# INDICATIONS AND SAFETY OF CHORIONIC VILLUS SAMPLING ANDAMNIOCENTESIS: A TERTIARY CARE HOSPITAL BASED STUDY

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**Abstract:**
**Background:** Chorionic villus sampling (CVS) and amniocentesis are prenatal tests that help to detect genetic or chromosomal abnormalities in fetuses and help to make important healthcare decisions especially in the era when late marriages are very common.
**Objectives:** The objectives of the study were to identify the common indications of performing chorionic villus sampling and amniocentesis and to compare safety of chorionicvillus sampling and amniocentesis.
**Results:** The most common indication in 139 (49.1%) participants was the history of singlegene disorder in the family followed by positive screening test in 79 (27.9%), family historyof chromosomal disorder in 23 (8.1%), soft marker in ultrasonography in 19 (6.7%), majorstructural abnormality on USG in 10 (3.5%), both soft marker in USG and positive screentest in 7 (2.5%) while as 3 each (1.1%) had fetal hydrops and other minor indications. Overall 98.2% cases of amniocentesis and 97.9 % cases of CVS were uneventful.
**Conclusion:** Both the procedures are safe and the common indication still remains the history of genetic disorder in the family.

**Key Words:** Chorionic villus sampling; Amniocentesis; Indications; Safety;Complications

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## INTRODUCTION:

Pregnant women are offered prenatal diagnostic tests like amniocentesis or chorionic villussampling (CVS) for a variety of reasons including a family history of genetic or chromosomal disorder, positive screening test or higher chance of aneuploidy and fetal structural anomaly on ultrasonography. Despite the increasing use of cell free DNA testingfrom maternal blood both CVS and amniocentesis remain, at present, the only definitive diagnostic tests for aneuploidy in pregnancy.

There is an advantage of detecting genetic abnormalities in the first trimester and giving parents the opportunity of evidence based decision making in continuation of pregnancy. However, there are also many risks associated with the procedure itself and hence counseling the parents before the procedure is equally important. An important risk is the

risk of miscarriage (which has been attributed to 0.5%-1.0% of CVS procedures and 0.25%-0.50% of amniocentesis procedures), chorioamnionitis, bleeding and risk for birth defects like digital or limb deficiency after the procedure. [1,2]

This current study provides information on indications for the use of CVS and amniocentesis, and compares the benefits and risks of the two procedures. The study has been carried out in a single facility where most commonly these procedures are done due to high risk of chromosomal anomalies seen with advanced maternal age.

## AIMS and OBJECTIVE:

The objectives of the study were to identify the common indications of performing chorionic villus sampling and amniocentesis and to compare safety of chorionic villus sampling and amniocentesis.

## MATERIAL and METHODS:

The study was a prospective study and was conducted by postgraduate Department of Fetal Medicine and Medical Genetics, Mahatma Gandhi Hospital, Jaipur, India. A total of 283 pregnant women agreed to participate in the study during a 1 year period (2020-21). Data was collected on self designed proforma and written informed consent was taken from the participants. Individualized counseling of the merits and demerits of CVS and amniocentesis was also provided for the parents undergoing the procedure.

**Chorionic villus sampling:** It was performed at $11^{+0}$ to $13^{+6}$ weeks of gestation. Trans- abdominal approach under continuous ultrasound guidance was used under aseptic technique. Ideal site exposing the longest axis of placenta was identified in supine position. Abdomen was cleaned with chlorhexidine or iodine solution and sterile drapes were placed to create sterile field. Under local anesthetic (10 ml xylocaine) 18 gauge spinal needle was inserted into the placenta under continuous ultrasound guidance. 20 cc syringe containing collection media was attached to the end of the needle once stylet was removed.Negative pressure was created, and needle moved up and down through the placenta, collecting the tissue. Once the sample was collected, it was examined to ensure sufficient chorionic villus sample was aspirated.

**Amniocentesis:** It was performed at $16^{+0}$ to 20 weeks of gestation. Trans-abdominal approach under continuous ultrasound guidance using an aseptic technique was again usedfor amniocentesis. Needle was introduced at an angle of 45° with respect to the maternal mid-sagittal plane, contralateral to the probe, so that the probe and the needle are at a 90° angle with respect to each other. Needle was inserted lateral to the probe, directly under

the middle of the ultrasound beam. The needle advanced about 3 cm pointing towards the middle of the MVP. Once the needle was located correctly in the uterine cavity, the stylet was removed to connect syringe. Approximately 20 ml amniotic fluid was obtained from the procedure, ideally without contamination by maternal blood cells.

