

Chorionic Villus Sampling in the Era of Genomic Medicine: A Gateway to Early and Personalized Prenatal Diagnosis

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Purpose: Despite the rapid expansion of noninvasive genomic technologies, invasive procedures such as chorionic villus sampling (CVS) remain indispensable for providing definitive, early prenatal genetic diagnoses. This study aimed to assess the diagnostic value and effectiveness of CVS in the early detection of chromosomal and genetic abnormalities in a cohort of 912 Polish women.

Patients and Methods: This retrospective cohort study included 912 CVS procedures performed between 2010 and 2024 at a tertiary referral center. Indications, sampling success rates, and genetic results were analyzed. Fetal samples were examined using conventional karyotyping, chromosomal microarray analysis, and digital PCR.

Results: Of 912 procedures, 903 (99.0%) were technically successful, with 844 included in the final cytogenetic analysis. The most common indication was abnormal ultrasound findings (79.9%). Chromosomal abnormalities were found in 40.05% of cases, with trisomy 21 (16.8%), trisomy 18 (8.8%), trisomy 13 (3.1%) and monosomy X (4.6%) being the most frequent. Mosaicism was detected in 8 cases, and maternal cell contamination in 9.

Conclusion: CVS is a valuable method of early prenatal genetic diagnosis, especially in high-risk pregnancies, where early and personalized genomic assessment can have a significant impact on clinical decision-making. Emerging genomic technologies are likely to complement CVS, underscoring its continued relevance in genomic medicine and personalized prenatal care.

Keywords: prenatal diagnosis, chromosomal abnormalities, molecular techniques, high-risk pregnancy, early detection, personalized medicine

Introduction

In the era of personalized medicine, early and accurate prenatal diagnosis plays a pivotal role in reproductive decision-making and risk management. While non-invasive techniques have become widespread, invasive procedures like amniocentesis (AC) or chorionic villus sampling (CVS) remain the gold standard for definitive genetic diagnosis, particularly in high-risk pregnancies.

Since the 1990s, aneuploidy screening between 11 and 13+6 weeks of gestation has become a standard component of prenatal care, with nuchal translucency (NT) recognized as the most effective ultrasound marker for detecting chromosomal abnormalities.^{1,2} Prenatal screening and diagnosis enable the early detection of congenital defects, structural abnormalities, and genetic conditions in the fetus, allowing for appropriate medical interventions and helping parents prepare for treatment and care before the child is born.³

Prenatal testing includes both non-invasive and invasive diagnostic techniques. Non-invasive methods comprise ultrasound examinations, maternal serum screening, and non-invasive prenatal testing (NIPT). Invasive diagnostic

methods include chorionic villus sampling, amniocentesis, and cordocentesis. NIPT is a prenatal genetic screening test based on the analysis of cell-free fetal DNA circulating in maternal blood, typically performed after the 10th week of gestation. It is primarily used to detect common autosomal aneuploidies (such as trisomy 21, 18, and 13), abnormalities in sex chromosomes, and selected microdeletion and microduplication syndromes.

In Poland, non-invasive prenatal testing is increasingly recommended in high-risk pregnancies, according to the joint guidelines of the Polish Society of Gynecologists and Obstetricians (PTGiP) and the Polish Society of Human Genetics (PTGC). The NIPT test should be offered to pregnant women when the risk calculated based on the combined first-trimester screening result falls between 1:300 and 1:1000. In cases where the estimated risk lies between 1:100 and 1:300, it is justified to propose either NIPT or invasive diagnostic testing. If the risk exceeds 1:100, invasive diagnostic testing should be offered without delay.⁴ While NIPT provides high sensitivity and specificity for selected chromosomal abnormalities, it remains a screening test and can occasionally yield false positive or false negative results, which may lead to additional anxiety for patients and necessitate further testing, potentially increasing healthcare costs.^{5,6} Confirmatory diagnostic procedures include invasive procedures such as CVS or amniocentesis, which allow for direct genetic analysis of fetal material.

Chorionic villus sampling is an early prenatal diagnostic procedure involving the collection of placental tissue that reflects the genetic profile of the fetus. An amniocentesis, usually conducted between the 15th and 20th week, involves aspirating amniotic fluid through a thin needle inserted into the uterus, which contains fetal cells for genetic testing. Cordocentesis, performed after the 18th week of pregnancy, involves taking a sample of fetal blood from the umbilical cord. The material obtained through invasive procedures is further analyzed for genetic abnormalities using techniques such as chromosome analysis and DNA analysis to detect chromosomal and monogenic abnormalities.

