INDICATIONS AND COMPLICATIONS OF CHORIONIC VILLUS SAMPLING

Humaira Ahmed, *Nadra Sultana

Combined Military Hospital, Rawalpindi, *Fauji Foundation Hospital, Rawalpindi

ABSTRACT

A descriptive study was conducted to highlight the use of Chorionic Villus Sampling (CVS) as a method of prenatal diagnosis in the first and the early second trimester of pregnancy and to identify the complications occurring in these patients. 264 patients were recruited from the antenatal clinics for this purpose on the basis of high risk factors in their history. The main indications for which CVS was carried out in the study were screening for Thalasemia, Down's syndrome, Hemophilia, Douchenne Muscular Dystrophy and Congenital Adrenal Hyperplasia.

The Double Needle Technique was used to perform CVS through transabdominal route under ultrasound guidance. Difficulties were encountered due to obesity, posterior low lying placenta, anterior uterine wall fibroid and extremely anxious patients. Early complications included amniotic cavity puncture in 1.5%, uterine cramps in 1.89%, vaginal bleeding in 1.1%, vaginal leaking and chorioamnionitis in 0.3% of the patients. Abortions both spontaneous and missed were seen in 4.1% of the cases. Abortions occurring till two weeks after CVS were considered as procedure related.

Keywords: Prenatal diagnosis, chorionic villus sampling, complications, indications, double needle technique.

INTRODUCTION

With the continuing pressure for the earliest possible detection of pregnancy abnormalities, first trimester screening has not been restricted to non-invasive modalities. With invasive prenatal testing delayed until the middle of the second trimester, subsequent elective termination of the pregnancy for a detected fetal abnormality can be problematic. Not only are the fetal movements perceivable by this time encouraging maternal – fetal bonding, but the pregnancy has also become evident to others. [1,2,3].

CVS is a well-established method of fetal sampling. Theoretically, first trimester amniocentesis and CVS performed after 10 weeks gestation have a similar success rate in obtaining cells for culture and chromosomal analysis and comparable harvest time. However, before 10 weeks gestation, amniotic fluid samples contain fewer cells, require long harvest time (up to 40 days more) and have a culture success rate of only 50% compared with villus samples. CVS produces larger samples, which is more convenient when rapid cell culture and DNA analysis are planned. [4,5]

Correspondence: Dr Humaira Ahmed, Classified Gynaecologist, CMH Rawalpindi.

Sampling of chorionic villi from the fetus is performed between 9-12 weeks of gestation. The biopsy is usually taken under ultrasound guidance via a Transabdominal or Transcervical approach. [6,7] Each biopsy yields 05-30 mg of tissue that can be used for fetal sexing, karyotyping, biochemical studies and DNA analysis. A direct fetal chromosomal analysis on cultured cells is possible within 24 hours. However, given the problem with mosaicism in CVS samples this should always be followed by chromosomal analysis on cultured cells from the sample 2-3 weeks later. An advantage of CVS is that the termination of pregnancy can be completed in the first trimester when it is technically easier. [8]

The purpose of this study was to emphasize the use of chorionic villus sampling in the first trimester and early second trimester of pregnancy as a reliable method of prenatal diagnosis. Careful follow up of these patients helped us to assess the

immediate and late complications of this procedure.

SUBJECTS AND METHODS

This descriptive study was carried in the Department of Gynecology and Obstetrics, Military Hospital Rwalpindi,for two years lasting from 1st January 1999 to 1st January 2001. A separate CVS office has been established in the unit. This unit is working since November 1994 and has extended prenatal diagnostic services to approximately 600 patients uptil now. This unit is working in collaboration with the Armed Forces Institute of Pathology where analysis of the test samples is done. The data of the patients is being maintained both in the department and in AFIP.

During this two year period a total of 17650 patients attended the antenatal clinic. Total number of admissions in gynecology ward was 13200 that included both emergency and OPD admissions. A total of 264 patients underwent CVS. Eleven patients had abortion, 07 inevitable and 04 missed.

Patients were counseled in detail about the procedure and the nature of the study. A written consent was obtained from the couple. All the relevant details of the history and examination were endorsed in the proforma designed for the study. After this preliminary data collection and endorsement, the couple was called for CVS. Double Needle Technique through transabdominal route was used and the sample was sent to AFIP for DNA analysis and chromosomal studies. The findings of the patients were documented in the register.

