methods, post-procedural complications, the need for repeat invasive testing, and subsequent pregnancy and neonatal outcomes, this study aims to provide contemporary outcome data from a high-risk referral population and to help inform clinical counseling and decision-making.

METHODS

This retrospective cohort included singleton pregnancies that underwent CVS between October 2023 and June 2025 at the Maternal–Fetal Medicine Unit of the University of Health Sciences Türkiye, İzmir City Hospital. The study protocol was approved by the University of Health Sciences Türkiye, İzmir City Hospital Ethics Committee (approval number: 2025/325, date: 09.07.2025).

Study Population and Indications

Pregnancies in which CVS was performed for genetic diagnosis were included in the study. Maternal age, gravidity, parity, number of living children, and GA at the time of the procedure were recorded. GA was determined by the last menstrual period or by first-trimester crown–rump length. Indications for CVS were categorized as follows: maternal anxiety, high-risk combined first-trimester screening test (cut-off >1/250), positive NIPT result, sonographic soft markers, major fetal structural anomalies, history of a previous child with aneuploidy or a genetic disease, parental carrier status for a chromosomal abnormality, and multiple indications (defined as the presence of more than one indication in the same patient).

Nuchal translucency (NT), included in the sonographic marker group, was measured by a maternal–fetal medicine specialist in accordance with the guidelines of the American Institute of Ultrasound in Medicine. Increased NT was defined as a measurement ≥3.0 mm during first-trimester sonography.[14]

All patients underwent a standardized first-trimester ultrasound examination in accordance with the ISUOG guidelines.[15] All ultrasound examinations were performed using a Voluson E8 system (GE Healthcare, Wauwatosa, WI, USA) equipped with a 2–9 MHz convex transducer.

CVS Technique

All procedures were performed between 11 and 14 weeks of gestation. Prior to CVS, detailed counseling was provided about the results of screening tests, available invasive diagnostic options, and the benefits and limitations of each option. This was a retrospective study, and written informed consent was obtained from all patients.

Fetal viability, presentation, and placental location were evaluated before the procedure. CVS was performed under continuous ultrasound guidance using a double-needle technique, with the same ultrasound system and standardized protocol used for the first-trimester screening examinations. An 18-gauge needle was introduced transabdominally, without local anesthesia, to reach the placenta. After removal of the stylet, an assistant inserted a 20-gauge aspiration needle and manually aspirated placental villi. All procedures were carried out under aseptic conditions by a fellow physician under the direct supervision of a maternal–fetal medicine specialist. Immediately after the procedure, fetal heart activity, amniotic fluid volume, and the presence of any hemorrhage were assessed. Rh-negative and indirect Coombs-negative patients received 300 µg of anti-D immunoglobulin for prophylaxis against alloimmunization.

Genetic Testing Protocol

All specimens were processed in the institutional genetics laboratory. Quantitative fluorescence polymerase chain reaction (QF-PCR) and conventional karyotyping were routinely performed.

Chromosomal microarray analysis (CMA) is not routinely performed in our clinic; instead, it is reserved for pregnancies with major fetal structural anomalies or increased NT, as well as for cases in which conventional karyotyping yields no result or yields a normal result despite high clinical suspicion. Next-generation sequencing (NGS) or Multiplex Ligation-dependent Probe Amplification (MLPA) was performed in a limited number of cases, including pregnancies with a relevant family history or suspicion of a single-gene disorder. The total number of patients evaluated with each genetic method was recorded.

Patients with abnormal results on any genetic test were assigned to the pathological group. Those in whom no results could be obtained from any genetic test were categorized as the no-result group. The number of pregnancy terminations within each indication group was also recorded.