Chorionic villus sampling and amniocentesis are the most frequently performed invasive prenatal diagnostic procedures, valued for their early applicability and safety. Modern, well-designed studies have shown that both procedures carry similarly low risks of procedure-related miscarriage - typically well under 0.5%, which is considerably lower than older estimates of 1–2% and significantly lower than the risk associated with cordocentesis (1–2%).^{7,8} The risks of chorionic villus sampling are similar to those of amniocentesis and include pregnancy loss, bleeding, infection, rupture of membranes, and uncertain results. The major drawback of CVS is procedure-related pregnancy loss, with published estimates varying between 0.29% and 2%.^{8–10} It is currently thought that the risk of pregnancy loss associated with the CVS procedure is similar to that after amniocentesis and is not significantly different from that in women who have not undergone any invasive procedure.¹¹

It is now consensual that the increase of procedure-induced limb defects is insignificant if sampling occurs after the 10th week of gestation.^{12,13}

CVS and AC have been well recognized as procedures for definitive diagnosis in patients with a high-risk result. Both procedures have been reported to be safe options for accurate genetic assessment.

Chorionic villus sampling has gained significant attention for its early diagnostic capabilities. The development of the trophoblast biopsy technique is attributed to the work of key research teams in Italy and the UK, who played a significant role in its refinement and implementation as a standard diagnostic method in prenatal genetics in the 1970s and 1980s.

This procedure was first performed in Milan by Italian biologist Giuseppe Simoni, scientific director of Biocell Center, in 1983.¹⁴ Brambati and Simoni presented a diagnosis of trisomy of chromosome 21 at 11 weeks' gestation.¹⁴ The continuous clinical implementation of CVS started in 1983, developed by Denis Fairweather and Humphrey Ward, of the University College of London, for the diagnosis of the hemoglobinopathies.^{12,15,16}

CVS is typically performed between the 11th and 14th weeks of gestation, earlier than amniocentesis or percutaneous umbilical cord blood sampling. It is the preferred technique before 15 weeks. In specific circumstances, its use has been described as early as the eighth week.¹⁷ Chorionic villus sampling (CVS) can be performed via two approaches: the transabdominal and the transcervical route.⁷ While both methods are guided by real-time ultrasound and aim to obtain placental tissue for genetic analysis, the transcervical approach is generally considered technically more demanding. It requires precise navigation through the cervical canal and is more dependent on operator experience and uterine anatomy. Moreover, the transcervical route has been associated with a slightly higher risk of procedure-related complications, including vaginal bleeding, infection, and, in some studies, a marginally increased risk of pregnancy loss. In contrast, the

transabdominal approach is typically better tolerated, technically more straightforward in most cases, and carries a lower complication rate, particularly in centers with established expertise. Consequently, when both routes are feasible, the transabdominal method is often preferred.⁷

CVS is typically performed under local anesthesia using lidocaine, in contrast to amniocentesis, which is often conducted without anesthesia. This distinction arises from differences in needle gauge and associated patient discomfort. The needle used in CVS is of a larger diameter, which may cause greater procedural discomfort compared to the finer needle employed in amniocentesis. Moreover, during amniocentesis, the discomfort associated with needle insertion is generally comparable to that experienced during administration of local anesthesia itself. In this procedure, however, the use of local anesthetic is effective in mitigating the increased discomfort resulting from the use of a thicker needle and more extensive manipulation required for placental sampling.

When considering the use of CVS, several factors may indicate the need for this procedure to provide a definitive diagnosis. Indications may include:

- abnormal screening results in the first trimester of pregnancy
- increased nuchal translucency or other abnormal ultrasound findings
- family history of chromosomal abnormalities or other genetic disorders
- parents known to be carriers of a genetic disorder
- advanced maternal age (AMA, defined as age 35 years or older)
- maternal anxiety and request for CVS
- ultrasound marker and positive biochemical maternal serum screening
- oligohydramnios or absence of amniotic fluid.

One important feature of CVS is that chorionic villi provide a more abundant and higher-quality source of fetal DNA compared to amniotic fluid, but it also has its limitations. A small percentage (1–2%) of pregnancies have confined placental mosaicism (CPM), where some but not all of the placental cells tested in the CVS are abnormal, even though the pregnancy is unaffected.¹⁸ The detection of CPM during this procedure often causes significant patient anxiety and necessitates a confirmatory procedure, typically amniocentesis. However, from another perspective, the identification of CPM provides valuable insight into potential placental dysfunction, allowing for more vigilant monitoring of the pregnancy. From a clinical standpoint, this finding may offer prognostic value. Cells from the mother can be mixed with the placental cells obtained from the CVS procedure. Occasionally if these maternal cells are not completely separated from the placental sample, this can lead to discrepancies with the results. This phenomenon is called Maternal Cell Contamination (MCC).¹⁸

Although this procedure is mostly associated with testing for common chromosomal abnormalities, including trisomy 21, trisomy 18 and trisomy 13 (Down, Edwards and Patau syndromes), overall, CVS can detect a wide range of genetic disorders.