**Inclusion and Exclusion criteria**: All pregnant women undergoing CVS or amniocentesis at Department of Fetal Medicine and Medical Genetics, Mahatma Gandhi Hospital during the period of study (1 year) were considered for participation in the study. Women who refused to participate in the study were excluded.

## RESULTS:

**Table 1:** Characteristics of participants undergoing amniocentesis and chorionic villus sampling

| Procedure | Age of participant(years) Mean ± SD | Gestational age(weeks) Mean ± SD |
|---|---|---|
| Amniocentesis (N=170) | 28.96 ±4.585 | 17.92 ±1.860 |
| Chorionic Villus Sampling (N=113) | 28.34 ±4.085 | 11.66 ±0.475 |
| Total (N= 283) | 28.71 ±4.395 | 15.42 ±3.403 |

Table 1 shows mean age of the participants and mean gestational age at the time of procedure. The mean age in amniocentesis and chorionic villus sampling was 28.96 ±4.585years and 28.34 ±4.085 years, respectively. The mean gestational age in weeks at the time of amniocentesis was 17.92 ±1.860 while as it was 11.66 ±0.475 in case of chorionic villussampling.

**Table 2:** Indications for amniocentesis and chorionic villus sampling in the study population

| | Procedure | | | | Total | |
|---|---|---|---|---|---|---|
| | Amniocentesis | | Chorionic Villus Sampling | | | |
| | N | Percent | N | Percent | N | Percent |
| Family history of Single gene disorder | 29 | 17.1% | 110 | 97.3% | 139 | 49.1% |
| Screening test positive | 78 | 45.9% | 1 | 0.9% | 79 | 27.9% |
| Family history of chromosomal disorder | 23 | 13.5% | 0 | 0.0% | 23 | 8.1% |
| Soft marker in USG | 19 | 11.2% | 0 | 0.0% | 19 | 6.7% |
| Major structural abnormality on USG | 10 | 5.9% | 0 | 0.0% | 10 | 3.5% |
| Soft marker in USG and screen test positive | 6 | 3.5% | 1 | 0.9% | 7 | 2.5% |
| Fetal hydrops | 2 | 1.2% | 1 | 0.9% | 3 | 1.1% |
| Other indication | 3 | 1.8% | 0 | 0.0% | 3 | 1.1% |
| Total | 170 | 100.0% | 113 | 100.0% | 283 | 100.0% |

The indication for amniocentesis and chorionic villus sampling is shown in table 2. The most common indication in 139 (49.1%) participants was the history of single gene disorder in the family. 79 (27.9%) had positive screening test, 23 (8.1%) had family history of chromosomal disorder, 19 (6.7%) had soft marker in ultrasonography, 10 (3.5%) had major structural abnormality on USG, 7 (2.5%) had both soft marker in USG and positivescreen test while as 3 each (1.1%) had fetal hydrops and other minor indications. The most common indication for amniocentesis was positive screening test in 78 (45.9%) while as most common indication for chorionic villus sampling was family history of single gene disorder in 110 (97.3%) of the participants.

**Table 3:** Test results (fetal status) following amniocentesis and chorionic villussampling among the study population.

| | RESULT/ Fetal status | | Total | p-value |
|---|---|---|---|---|
| | Abnormal | Normal | | |
| Amniocentesis | 14 | 156 | 170 | 0.024 |
| | 8.2% | 91.8% | 100.0% | |
| Chorionic Villus Sampling | 20 | 93 | 113 | |
| | 17.7% | 82.3% | 100.0% | |
| Total | 34 | 249 | 283 | |
| | 12.0% | 88.0% | 100.0% | |

The results received following amniocentesis and chorionic villus sampling are shown in table 3. Out of 170 participants who underwent amniocentesis 14 (8.2%) of their fetuses had genetic disorder while as in case of CVS 20 (17.7%) out of 113 had genetic disorder.

**Table 4:** Comparison of complications of amniocentesis and chorionic villus sampling

| | Procedure | | | | Total | |
|---|---|---|---|---|---|---|
| | Amniocentesis | | Chorionic Villus Sampling | | | |
| | N | Percent | N | Percent | N | Percent |
| Pregnancy loss | 1 | 0.6% | 1 | 0.9% | 2 | 0.7% |
| Bleeding | 0 | 0.0% | 2 | 1.8% | 2 | 0.7% |
| Infection | 1 | 0.6% | 0 | 0.0% | 1 | 0.4% |
| Rupture of membranes | 1 | 0.6% | 0 | 0.0% | 1 | 0.4% |
| No complication | 167 | 98.2% | 110 | 97.1% | 277 | 97.9% |
| Total | 170 | 100.0% | 113 | 100.0% | 283 | 100.0% |

The complications observed following amniocentesis and CVS are shown in table 4. In amniocentesis we had one case (0.6%) each of pregnancy loss, infection and rupture of membranes. While as in CVS we observed one (0.9%) pregnancy loss and 2 (1.8%) participants had bleeding per vagina. Overall 98.2% cases of amniocentesis and 97.9 % cases of CVS were uneventful.