Patients were detained for sometimes in the hospital to look for abdominal pain, vaginal bleeding or leaking and any other disturbing symptoms. Later the patient, preferably the couple was called with the CVS report and advised accordingly. All Rh-ve ladies were given Anti- D prophylaxis.

Inclusion Criteria

a. Patients above 35 years of age
b. Patients with children suffering from genetic, hereditary, endocrinal or muscular diseases for which laboratory diagnosis is available
c. Patients with recurrent pregnancy losses
d. Patients willing for termination of pregnancy in case of abnormal result
e. Patients with personal or family history of blood disorders for which laboratory diagnosis is available

Exclusion Criteria

a. Non viable pregnancy
b. Obvious fetal and placental anomaly
c. For neural tube defects or spine defects
d. Presence of vaginal bleeding
e. Patients with medical or psychological problems

RESULTS

The procedure was successful in majority of the patients. 64.3% of the patients were in the age group of 21-30 years. 33.3% were 31 years and above and only 2.2% were between 16–20 years of age (table-1). Majority of the patients were in their third, fourth and fifth pregnancies. Only 3.7% were primigravida. Highest gravidity was gravida 7 in two patients included in the study (table-2). Patients mainly belonged to low socioeconomic class. Civilian patients were referred from various parts of the country like Peshawar and Northern Areas. Patients of the middle class were either wives of army officers or were from educated class for example doctors and lawyers. Consanguinity is a major risk factor for a number of genetically transmissible diseases. 60.2% were first cousins, 30.3% were distant relatives and 9.4% were unrelated (table-3).

In this study, 62.1% were illiterate and 37.8% were literate which also included those who had read Quran only or went to madrassahs (fig. 1). 85.2% were housewives and had large families with the average of 5-6 pregnancies regardless of the outcome. 13.2% were primary school teachers and 1.5% were private assistants. They had less number of children and even included primigravida who were conscious of their medical problems and seeked hospital help earlier (table-4).

Detailed ultrasound evaluation of the fetus, placenta and liquor was done. Three cases of twin pregnancies were seen. The difficulties were encountered in performing CVS mainly due to the thick abdominal wall in 4.54%, posterior placenta

in 56.8%, anterior fibroids in 0.75%, anxiety of the patients in 5.3% and the procedure failed in 2 cases (fig. 2).

Complications of CVS were divided into two groups. Immediate complications were those that were seen at the time of performing the procedure and included uterine cramps in 1.8% patients which was treated symptomatically, vaginal bleeding in 1.13% which got settled by bed rest and mild sedation. Amniotic cavity got punctured in 1.51% cases. One of who aborted the next day and one developed missed abortion. Only one patient 0.37% had vaginal leaking after the procedure. She later developed chorioamnionitis and was put on broad spectrum antibiotics. Her pregnancy was terminated.

Late complications included Abortions both spontaneous and missed. A total of 11 patients had abortion that constitutes about 4.1% of all the patients (fig. 3). 7 patients reported back in the hospital with inevitable abortion. 4 patients during their follow up were found to have missed abortion. Their pregnancies were terminated with the cervical foley catheter and prostaglandin F2 alpha.

DISCUSSION

CVS has been used as a successful and safe first trimester prenatal diagnostic technique for over 20 years [9]. It has rapidly has become a primary tool for diagnosis of fetal cytogenetic, molecular and biochemical disorders [10]. Except for the high abortion rate, CVS retains its superiority over amniocentesis in both first and second trimesters in producing rapid results [11,12,13]. Brambuti, Tului and Alberti carried out a study on Prenatal Diagnosis by CVS and found that CVS retains its great advantage in producing early results with rapid analytical techniques [14].

The present study used CVS for a number of indications and the main objective was to analyze the complications of this procedure. This was the first study carried out in the Military Hospital on this subject.

CVS was used mainly for the diagnosis of Thalasemia and Down's syndrome. Since Thalasemia is more prevalent on our side of the globe so more patients reported for this indication. Due to lack of awareness, people seeked less for

Table-1: Age and number of patients distribution

Age Years	No of Patients	Percentage
16-20 Yrs	6	2.2%
21-30 Yrs	170	64.3%
31 Yrs	88	33.3%

Table-2: Gravidity of the patients

Gravida	No. of Patients	Parentage
Primigravida	10	03.7%
Second	33	12.5%
Third	69	26.1%
Fourth	72	27.2%
Fifth	53	20.0%
Sixth	25	09.46%
Seventh	02	0.75%