A key advantage of this procedure is its ability to provide early and comprehensive genetic information, aiding in clinical decision-making for expectant parents. Direct access to fetal DNA from chorionic villi enables detailed molecular analyses, including chromosomal microarray analysis (CMA), single-gene testing, and emerging epigenetic studies.¹⁹ The integration of next-generation sequencing (NGS), including genome and exome sequencing, into prenatal diagnostics has further expanded the scope of CVS, allowing for a more precise assessment of monogenic disorders and polygenic risk scores, which are becoming increasingly relevant in the era of individualized prenatal medicine.^{20,21} These advancements contribute to a more tailored approach in managing pregnancies at risk for genetic conditions, improving diagnostic accuracy and counseling options.

Chorionic villus sampling, as one of the earliest available sources of fetal genetic material, remains a cornerstone in the era of genomic medicine - offering a gateway to early and personalized prenatal diagnosis.

The aim of this study was to evaluate the diagnostic utility and effectiveness of chorionic villus sampling in detecting chromosomal abnormalities and genetic disorders in a large cohort of Polish patients. Particular attention is given to the

types of abnormalities detected, indications for the procedure, and the integration of molecular methods such as chromosomal microarray analysis and digital PCR into routine practice.

Materials and Methods

This retrospective cohort study investigated 912 patients who underwent chorionic villus sampling for prenatal genetic diagnosis between September 2010 and August 2024 at the Polish Mother's Memorial Hospital Research Institute in Lodz, specifically in the Department of Genetics; Clinic of Gynecology, Reproduction and Fetal Therapy; Infertility Diagnostics and Treatment; and Clinic of Perinatology, Obstetrics and Gynecology. All participants signed a written informed consent after receiving detailed pretest genetic counseling conducted by trained clinical geneticists, which included comprehensive information about the diagnostic procedures and associated risks.

The study included 912 Polish women aged 18–48 years (mean age 32.28 ± 5.51 years).

In our centre, the main indications for trophoblast biopsy were abnormal ultrasound findings and biochemical tests indicating an increased risk of chromosomal aberrations or fetal abnormalities. All chorionic villus sampling procedures were performed by the transabdominal method using a sterile 18G $\times$ 100 mm FNA Chiba needle, under ultrasound guidance and local anesthesia. Anti-D immunoglobulin was administered to Rh-negative, unsensitized patients. In some patients with a retroverted uterine position, the chorion was not safely accessible for CVS, and the sampling was delayed until 15 weeks, when amniocentesis was feasible. However, in a substantial proportion of such cases, an approach for sampling could still be identified. Therefore, a retroverted uterus should not be considered an absolute contraindication for CVS.

A satisfactory amount of tissue was obtained on the first attempt in 99% of cases. The procedure was carried out at a mean of 13 weeks, the earliest case being collected at 10 weeks and the latest at 22 and 23 weeks of gestation in specific circumstances (anhydramnios).

Fetal samples obtained by CVS were analyzed by various techniques including chromosome analysis, chromosomal microarray analysis, fluorescence in situ hybridization (FISH), and digital PCR.

For cytogenetic and molecular studies, the villi were separated from maternal tissue under an inverted microscope and cleaned in an appropriate wash medium (the cell culture medium routinely used in our laboratory). After separation, chromosome preparations were obtained by a direct and a long-term culture method following previously described procedures with slight modifications.^{22,23}

For chromosome analysis, the material was processed using both a direct method and culture method. Metaphases were initially the trypsin-Giemsa banding technique. The result of short-term culture was obtained within 3 days, while long-term culture took about 10 days. The average turnaround time for the result was 14 days and was in accordance with the European guidelines for constitutional cytogenomic analysis.²⁴ Karyotypes were described according to the current International System for Human Cytogenetic Nomenclature (ISCN) guidelines.

DNA extraction and additional studies were done according to standard procedures and disease-specific techniques. All data were recorded in an electronic database. Direct identifiers were removed and replaced with coded identifiers. Numerical variables are presented as means, and categorical variables are expressed as absolute numbers and percentages.

Ethical Approval

The study was conducted in accordance with the principles of the Declaration of Helsinki and approved by the Bioethics Committee of the Polish Mother's Memorial Hospital Research Institute (approval number: KB-89/2025).

Written informed consent was obtained from all participants (or their legal guardians, in the case of minors) prior to inclusion in the study.

Results

Out of 912 chorionic villus sampling procedures performed, 903 were successfully completed. The failure of 9 procedures was due to sampling errors, such as the collection of non-villous tissue or an insufficient amount of chorionic villi, which resulted in unsuccessful culture growth. Of the 903 successful procedures, 844 cases were included in the final cytogenetic analysis. The remaining 59 cases were excluded due to the absence of results (38 cases - mainly due to

culture failure or technical limitations) or inconclusive/non-informative findings (21 cases). All patients with unavailable or ambiguous results were offered an amniocentesis for further diagnostic evaluation.