Maternal, Pregnancy, and Neonatal Outcomes

Maternal, pregnancy, and neonatal outcomes included complications and pregnancy loss, such as vaginal bleeding, preterm premature rupture of membranes (PPROM), chorioamnionitis, and miscarriage. To provide more detailed information and to address potential discrepancies in definitions, we categorized all spontaneous losses into the following time intervals: 0–48 hours, 2–7 days, 7–14 days, and 2–24 weeks post-procedure. Patients who required repeat invasive testing, as well as those who accepted or declined repeat sampling, were recorded. Additional follow-up data included counseling on pregnancy termination; the number of terminations performed; maternal or fetal complications; hospital admissions and their indications; and stillbirths and live-birth outcomes. For subsequent pregnancies following CVS, follow-up data were collected from both hospital records and structured telephone interviews to investigate additional complications not documented in medical records. Birth characteristics, including preterm or term delivery, mode of delivery, and neonatal outcomes, were recorded for all live births. However, third-trimester follow-up data were unavailable for six patients. Therefore, variables related to late-pregnancy follow-up, hospital admissions, associated maternal–fetal conditions, and delivery and neonatal outcomes were evaluated in the remaining 64 patients.

Outcome Definitions

Primary outcomes were the diagnostic yield of CVS (proportion of pathological genetic findings across QF-PCR, karyotyping, CMA, NGS, and MLPA) and pregnancy loss rates (miscarriage, intrauterine death, stillbirth) from the procedure to neonatal follow-up.

Secondary outcomes included post-procedure complications (vaginal bleeding, PPROM, chorioamnionitis); need for repeat invasive testing; pregnancy termination rates; maternal/fetal complications [e.g., preeclampsia, fetal growth restriction (FGR)]; delivery characteristics (preterm birth, mode of delivery); and neonatal outcomes [birth weight, Apgar scores, neonatal intensive care unit (NICU) admission, neonatal loss].

In the present study, procedure-related pregnancy loss was not defined using a strict causal attribution model. Instead, pregnancy losses were categorized descriptively by the time interval following CVS and by the presence or absence of major fetal structural or chromosomal abnormalities.

Statistical Analysis

Descriptive statistical analyses were performed using the Statistical Package for the Social Sciences, version 26.0 (IBM Corp., Armonk, NY). Continuous variables were summarized as mean ± standard deviation, and as ranges when appropriate, while categorical variables were reported as frequencies and percentages. Exact binomial 95% confidence intervals (CIs) were calculated for key proportions. Exploratory subgroup comparisons were performed using Fisher's exact test. Univariable logistic regression analysis was conducted to evaluate predictors of pathological genetic findings.

RESULTS

A total of 80 patients were initially scheduled for CVS between 2023 and 2025. The procedure could not be performed in 10 patients (12.5%): nine due to an unfavorable placental location (posterior; 11.3%) and one due to a pre-procedural missed miscarriage (1.3%), resulting in a final study cohort of 70 patients. A total of seven patients who were Rh-negative and indirect Coombs-negative received 300 µg of anti-D immunoglobulin. The mean maternal age was 32.2±5.8 years, and CVS was performed at a mean GA of 12.9±0.8 weeks. Demographic characteristics of the study population are summarized in Table 1.

Table 2 presents the indications for CVS and associated diagnostic outcomes. Major fetal structural anomalies were the most frequent indication (40%, 28/70), among which there were 11 pathological results (39.3%) and 16 terminations (57.1%). An increased risk on the first-

trimester combined screening test accounted for 22.9% of cases; none of these cases yielded pathological genetic results. Maternal anxiety was the indication in 3 cases (4.3%), whereas an increased risk on NIPT (2.9%) resulted in abnormal findings in both patients. Sonographic soft markers represented 10% of indications, most commonly increased NT. One pathological result (14.3%) was identified in this group.

A prior pregnancy affected by a chromosomal abnormality was the indication for 6 patients (8.6%); none of these pregnancies showed a pathological finding, although one pregnancy was later terminated after micromelia suggestive of a skeletal dysplasia. Parental carrier status accounted for 2 cases (2.9%); one pathological result and one inconclusive result. Multiple indications were present in 6 patients (8.6%), including one patient with a pathogenic neurofibromatosis type 1 (NF1) variant. In another case, MCC was inconclusive, and the patient subsequently underwent AC, which identified a homozygous osteogenesis imperfecta-related variant, leading to pregnancy termination. Exploratory subgroup comparisons of diagnostic yield across indication groups were performed using Fisher's exact test. The rate of pathological findings was significantly higher in pregnancies with major fetal structural anomalies than in those with other indications ($p<0.001$). Univariable logistic regression analysis demonstrated that the presence of major fetal structural anomalies was significantly associated with pathological genetic findings (odds ratio 10.7%; 95% CI: 3.1–36.2; $p<0.001$). Overall, pathological genetic findings were identified in 15 of 70 cases (21.4%; 95% CI: 12.8–32.3). No diagnostic result was obtained in 4 of 70 cases (5.7%; 95% CI: 1.6–13.9), and pregnancy termination was performed in 20 of 70 cases (28.6%; 95% CI: 18.4–40.6).