Table-3: Consanguinity and number of patient distribution

Consanguinity	No. of patients	Percentage
First Cousins	159	60.2%
Unrelated	25	9.4%
Distant Relatives	80	30.3%

Table-4: Occupation of the patients

Occupation	No of Patients	Percentage
Housewives	225	85.2%
Primary School Teachers	35	13.2%
Private Assistants	04	1.5%

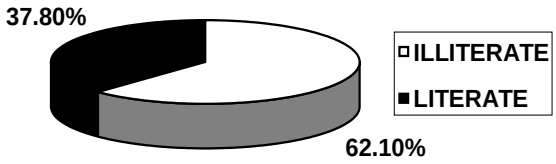
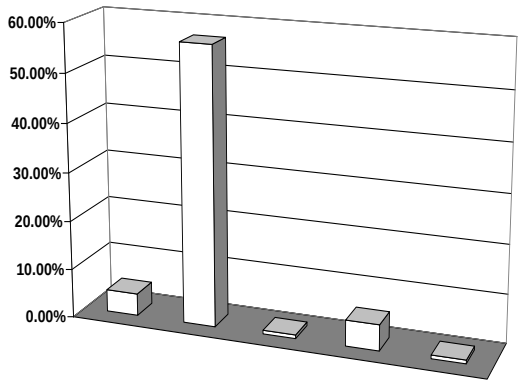


Fig. 1: Education standard



	Thick Abdominal Wall	Posterior Placenta	Anterior Fibroids	Anxious Patients	Failed Procedures
PATIENTS	4.54%	56.80%	0.75%	5.30%	0.75%

Fig. 2: Difficulties in the procedure

other indications like Hemophilia and Muscular Dystrophy. Majority of the patients belonged to 21-30 years age group and even those above 30 years included more for Thalasemia. In the western centers where people are more educated and informed about the health care system, advanced maternal age, Down's syndrome and pregnancy after artificial reproduction techniques are the main indications [15]. Therefore, more women belong to 30 years and above age group. These females are knowledgeable about genetic and chromosomal disorders than their counterparts in this study where 62.1% were illiterate. Amongst the literate those patients were also included who had not received any formal education that again showed lack of medical awareness.

Majority of the patients reported only when they already had abnormal babies, so they were multigravida. This study did not include a large number of twin pregnancies. Only three such cases were seen and the procedure was successful in each one of them. Liebaers and Foulon did a study on the outcome of twin pregnancies after first trimester CVS. The main indication was the advanced maternal age and conception after artificial reproduction techniques. It showed a fetal loss rate of 5.5% and concluded that CVS is an accurate means for prenatal genetic diagnosis in twin pregnancies [16].

The significant early complications were vaginal bleeding and leaking. Abortion rate was 4.1%. The abortion rate with CVS ranges from 1-5% in various studies [10,11,17]. The analysis of the limb reduction defects among CVS cases reported to WHO-Registry from a number of research trials has been unable to find any relationship between sampling and fetal malformations. The abortion rate is between 3-5% evident from these controlled trials [18,19,20].. Hence, first trimester CVS should be considered a gold standard procedure for the prenatal diagnosis of genetic diseases.

Difficulties that were faced during the post procedure follow up since most of the patients did not feel the responsibility to report back to the hospital themselves. So, we had to contact them and enquire about the complications and the pregnancy outcome. Illiteracy, ignorance about the lethal diseases, lack of awareness of the medical facilities, social taboos and the false religious

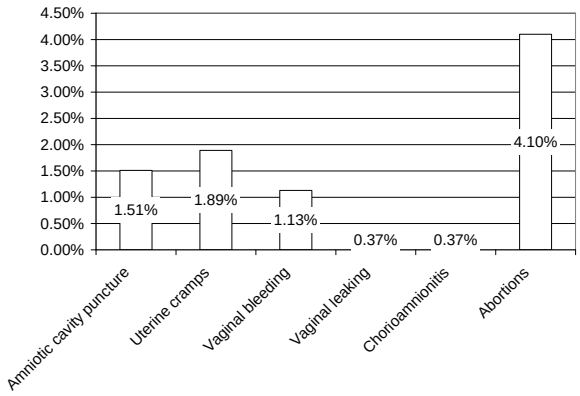


Fig. 3: Complications of chorionic villus sampling

beliefs all hampered our efforts. But now over a period of time many people are understanding this preventive field of obstetrics and approaching with keen interest.