Long-term follow-up of pregnant patients was beyond the scope of our study. The role of our center was limited to performing the trophoblast biopsy procedure and providing the diagnostic result. In the absence of immediate complications, patients returned to their referring physicians for further prenatal care. Consequently, our dataset does not include information on pregnancy outcomes such as miscarriage or late complications. Given this limitation, these aspects were not included in our analysis.

Among the 844 chorionic villus sampling procedures analyzed in this cohort, the most common indication was abnormal ultrasound findings, reported in 674 cases (79.9%). Other indications included abnormal first-trimester screening results in 76 cases, (9%), advanced maternal age in 17 cases (2.0%), family history of chromosomal abnormalities or other genetic disorders in 27 cases (3%), both advanced maternal age and positive family history in 3 cases (0.4%), and a group classified as “others” in 23 cases (2.7%). 24 procedures are lacking specified indications which is 2.8%. The “others” category comprised cases where the indication for CVS was either maternal anxiety or suspected cytomegalovirus (CMV) infection.

Of the 844 CVS results, 506 (59.9%) were cytogenetically normal. The analysis of 844 CVS procedures performed in our center revealed an abnormal karyotype in approximately 40.05% of cases. The most frequently diagnosed chromosomal abnormality was trisomy 21, identified in 142 cases (16.8%), with the vast majority (131 cases) associated with abnormal ultrasound findings. Trisomy 18 was detected in 74 cases (8.8%), predominantly in patients with abnormal ultrasound results. Trisomy 13 was diagnosed in 26 cases (3.1%), also primarily linked to abnormal ultrasound findings. Monosomy X (45,X), indicative of Turner syndrome, was found in 39 cases (4.6%), while sex chromosome aneuploidy 47,XXY was present in 4 cases (0.5%). Triploidy was observed in 24 cases (2.8%), almost exclusively in association with ultrasound abnormalities. Additionally, 29 cases (3.4%) were categorized as “other abnormalities”, which included structural or rare chromosomal anomalies such as deletions, balanced and unbalanced translocations, additions, inversions, trisomy 22, and mosaic rearrangements. A detailed distribution of cytogenetic results by clinical indication is presented in [Table 1](#).

Abnormal ultrasound findings emerged as the predominant clinical indication for chorionic villus sampling and were associated with the highest diagnostic yield across all categories of chromosomal abnormalities. The vast majority of significant findings - including trisomy 21 (131 of 142 cases), trisomy 18 (69 of 74), trisomy 13 (25 of 26) and monosomy X (38 of 39) - were detected in pregnancies with ultrasound-detected anomalies. In contrast, other clinical indications such as advanced maternal age (AMA) or a positive family history contributed minimally to the detection of genetic abnormalities. These findings emphasize the pivotal role of detailed fetal ultrasound in selecting candidates for invasive testing, even without other risk factors.

Mosaicism was identified in 8 cases using conventional karyotyping, underscoring the importance of comprehensive cytogenetic evaluation in prenatal diagnostics. The detected mosaic karyotypes included mos 45,X/46,XX (n=3), mos 47,XXY/46,XY (n=2), and other rare forms such as mos 47,XY,+21/46,XY (n=1), mos 69,XXX/46,XX (n=1), and 46,XX/46,XY (n=1). In one of these cases, confined placental mosaicism (CPM) was suspected, prompting referral for follow-up amniocentesis, which confirmed a normal fetal karyotype.

Maternal cell contamination (MCC) was identified in 9 cases, necessitating cautious interpretation of cytogenetic findings and, in some instances, additional confirmatory testing.

Karyotyping was the first-line diagnostic method and was performed for all cases included in the study. Since the routine implementation of array comparative genomic hybridization (aCGH) in our prenatal diagnostic workflow in 2019, aCGH has been performed selectively - primarily in pregnancies with abnormal ultrasound findings or in situations where a rapid and more detailed genomic assessment was clinically required. During the study period, a total of 235 aCGH analyses were performed. Among these, abnormal results were identified in 74 cases. Most abnormalities represented common numerical aneuploidies (n = 56), including trisomy 13 (6 cases, including one mosaic karyotype), trisomy 18 (17 cases), trisomy 21 (20 cases, including two mosaic karyotypes), trisomy 22 (1 case), monosomy X (11 cases), and one case of 47,XXY. In addition, aCGH revealed several pathogenic submicroscopic chromosomal abnormalities, including del 22q12.3q13.1, del 22q11.21, del 2q37.3, dup 7p22.3q11.21, del 17q12, del 8p23.3p23.1, del Xp22.31,

Table 1 Distribution of Chorionic Villus Sampling (CVS) Results by Clinical Indication