Table 1. Demographic characteristics of the study population

n=70	Mean ± SD (min–max)
Age	32.2±5.8 (20–43)
Gravidity	2.3±1.4 (1–7)
Parity	0.94±0.98 (0–4)
Living children	0.90±0.97 (0–4)
Abortions	0.40±0.97 (0–5)
Gestational age (weeks)	12.9±0.8 (11–14)

SD: Standard deviation, min: Minimum, max: Maximum

Table 3 summarizes the genetic test results. QF-PCR identified 9 pathological findings (12.9%), including 45, X (monosomy X; Turner syndrome), trisomy 21 (n=3), trisomy 18 (n=3), and trisomy 13 (n=2), while 14 samples were non-informative. Conventional karyotyping detected 12 abnormalities (17.1%), including del(6)(p22), monosomy X, mosaic Turner syndrome, and multiple autosomal trisomies. Nineteen samples were inconclusive due to low band resolution, culture failure, MCC, or technical issues.

CMA was performed in 13 cases and identified three abnormalities (23.1%): a pathogenic 6p25.3–p24.1 microdeletion, trisomy 21, and monosomy X. The latter two had already been detected by karyotyping; thus, the 6p25.3–p24.1 microdeletion represented the additional diagnostic yield of CMA beyond conventional karyotyping (1/13 cases; 7.7%). NGS identified two likely pathogenic variants (NF1 and COL1A1), while one sample could not be analyzed due to MCC. MLPA confirmed one homozygous

Table 2. Clinical indications for CVS and associated diagnostic outcomes

n=70	n (% of total)	Pathological result n (% within group)	No result n (% within group)	TOP n (% within group)
Maternal anxiety	3 (4.3)	-	1 (33.3)	-
Screen-positive test (1st trimester)	16 (22.9)	-	-	-
Increased risk in NIPT	2 (2.9)	2 (100)	-	2 (100)
Sonographic markers	7 (10)	-	1 (14.3)	-
Increased NT	5 (7.1)	-	-	-
Others	2 (2.9)	-	1 (50)	-
Major fetal structural anomaly	28 (40)	11 (39.3)	1 (3.6)	16 (57.1)
Previous pregnancy with chromosomal abnormality	6 (8.6)	-	-	1 (16.7)
Parental chromosomal rearrangement carrier	2 (2.9)	1 (50)	1 (50)	1 (50)
Multiple indications	6 (8.6)	1 (16.7)	-	1 (16.7)
Total	70 (100)	15 (21.4)	4 (5.7)	20 (28.6)

TOP: Termination of pregnancy, NIPT: Non-invasive prenatal testing, NT: Nuchal translucency, CVS: Chorionic villus sampling

Table 3. Genetic test results

Type of test n=70	n (% of total)	Pathological result n (%)	Normal result n (%)	No result n (%)
QF-PCR	70 (100)	9 (12.9) 1 45,X 3 T21 3 T18 2 T13	47 (67.1)	14 (20)[a]
KT	70 (100)	12 (17.1) 1 del(6)(p22) 1 45,X 1 47,XXX/45,X/46,XX (mosaic Turner syndrome) 3 T21 3 T18 3 T13	39 (55.7)	19 (27.1)[b]
CMA	13 (18.6)	3 (23.1) 1 6p25.3–p24.1 del (pathogenic) 1 T21 1 45,X	8 (61.5)	2 (15.4)[c]
NGS	4 (5.7)	2 (50) 1 NF1 c.1466A>G (p.Tyr489Cys) 1 COL1A1 p.Gly626Asp (heterozygous, likely pathogenic)	1 (25)	1 (25)
MLPA	1 (1.4)	1 (100) SMN1 exons 7–8 (homozygous deletion)		