**DISCUSSION**:

Typically, the gestational age for CVS is 11-13 weeks' and for amniocentesis is 15-20 weeks'. In our study the mean gestational age in weeks at the time of amniocentesis was 17.92 ±1.860 while as it was 11.66 ±0.475 in case of chorionic villus sampling. Further theevidence shows that there are high chances of pregnancy loss and potential for talipes equinovarus development if amniocentesis is performed before 15+0 weeks' gestation.[3,4] Early amniocentesis may also lead to increased chances of multiple insertions [5] besides cytogenetic implications, increased risk of failed culture and false negative results.[6] The increased risk of complications is also gestation dependant and hence guidelines also discourage performing CVS before $10^{+0}$ weeks.[3,7] Additionally, due to underdeveloped placenta the CVS before $11^{+0}$ weeks' gestation can be more technically challenging.

The mean age of the participants in amniocentesis and chorionic villus sampling was 28.96 ±4.585 years and 28.34 ±4.085 years, respectively. The main reason for amniocentesis andCVS in our study was genetic and chromosomal disorders. However, in United States, CVS and amniocentesis is offered almost to all pregnant women who are greater than or equal to 35 years of age as there is increased risk of Down's syndrome and aneuploidy withadvanced maternal age [1], hence the mean age may be higher than our study.

The indication for amniocentesis and chorionic villus sampling is shown in table 2. The most common indication in 139 (49.1%) participants was the history of single gene disorder in the family. The most common indication for amniocentesis was positive screening test in 78 (45.9%) while as most common indication for chorionic villus sampling was family history of single gene disorder in 110 (97.3%) of the participants. Thepreference of CVS in single gene disorder in our study was due to the fact that there was already an indication at the start of pregnancy. [8] The advantage of CVS over amniocentesis is that intervention like medical termination of pregnancy in case an abnormality is detected is more acceptable in first trimester than in the second trimester [9]. Further the DNA-based diagnosis of single gene disorders such as cystic fibrosis, hemophilia, muscular dystrophy, and hemoglobinopathies, can be made by direct analysis of uncultured chorionic villus cells[10]. In ourstudy we were able to detect 17.7% of the genetic disorders through CVS and only 8.2% of the genetic disorders through amniocentesis because of the preference of CVS over amniocentesis in case of known genetic disorders in the family.

The complications observed in our study following amniocentesis and CVS are shown in table 4. Overall 98.2% cases of amniocentesis and 97.9 % cases of CVS were uneventful in our study. The slightly higher complication rate in our study is similar to the observed fetal-loss in a previous study.[11] Another systematic review reported weighted pooled procedure-related risk of pregnancy loss of 0.11% (95% CI 0.04–0.26) for amniocentesis and 0.22% for CVS (95% CI 0.71–1.16).[7] The updated study by the authors showed weighted pooled procedure-related risk of pregnancy loss as 0.35% for both procedures.[12] A randomized trial had 1% miscarriage rate in amniocentesis, however, the risks for miscarriage from other amniocentesis studies range from 0.25%- 0.50% [1,13]. The miscarriage rate after CVS vary widely by the center [14] and after adjusting for confounding factors the CVS-related miscarriage rate was found to be approximately 0.5%-1.0%. [1]. Although uterine infection may lead to miscarriage after the procedure but the overall infection rates were <0.1% after either CVS or amniocentesis[13].

Maternal morbidity and mortality associated with induced abortion increase significantly with increasing gestational age as major complication rate was 0.8% at 11-12 weeks' gestation, compared with 2.2% at 17-20 weeks' gestation [15]. However, the risk for developing major complications from abortion at any gestational age decreased with time.As per the CDC surveillance data from 1972 through 1987, the risk for abortion-related death was 1.1 deaths per 100,000 abortions performed at 11-12 weeks' gestation comparedwith 6.9 deaths per 100,000 abortions for procedures performed at 16-20 weeks' gestation [16]. The lower risk associated with first-trimester abortions may be an important factor for prospective parents who are deciding between CVS and amniocentesis.

**CONCLUSION**:

Amniocentesis and CVS are safe procedures with minimal risk to fetus and mother when performed by expert hands. Timing of the procedure must be weighed against the risks and benefits to the parents. When there is a clear indication for the procedure CVS must be preferred over amniocentesis as this will leadto less physical and psychological trauma to the parents in case an abnormal fetus is detected.

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