CVS Results	Indications							
	Abnormal Ultrasound Findings	Abnormal Screening Results in the First Trimester of Pregnancy	Advanced Maternal Age	Family history of Chromosomal Abnormalities or Other Genetic Disorders	Both Advanced Maternal Age and Family History of Chromosomal Abnormalities or Other Genetic Disorders	Others	Unspecified	Total
Normal	363	61	15	23	3	21	20	506
Trisomy 21	131	8	1	0	0	1	1	142
Trisomy 18	69	4	0	0	0	0	1	74
Trisomy 13	25	1	0	0	0	0	0	26
45,X	38	0	0	0	0	1	0	39
47,XXY	4	0	0	0	0	0	0	4
Triploidy	21	1	1	0	0	0	1	24
Others	23	1	0	4	0	0	1	29
Total	311	15	2	4	0	2	4	338
abnormal								
Total	674	76	17	27	3	23	24	844

Abbreviations: aCGH, array comparative genomic hybridization; CMA, chromosomal microarray analysis; CVS, chorionic villus sampling; FBS, fetal blood sampling; MCC, maternal cell contamination; NIPT, noninvasive prenatal testing.

and others. These findings highlight the added diagnostic value of aCGH, particularly in cases where conventional karyotyping did not explain abnormal ultrasound findings or when rapid genomic clarification was necessary.

The integration of aCGH into the diagnostic workflow has therefore substantially increased the overall detection rate of clinically significant chromosomal abnormalities, especially in high-risk pregnancies with inconclusive cytogenetic results.

Digital PCR (dPCR) was introduced at our center in 2018 as part of a development project aimed at implementing a rapid method for detecting the most common fetal aneuploidies.²⁵ The assay was systematically optimised by the staff of the Department of Genetics, ICZMP, and implemented into routine laboratory practice using the QuantStudio 3D Digital PCR platform, in adherence to the established methodology.^{26,27} The technique has since been used as a screening tool enabling preliminary results within 24 hours of sample collection. During the study period, a total of 207 dPCR analyses were performed, of which 88 yielded abnormal findings. Every abnormal dPCR result was subsequently confirmed by conventional karyotyping, with complete concordance and no observed discrepancies. These data highlight the utility of dPCR as a rapid and reliable complementary method, particularly valuable in situations requiring expedited assessment of major aneuploidies prior to the availability of comprehensive cytogenetic or microarray results.

Discussion

Over the past decade, prenatal diagnosis has substantially evolved due to technological advancements and changing societal expectations. The increasing use of genome-wide non-invasive prenatal testing (NIPT) has notably reduced the demand for invasive procedures in general prenatal care.²⁸

Despite this trend, our data reaffirm the enduring value of invasive procedures - especially chorionic villus sampling (CVS) - in high-risk populations. In our cohort, the overall detection rate of chromosomal abnormalities reached 40.05%, which is consistent with findings from Cnota et al (39%), but much higher than that reported by other authors Kuyucuet al (21.1%), Öztürk et al (25.5%), Martins et al (26.6%) and reflects the high-risk population in our tertiary referral center.^{29–32} This discrepancy likely reflects differences in patient selection and referral patterns, particularly the concentration of high-risk cases in centers such as ours.

Data published from Poland based on invasive prenatal procedures - including amniocentesis (AC), chorionic villous sampling (CVS), and fetal blood sampling (FBS) - showed a detection rate of chromosomal abnormalities of 9.7%.³³ Meng et al reported a similar rate of genomic abnormalities in their study (9.6%), but they used both routine karyotyping as well as aCGH for genetic testing.³⁴

Similarly, in a recent Polish cohort of 1746 invasive procedures, including CVS, amniocentesis, and cordocentesis, classical karyotyping revealed chromosomal abnormalities in 19.1% of cases, with an additional 5.0% of clinically significant findings detected using aCGH.¹⁹

In the study by Jorge et al, based on 491 CVS procedures performed over 26 years, abnormal results were identified in 23.7% of cases, encompassing cytogenetic, molecular, and combined methods.¹² When considering only cases referred for conventional karyotyping, chromosomal abnormalities were detected in 6.1% of cases. Taken together, these findings highlight the consistent diagnostic yield of invasive prenatal testing across different populations and underscore the added value of molecular approaches in complementing conventional cytogenetics.

In some centers, a shift in prenatal diagnostic practice has been observed, with increasing preference for chorionic villus sampling over amniocentesis.³⁵ This change reflects advancements in imaging technology, greater clinical experience, and rising patient awareness, despite the relatively low detection rate of abnormal karyotypes following CVS.