[a]In 8 cases, no result was obtained due to maternal cell contamination. It was recommended to wait for the cytogenetic results for 2 patients with chromosome 13 anomaly, 1 patient with chromosome 18 anomaly, and 2 patients with sex chromosomes

[b]No result due to low band resolution (n=3), maternal cell contamination (n=3), culture failure (n=7), or technical issues (n=6)

[c]No result due to maternal cell contamination (n=1) or technical issues (n=2)

Maternal cell contamination was observed in 20 cases overall and contributed to inconclusive results in QF-PCR (n=4), karyotyping (n=2), QF-PCR + karyotyping (n=2), and QF-PCR + CMA (n=2). For each test modality, percentages in the "Pathological," "Normal," and "No result" columns reflect within-group distributions, calculated relative to the number of patients who underwent that specific test ("n tested").

QF-PCR: Quantitative fluorescence polymerase chain reaction, CMA: Chromosomal microarray analysis, KT: Conventional karyotype analysis, NGS: Next-generation sequencing, MLPA: Multiplex ligation-dependent probe amplification, T: Trisomy

Note: For each test modality, percentages in the "pathological," "normal," and "no result" columns reflect within-group distributions, calculated relative to the number of patients who underwent that specific test ("n tested")

SMN1 deletion. Overall, pathological findings in the cohort included trisomy 21 (4.3%), trisomy 18 (4.3%), trisomy 13 (4.3%), monosomy X (1.4%), mosaic Turner syndrome (1.4%), a pathogenic 6p deletion (1.4%), an NF1 variant (1.4%), a homozygous SMN1 deletion (1.4%), and a likely pathogenic COL1A1 variant (1.4%).

A total of 70 CVS procedures were evaluated for short- and intermediate-term outcomes (Table 4). No immediate complications occurred within the first 48 hours. Two patients experienced early pregnancy loss within the first two weeks (2.8%; 95% CI: 0.3–9.7). Repeat invasive testing was required in 12 patients (17.1%) because initial results were inconclusive or incomplete, most commonly secondary to MCC, culture failure, or other technical limitations.

Termination of pregnancy was recommended in 23 cases (32.9%) and performed in 20 cases (28.6%). The mean GA at termination was 15.4±3.3 weeks (range: 11–22). Additional maternal–fetal complications occurred in two pregnancies (3.1%): one pregnancy developed preeclampsia with placental abruption, and the other involved a fetus with trisomy 21 that demonstrated early-onset FGR. Hospitalization was required in three cases (4.7%): one case due to FGR related to trisomy 21 and two cases due to complications associated with diabetes.

Stillbirth occurred in two pregnancies (3.1%): one associated with multiple fetal anomalies and the other in the setting of severe preeclampsia with placental abruption. Among the 64 pregnancies with available delivery outcomes, 36 resulted in live births, in line with expectations for a clinically high-risk CVS population.

Pregnancy loss between 2–24 weeks occurred in two additional cases (2.9%), both were associated with major fetal anomalies: megacystis with trisomy 13 and cystic hygroma with trisomy 18. The detailed clinical characteristics of all pregnancy loss cases are summarized in Table 5.

Table 4. Pregnancy outcomes after CVS		
	Mean ± SD or n (%)	**Description/notes**
Early and ıntermediate outcomes (n=70)		
Complication/loss (0–2 days)	0 (0)	
Complication/loss (2–7 days)	1 (1.4)	
Complication/loss (7–14 days)	1 (1.4)	
Complication/loss (2–24 weeks)	2 (2.8)	
Repeat invasive procedure required	12 (17.1)	5/12 (41.7%) accepted repeat testing*
Termination recommended	23 (32.9)	
Termination performed	20 (28.6)	
Gestational age at termination (weeks)	15.4±3.3 (range 11–22)	
Late pregnancy and delivery outcomes (n=64)		
Maternal/fetal complications	2 (3.1)	1 severe preeclampsia with placental abruption 1 early-onset FGR associated with T21
Hospitalization required	3 (4.7)	1 early-onset FGR associated with T21 2 preterm labor
Stillbirth	2 (3.1)	1 multiple anomalies 1 preeclampsia with abruption
Live birth	36 (56.3)	