There is a great need for such study programmes to be continued over a longer period of time and with more vigilance. It is also required that we compare CVS with Amniocentesis and assess their suitability for our community. We should also get registered with the WHO-CVS Registry and report our cases there.

CONCLUSION

CVS is a safe and reliable option for the prenatal diagnosis in the early pregnancy. This is one such field where immense help can be afforded towards families and community by preventing the birth of abnormal children or with disease not amenable to treatment. Although the procedure requires expertise but in trained hands the complication rate is less and compares favorably with the centers in the world.

REFERENCES

1. Holzgreve W, Miny P. Chorionic Villus Sampling and Placental Biopsy. In: James DK, Steer PJ, Weiner CP, Gonick B. High Risk **Pregnancy Management Options. 2nd ed. London : Saunders WB 2003.**

2. Laughlin D. Genetic Disorders and Sex Chromosome Abnormalities. In : Decherney AH, Nathan L. Current Obstetric and **Gynecologic Diagnosis and Treatment. 9th ed. Newyork : McGraw Hill 2003: 99-129.**

3. Willner JP. Reproductive Genetics and patients option: Prenatal Diagnosis. **Mt-Sinai-J-Med 1998; 65(3): 173-7.**

4. Wapner RJ. Chorionic villus sampling. **Obstet-Gynecol-Cli-North-Am 1997; 24(1): 83-110**

5. Smidt J, Permin M, Philip J. Sampling success and risk by Transabdominal CVS, Transcervical CVS and Amniocentesis. Ultrasound in **Obstetrics and Gynaecology 1991; 1: 86-90.**

6. Smidt J, Hahneman N. Transabdominal fine needle biopsy from chorionic villi in first trimester. **Prenatal Diagnosis 1984; 4: 163-69.**

7. Ward RT, Modell B, Petrou M, Karagozlu F, Douratsos E. Method of sampling chorionic villi in the first trimester of pregnancy under guidance of real time ultrasound. **BMJ 1983; 286: 1542.**

8. Philips OP, Tharapel AT, Lerner JL et al. Risks of fetal mosaicism when placental mosaicism is diagnosed by CVS. **Am J Obstet Gynecol 1996; 174: 850-55.**

9. Tintung Hospital of Anshan Steel Works, Department of Obstetrics and Gynaecology. Fetal sex prediction by sex chromatin of chorionic villi cells during early weeks of pregnancy. **Chinese Med J 1975; 1: 117-26.**

10. Rhoads GC, Jackson LG, Schlessman SL et al. The safety and efficacy of CVS for early prenatal diagnosis of cytogenetic abnormalities. **New Engl J Med 1989; 320: 609.**

11. Savia R, Longy M, Horovitz J et al. Risks of Transabdominal CVS before 12 weeks of amenorrhoea. **Prenatal Diagnosis 1990; 10: 461-67.**

12. Holzgreve W, Miny P, School R. 'Late CVS' International Registry Compilation of data from 24 centers. **Prenatal Diagnosis 1990; 10:: 159-67.**

13. Pertl B, Kopp S, Krooisel PM et al. Rapid detection of chromosome aneuploidies by quantitative flourescene PCR on 247 CVS samples. **J Med Genet 1999; 36(4): 300-3.**

14. Brambuti B, Tului L, Alberti E. Prenatal Diagnosis by CVS. **Eur-J-Obstet-Gynecol-Reprod-Biol 1990; 65: 11-6.**

15. Young Y, Park YW, Kim SK et al. Chorionic Villus Sampling, clinical experience of 750 cases. **J-Obstet-Gynecol-Res 1996; 22(2): 143-9.**

16. Liebares I, Foulun W. Outcome of twin gestation after first trimester chorionic villus sampling. **Obstet-Gynecol 2000; 96: 714-20.**

17. MRC Working party on evaluation of chorionic villus sampling. **Medica Researh Council European trial of CVS. Lancet 1991; I: 1499.**

18. Canadian collaborative **CVS-Amniocentesis. Lancet 1989; I: 16.**

19. Jahoda MGJ, Branderburg H, Reuss A et al. Transcervical and transabdominal CVS for prenatal diagnosis in Rotterdam experience with 3611 cases. **Prenatal Diagnosis 1991; 11: 559-61.**

20. Young SR, Shipley CF, Wade RV et al. Single center comparison of results of 1000 prenatal diagnosis with CVS and 1000 with Amniocentesis. **Am J Obstet Gynecol 1991; 165: 255-63.**