The significant advancements in imaging technology, particularly the advent of high-resolution ultrasound, have markedly enhanced the detection of fetal abnormalities. Equally important is the careful selection of patients for invasive testing, which is optimally achieved through comprehensive evaluation by a geneticist–obstetrician skilled in prenatal ultrasound. Our observations align with the findings reported by Bijok et al, underscoring that targeted patient selection based on detailed genetic counseling and improved imaging techniques leads to a higher detection rate of chromosomal abnormalities.³³ This refined approach likely reflects a shift in the baseline risk profile of women undergoing invasive procedures, thereby improving the diagnostic yield of the procedure.

As with any retrospective study, certain limitations may apply, such as variability in clinical practice over the 14-year study period, gradual introduction of new diagnostic methods (dPCR in 2018, aCGH in 2019), and occasional incomplete follow-up. However, these factors reflect the natural evolution of prenatal diagnostics and do not affect the overall interpretation or clinical significance of our results.

Equally critical is the evolution of diagnostic technologies. This method provides early access to fetal tissue and allows integration with advanced molecular methods such as chromosomal microarray analysis (CMA), next-generation sequencing (NGS), digital PCR, and optical genome mapping (OGM). These tools significantly increase the resolution and scope of prenatal diagnosis, enabling detection of not only common trisomies but also submicroscopic and repeat expansion disorders such as facioscapulohumeral muscular dystrophy (FSHD).³⁶ Importantly, NGS performed on CVS samples has enabled the identification of rare monogenic disorders, including a novel MCPH1 mutation associated with autosomal recessive primary microcephaly, highlighting the value of early sampling combined with high-throughput genomic technologies.²⁰

The originality of our study lies in its large Polish cohort and extended timeframe (2010–2024), providing valuable insights into evolving practices in prenatal diagnostics, including karyotyping, aCGH, and dPCR. Our results, viewed in the context of current global trends in genomic medicine and early prenatal testing, underscore the increasing integration of high-resolution molecular and epigenetic approaches and highlight the potential of novel biomarkers to complement conventional cytogenetic and molecular methods. This trend is illustrated by recent epigenome-wide profiling of trisomy 18 in first-trimester chorionic villi, which used high-resolution MC-seq to identify differentially methylated regions as potential early non-invasive biomarkers.³⁷

The results of this study highlight the continued relevance of CVS testing as a reliable source of early fetal genetic material. With the integration of advanced molecular techniques such as chromosomal microarray analysis (CMA), digital PCR, and next-generation sequencing (NGS), CVS offers enhanced diagnostic accuracy, especially in detecting single-gene disorders and submicroscopic chromosomal abnormalities. As prenatal diagnostics evolve toward more individualized and detailed genetic profiling, this procedure remains a key tool in early, comprehensive risk assessment and clinical decision-making.

Beyond its diagnostic utility, the safety of CVS has been a subject of extensive research and debate. A meta-analysis of invasive prenatal procedures show that in the hands of experienced experts performing CVS, the rate of fetal loss and complications is almost identical compared to amniocentesis and is less than 0.5%.^{10,31,38} Also, recent meta-analysis demonstrates that there is no significant difference in fetal loss before 24 weeks of gestation in women who undergo CVS or amniocentesis in specialized centers, compared to those who have no invasive prenatal diagnosis, and furthermore, the miscarriage rate following CVS is lower compared to amniocentesis.^{8,35} The safety profile of this method remains favorable, particularly in experienced hands, with low rates of complications and pregnancy loss. Its proven reliability, combined with compatibility with genomic techniques, makes it a key component of modern prenatal diagnostics.

Early prenatal diagnosis through CVS can provide critical information that may influence parental decision-making and pregnancy management, allowing timely counseling and planning for potential interventions or preparations for neonatal care.

In conclusion, CVS remains a cornerstone of invasive prenatal testing in high-risk pregnancies. When performed in specialized centers with integrated genetic services and state-of-the-art technology, it offers high diagnostic accuracy and reliability. Future directions include broader implementation of genome-wide technologies and optimization of referral pathways to ensure maximum diagnostic benefit.

Conclusion

In summary, despite the rise of non-invasive methods, chorionic villus sampling (CVS) continues to play a vital role in prenatal diagnosis, particularly in high-risk pregnancies, benefiting from technological and procedural advancements. This retrospective analysis of 912 cases confirms that CVS is a reliable and diagnostically valuable method for prenatal diagnosis in the first trimester of pregnancy in pregnancies at risk of chromosomal abnormalities and genetic disorders. Chorionic villus sampling remains a valuable and necessary procedure, especially when performed in specialized centers with integrated genetic services and state-of-the-art technology, ensuring optimal diagnostic accuracy and patient care. In the era of genomic medicine, CVS serves not only as a traditional diagnostic tool but also as a gateway to early and personalized prenatal diagnosis, enabling timely decision-making and tailored counseling based on increasingly precise molecular and cytogenetic findings. As emerging genomic and multi-omics technologies continue to advance, they are expected to complement CVS, further enhancing its role in comprehensive, individualized prenatal diagnostics.