*Structural evaluation was inconclusive due to maternal cell contamination (n=2), low band resolution (n=3), culture failure (n=6), or need for additional genetic investigations (n=1)

FGR: Fetal growth restriction, SD: Standard deviation, CVS: Chorionic villus sampling, T: Trisomy

Table 5. Detailed characteristics of pregnancy loss cases following CVS

Case	Maternal age	GA at CVS (weeks)	GA at pregnancy loss (weeks)	Structural anomaly	Genetic result	MCC	Culture failure	Clinical context
1	42	13	14	-	QF-PCR normal; culture failure	-	1	Screen positive test results
2	35	12	14	Megacystis, increased NT	T13	-	-	Megacystis, increased NT
3	31	13	13	Megacystis	Normal	1	-	Megacystis
4	31	11	14	Cystic hygroma	Normal	-	-	Cystic hygroma

GA: Gestational age, CVS: Chorionic villus sampling, MCC: Maternal cell contamination, QF-PCR: Quantitative fluorescence polymerase chain reaction, NT: Nuchal translucency

Overall, pregnancy loss occurred in 4 of 70 pregnancies (5.7%). Three losses were associated with major fetal structural or chromosomal abnormalities, whereas one occurred in a structurally normal fetus with inconclusive cytogenetic results. When pregnancies with major anomalies were excluded, the observed loss rate among structurally normal pregnancies was 1.4% (1/70).

Delivery outcomes among the 36 live births are summarized in Table 6. Of these, 35 (97.2%) delivered at term, while one patient (2.8%) delivered preterm at 35 weeks due to trisomy 21. Spontaneous vaginal delivery occurred in 25% of cases, and primary cesarean section occurred in 30.6% of cases. One neonatal death (2.8%) occurred due to cardiac failure related to trisomy 21. The mean GA at delivery was 38.2±1.1 weeks, and the mean birth weight was 3131±570 g. NICU admission was required for 13.9% of neonates; sex distribution was balanced (52.8% female and 47.2% male).

DISCUSSION

This study provides a detailed evaluation of CVS indications, diagnostic yield, and associated pregnancy and neonatal outcomes in this cohort. The results

Table 6. Delivery and neonatal outcomes	
n=36	**Mean ± SD or n (%)**
Term delivery	35 (97.2)
Preterm delivery (<37 weeks)	1 (2.8)*
Spontaneous vaginal delivery	9 (25)
Primary cesarean section	11 (30.6)
Repeat cesarean section	16 (44.4)
Neonatal loss	1 (2.8)**
Gestational age at birth (weeks)	38.2±1.1 (range 35–41)
Birth weight (g)	3131.3±570.1
Female newborns	19 (52.8)
Male newborns	17 (47.2)
Apgar score (1 min)	7.89±1.01
Apgar score (5 min)	9.03±0.97
NICU admission	5 (13.9)

*35 weeks, T21

**Neonatal death secondary to cardiac failure, T21

g: Grams, min: Minute, NICU: Neonatal intensive care unit, SD: Standard deviation, T: Trisomy

demonstrate that major fetal structural anomalies represent the leading indication for CVS and are associated with the highest rate of pathological genetic findings. This association was further supported by exploratory statistical analyses, including Fisher's exact test and univariable logistic regression, which showed a significantly higher likelihood of pathological findings in pregnancies with structural anomalies. In contrast, post-procedure pregnancy loss rates were low in this cohort and occurred predominantly in pregnancies with significant underlying fetal or maternal risk factors.