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Disclosure

The authors report no conflicts of interest in this work.

References

1. Nicolaides KH, Azar G, Byrne D, et al. Fetal nuchal translucency: ultrasound screening for chromosomal defects in first trimester of pregnancy. *Br Med J*. 1992;304:867–869. doi:10.1136/bmj.304.6831.867
2. Snijders RJ, Noble P, Sebire N, et al. UK multicentre project on assessment of risk of trisomy 21 by maternal age and fetal nuchal-translucency thickness at 10–14 weeks of gestation. Fetal medicine foundation first trimester screening group. *Lancet*. 1998;352:343–346. doi:10.1016/S0140-6736(97)11280-6
3. Okoror CEM, Arora S. Prenatal diagnosis after high chance non-invasive prenatal testing for trisomies 21, 18 and 13, chorionic villus sampling or amniocentesis? – Experience at a district general hospital in the United Kingdom. *Eur J Obstet Gynecol Reprod Biol X*. 2023;19:1–6.
4. Sieroszewski P, Haus O, Zimmer M, et al. Rekomendacje Polskiego Towarzystwa Ginekologów i Położników oraz Polskiego Towarzystwa Genetyki Człowieka dotyczące badań przesiewowych oraz diagnostycznych badań genetycznych wykonywanych w okresie prenatalnym. 2022;7(1):20–33.
5. Jayashankar SS, Nasaruddin ML, Hassan MF, et al. Non-Invasive Prenatal Testing (NIPT): reliability, challenges, and future directions. *Diagnostics*. 2023;13:1–21. doi:10.3390/diagnostics13152570
6. Liehr T. False - positives and false - negatives in non - invasive prenatal testing (NIPT): what can we learn from a meta - analyses on > 750 000 tests? *Mol Cytogenet*. 2022;15:1–10. doi:10.1186/s13039-022-00612-2
7. Alfirevic Z, Navaratnam K, Mujezinovic F. Amniocentesis and chorionic villus sampling for prenatal diagnosis. *Cochrane Database Syst Rev*. 2009;3:1–37.

8. Salomon LJ, Sotiriadis A, Wulff CB, et al. Risk of miscarriage following amniocentesis or chorionic villus sampling: systematic review of literature and updated meta-analysis. *Ultrasound Obstet Gynecol.* **2019**;54:442–451. doi:10.1002/uog.20353
9. Kollmann M, Haeusler M, Haas J, et al. Procedure-related complications after genetic amniocentesis and chorionic villus sampling. *Ultraschall Med.* **2013**;34:345–348.
10. Likar IP, Jere KS, Možina T, et al. Pregnancy loss after amniocentesis and chorionic villus sampling: cohort study. *Zdr Varst.* **2020**;60:25–29. doi:10.2478/sjph-2021-0005
11. Beta J, Zhang W, Geris S, et al. Procedure-related risk of miscarriage following chorionic villus sampling and amniocentesis. *Ultrasound Obstet Gynecol.* **2019**;54:452–457. doi:10.1002/uog.20293
12. Jorge P, Mota-Freitas M, Santos R, et al. A 26-year experience in chorionic villus sampling prenatal genetic diagnosis. *J Clin Med.* **2014**;3:838–848. doi:10.3390/jcm3030838
13. Firth HV, Huson SM, Boyd PA, et al. Analysis of limb reduction defects in babies exposed to chorionic villus sampling. *Lancet.* **1994**;343(8905):1069–1071. doi:10.1016/S0140-6736(94)90182-1
14. Brambati B, Simoni G. Diagnosis of fetal trisomy 21 in first trimester. *Lancet.* **1983**;1:586.
15. Ward RHT, Modell B, Petrou M, et al. Method of sampling chorionic villi in first trimester of pregnancy under guidance of real time ultrasound. *Br Med J.* **1983**;286:1542–1544. doi:10.1136/bmj.286.6377.1542
16. Old JM, Petrou RHTWM, Modell FK, et al. First-trimester fetal diagnosis for haemoglobinopathies: three cases. *Lancet.* **1982**;320:1413–1416. doi:10.1016/S0140-6736(82)91324-1
17. Wapner RJ, Evans MI, Davis G, et al. Procedural risks versus theology: chorionic villus sampling for Orthodox Jews at less than 8 weeks' gestation. *Am J Obstet Gynecol.* **2002**;186:1133–1136. doi:10.1067/mob.2002.122983
18. Wapner RJ. Invasive prenatal diagnostic techniques. *Semin Perinatol.* **2005**;29:401–404. doi:10.1053/j.semperi.2006.01.003
19. Wójtowicz A, Kowalczyk K, Szewczyk K, et al. Array Comparative Genomic Hybridization (aCGH) results among patients referred to invasive prenatal testing after first-trimester screening: a comprehensive cohort study. *Diagnostics.* **2024**;14:1–26. doi:10.3390/diagnostics14192186
20. Papoulidis I, Eleftheriades M, Manolakas E, et al. Prenatal identification of a novel mutation in the MCPH1 gene associated with autosomal recessive primary microcephaly (MCPH) using next generation sequencing (NGS): a case report and review of the literature. *Children.* **2022**;9:1–7. doi:10.3390/children9121879
21. Ji X, Li Q, Qi Y, et al. When NIPT meets WES, prenatal diagnosticians face the dilemma: genetic etiological analysis of 2328 cases of NT thickening and follow-up of pregnancy outcomes. *Front Genet.* **2023**;14:1–8. doi:10.3389/fgene.2023.1227724
22. Barch MJ, Knutsen T, Spurbeck JL. *The Agt Cytogenetics Laboratory Manual.* **1997**.
23. Zneimer SM. *Cytogenetic Laboratory Managment: Chromosomal, FISH and Microarray-Based Best Practices and Procedures.* **2016**.
24. Silva M, de Leeuw N, Mann K, et al. European guidelines for constitutional cytogenomic analysis. *Eur J Hum Genet.* **2019**;27:1–16. doi:10.1038/s41431-018-0244-x
25. Nykel A, Kaszkowiak M, Fendler W, et al. Chip-based digital PCR approach provides a sensitive and cost-effective single-day screening tool for common fetal aneuploidies - a proof of concept study. *Int J Mol Sci Artic.* **2019**;20:1–11.
26. Nykel A, Woźniak R, Gach A. Clinical validation of novel chip-based digital PCR platform for fetal aneuploidies screening. *Diagnostics.* **2021**;11:1–11. doi:10.3390/diagnostics11071131
27. Nykel A, Woźniak R, Gach A. The influence of maternal cell contamination on fetal aneuploidy detection using chip-based digital PCR testing. *Diagnostics.* **2021**;11:1–10. doi:10.3390/diagnostics11091607
28. Srebnik MI, Knapen MFCM, Govaerts LCP, et al. Social and medical need for whole genome high resolution NIPT. *Mol Genet Genomic Med.* **2020**;8:8–11. doi:10.1002/mgg3.1062
29. Cnota W, Grolik B, Szoltyś-Szot M, et al. Przezbrzuszną biopsję kosmówki w prenatalnej diagnostyce zaburzeń chromosomowych - doświadczenia własne. *Ginek Pol.* **2013**;84:412–417. doi:10.17772/gp/1597
30. Kuyucu M, Erdogan KM, Adiyaman D, et al. Consecutive 5-year outcomes of chorionic villus sampling at a tertiary center. *Med.* **2025**;104:1–5.
31. Öztürk FH, Öcal FD, Erol SA, et al. Fetal genetic diagnosis by chorionic villus sampling: evaluation of the five-year experience from a single center. *Fetal Pediatr Pathol.* **2021**;40:281–289. doi:10.1080/15513815.2019.1707919
32. Martins AT, Francisco C, Correia H, et al. Chorionic villus sampling: 10 years of experience in a University referral center. *J Gynecol Obstet Hum Reprod.* **2020**;49:1–5.
33. Bijok J, Kucińska-Chahwan A, Massalska D, et al. In-house genetic counseling increases the detection of abnormal karyotypes - a 26-year experience in prenatal diagnosis in a single tertiary referral hospital in Poland. *J Assist Reprod Genet.* **2020**;37:1999–2006. doi:10.1007/s10815-020-01812-8
34. Meng J, Matarese C, Crivello J, et al. Changes in and efficacies of indications for invasive prenatal diagnosis of cytogenomic abnormalities: 13 years of experience in a single center. *Med Sci Monit.* **2015**;21:1942–1948. doi:10.12659/MSM.893870
35. Monni G, Corda V, Iuculano A, et al. The decline of amniocentesis and the increase of chorionic villus sampling in modern perinatal medicine. *J Perinat Med.* **2020**;48:307–312. doi:10.1515/jpm-2020-0035
36. Li M, Hao N, Chang J, et al. The distribution of D4Z4 repeats in China and direct prenatal diagnosis of FSHD by optical genome mapping. *Orphanet J Rare Dis.* **2025**;20:1–10. doi:10.1186/s13023-025-03591-w
37. Kim JY, Yang SJ, Kim JW, et al. Epigenome-wide profiling of trisomy 18 specific DNA methylation signatures in first- trimester chorionic villi. *Clin Clin Epigenet.* **2025**;1–13.
38. Akolekar R, Beta J, Picciarelli G, et al. Procedure-related risk of miscarriage following amniocentesis and chorionic villus sampling: a systematic review and meta-analysis. *Ultrasound Obstet Gynecol.* **2015**;45:16–26. doi:10.1002/uog.14636

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