Pathological genetic results were identified in 21.4% of cases. Although trisomy 21 is typically the most commonly reported aneuploidy, trisomy 18 occurred at a similar frequency in our cohort.[7,9,16] This pattern likely reflects the high prevalence of structural anomalies in our population (40%), which exceeds rates reported in most studies, in which an increased risk on first-trimester screening tests is usually the most common indication.[1,9,12] This may be related to the profile of a tertiary referral center with advanced ultrasound technology and experienced fetal imaging specialists. Moreover, the widespread adoption of NIPT in recent years has not only begun to replace traditional first-trimester screening but has also led to a reduction in invasive diagnostic procedures among women identified as high-risk by first-trimester screening.[17,18] This shift may also explain why elevated first-trimester screening risk is no longer the most common indication for CVS in our cohort. Current guidelines indicate that NIPT is a screening test requiring confirmation by invasive procedures such as CVS or AC.[19] Nevertheless, rare autosomal trisomies are frequently associated with fetal or confined placental mosaicism, which may result in discordance between placental and fetal genetic findings; therefore, AC may be preferred to confirm true fetal involvement when mosaicism is suspected.[20,21]

Changes in clinical practice have also affected the role of advanced maternal age (AMA). Current guidelines from ACOG no longer recommend AMA as a stand-alone indication for invasive testing.[22] Nevertheless, many published series still report that CVS procedures were performed solely for AMA.[1,9,23] In our cohort, no patients underwent CVS solely for AMA. Relatively few studies appear to reflect this recent shift in clinical practice.[12] Spinal muscular atrophy (SMA) carrier screening is now widely recommended.[24,25] Several studies have supported the use of CVS for prenatal diagnosis in pregnancies at risk for SMA.[26-29]

Although our sample size was limited, our findings highlight the relevance of CVS for SMA carrier couples. As carrier screening programs expand, prenatally diagnosed SMA cases are expected to increase, further strengthening the evidence base for this indication.

Reported pregnancy loss rates after CVS vary across studies, largely due to differences in study design and definitions of procedure-related pregnancy loss.[1,9,11-13] Previous studies have reported higher pregnancy loss rates in women aged ≥40 years, both following CVS and in the general obstetric population.[30] In addition, several studies have evaluated both the expected miscarriage risk based on maternal and fetal characteristics and the observed miscarriage rates following CVS.[12,31] In these analyses, no significant increase in miscarriage risk attributable to the procedure was observed. In our study, pregnancy losses were reported according to commonly used time-based categories. No immediate complications, such as vaginal bleeding or PPROM, were observed; however, four pregnancy losses occurred before 20 weeks. Three were associated with major structural or chromosomal abnormalities, while one occurred in a pregnancy without identifiable structural or chromosomal abnormalities. When anomaly-associated cases were excluded, the observed loss rate among structurally normal pregnancies was 1.4%. Pregnancy losses observed following CVS appeared to be predominantly attributable to underlying fetal pathology or AMA. Post-procedure loss rates remained low in this cohort. However, establishing any causal link to the procedure is difficult because of the retrospective design, small sample size, low number of events, and confounding by indication in this high-risk population.

CVS remains an important option when confirmatory testing is required for pregnancy termination decisions, despite advances in NIPT.[32] Published termination rates following CVS range from 16% to 29%, and our findings fall within the upper range of previously reported rates.[1,9,12] This finding likely reflects early and accurate prognostic assessment enabled by detailed ultrasound evaluation and contemporary genetic testing strategies.

Non-informative results can occur due to confined placental mosaicism, insufficient villus sampling, or limited cytogenetic resolution.[1,10] When considered individually, culture failures were observed in 27.1% of cases; however, only 5.7% of patients remained without a definitive diagnosis after applying additional genetic testing methods. These findings are consistent with the potential benefit of multimodal testing strategies. Nonetheless, 17.1% of patients required repeat invasive testing, and more than half declined a second procedure, highlighting the need to consider AC early, particularly when mosaicism is suspected.[9] MCC was an important cause of inconclusive genetic results in our cohort. Although MCC is a recognized limitation of CVS, the occurrence of MCC may also reflect sampling technique, placental characteristics, or laboratory processing factors. Therefore, reducing MCC rates through optimized sampling strategies and laboratory protocols may improve diagnostic efficiency and decrease the need for repeat invasive procedures. However, the determinants of CVS sampling failure remain incompletely understood.[10] Chevreau et al.[10] reported a 34% failure rate, independent of operator experience, and emphasized the need for careful pre-procedural assessment to reduce unsuccessful sampling and repeat procedures.

Regarding obstetric complications, Movahedi et al.[33] reported that PPROM and FGR were the most frequent observed complications following CVS, while no cases of chorioamnionitis were identified. In our cohort, no cases of PPROM were observed, and FGR occurred in only one pregnancy affected by trisomy 21. Similarly, other studies have reported chorioamnionitis as a rare complication following CVS.[33,34]

In our cohort, preeclampsia occurred in only one of 44 ongoing pregnancies that had third-trimester follow-up. This case was complicated by placental abruption and stillbirth. Although the overall prevalence was comparable to that reported in the general population (4.6%),[35] the severity of this case highlights the importance of close monitoring.

Neonatal outcomes following CVS have been evaluated in a limited number of studies.[36] In that large retrospective cohort, the mean GA at delivery was 38.4 weeks, with a preterm birth rate of 10.5%. Cesarean delivery occurred in 53.0% of cases; the mean birth weight was approximately 3158 g, and NICU admission was required in 13.0% of neonates; there was no significant increase in composite neonatal morbidity compared with AC. Our study provides a comprehensive evaluation of indications, genetic findings, and perinatal, obstetric, and neonatal outcomes within a single cohort. Despite the high-risk characteristics of the population, delivery outcomes were generally favorable. Most pregnancies reached term (mean GA of 38.2 weeks); preterm delivery occurred in only one case (2.8%; trisomy 21), and neonatal loss was limited to a single case of trisomy 21. Stillbirth (3.1%) was attributable to severe fetal or maternal pathology rather than to the CVS procedure. The high prevalence of previous cesarean deliveries reflected the underlying obstetric risk profile. Overall, obstetric and neonatal outcomes in this tertiary referral cohort were generally favorable, although these observations are tempered by the study's limitations.

The present study has several limitations. First, the relatively small sample size and the limited number of events reduce the statistical power of the analyses and preclude more extensive multivariable modeling. Second, the retrospective single-center design introduces the potential for referral bias, because our institution is a tertiary referral center that frequently receives high-risk pregnancies with suspected fetal anomalies. Third, confounding by indication cannot be excluded, since pregnancies undergoing CVS often have underlying clinical risk factors that may independently influence pregnancy outcomes. Fourth, no predefined adjudication criteria were applied to attribute pregnancy loss specifically to the CVS procedure rather than to underlying fetal or maternal pathology; therefore, causal attribution should be interpreted with caution. Although all procedures were performed by fellows under the supervision of maternal–fetal medicine specialists, operator experience may influence procedural success, MCC, and complication rates, and should therefore be considered when interpreting the results. Finally, long-term neonatal or neurodevelopmental follow-up data were not available, limiting the ability to assess potential late outcomes beyond the perinatal period.

CONCLUSION

These findings suggest that the indications for CVS are increasingly shifting toward pregnancies with structural fetal anomalies. Our findings indicate that CVS continues to play an important role in definitive prenatal diagnosis, accurate counseling, and timely pregnancy management and that observed post-procedure complication rates were low in both the prenatal and neonatal periods. Post-procedure pregnancy losses in this cohort predominantly occurred in pregnancies with significant fetal or maternal

risk factors and were less frequently observed in structurally normal cases. The results also emphasize the importance of informing families that, in selected cases, additional invasive testing may be required. However, given the retrospective design and single-center nature of the study, these observations should be interpreted cautiously and confirmed in larger, multicenter prospective studies to enhance generalizability and strengthen the evidence base for clinical practice.

Ethics

Ethics Committee Approval: The study protocol was approved by the University of Health Sciences Türkiye, İzmir City Hospital Ethics Committee (approval number: 2025/325, date: 09.07.2025).

Informed Consent: This was a retrospective study, and written informed consent was obtained from all patients.

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Footnotes

Authorship Contributions

Surgical and Medical Practices: Z.E.Ç., H.G., B.B., İ.G.A., H.A.A., E.B., S.K., A.K., A.E., Concept: Z.E.Ç., H.G., A.E., Design: Z.E.Ç., H.G., Data Collection or Processing: S.H.Ö., R.T., İ.G.A., H.A.A., E.B., Analysis or Interpretation: Z.E.Ç., S.H.Ö., Literature Search: Z.E.Ç., H.G., Writing: Z.E.Ç., H.G., A.E.

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