# AN EXPERIENCE OF CHORIONIC VILLUS SAMPLING IN LADY READING HOSPITAL, PESHAWAR

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## ABSTRACT

**Objective:** To determine the outcome of chorionic villus sampling for prenatal diagnosis of inherited diseases.

**Methodology:** This descriptive study was conducted on 70 antenatal ladies having 11 to 14 weeks singleton pregnancy and with history of genetic disorders in family or children. It was carried in the Department of Obstetrics and Gynaecology, Lady Reading Hospital, Peshawar. Chorionic villus sampling (CVS) was performed by Obstetrics and Gynae consultants via transabdominal route under local anaesthesia and ultrasound guidance. Written informed consent was taken from all the participating couples before starting the process. By using SPSS version 23, statistical analysis was done.

**Results:** A total of 70 samplings were done. Miscarriage as a result of the procedure occurred in 1/70 (1.42%), significant pain requiring intramuscular analgesia occurred in 40 (57%) patients and there were no reported cases of infection. Failure to retrieve sample occurred in 4 (5.7%) patients requiring repeat procedure after 10 days. 3 (4.2%) patients reported vaginal bleeding within a week after the procedure. After DNA analysis of the submitted samples, it showed thalassemia major 15 (21.42%), thalassemia minor 30 (42.85%), no mutation 22 (31.42%) and down syndrome 1 (1.42%).

**Conclusion:** Chorionic villus sampling was found to be a safe procedure for prenatal diagnosis of genetic disorders in first trimester.

**Key Words:** Chorionic villus sampling, Thalassemia, Down syndrome, Miscarriage, Pain

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## INTRODUCTION

Worldwide, morbidity and mortality are considered the most dreadful sequelae of genetic disorders. The majority of these inherited diseases are difficult to treat or if treatment is possible, it is unapproachable for the population[1]. One of the relevant and necessary elements of the genetic disorder management is early diagnosis and selective termination of the affected pregnancies. Chorionic villus sampling (CVS) is a technique by which samples can be collected through a transabdominal or transcervical route.

In 1970, in China, CVS was originally used as first-trimester diagnostic procedure by Anguo et al[2]. In 1983, CVS application for diagnosis of hemoglobinopathies came into use[3,4]. In Italy, it was subsequently introduced by Simoni et alin 1983[5]. Analysis of the chromosomes by direct preparation of tissue was further step ahead in fetal genetic diagnosis[3].

For CVS, two distinct approaches have been used, the transabdominal and transcervical route[4,5]. It's a day case procedure carried under ultrasound guidance using local anesthesia. The most crucial complications of CVS are fetal damage and loss directly related to this invasive procedure[6]. At present, in Pakistan, the most common procedure for prenatal diagnosis is CVS, to diagnose fetal cytogenetic, molecular and biochemical disorders[7]. In Pakistan, introduction, application and dissemination of the skill was pioneered by Dr Yasmeen Rashid, while first publication appeared in Pakistani literature in 1994 by Ahmad et al[8].

Despite the fact that CVS is practised in major cities of Pakistan for the last two decades for prenatal diagnosis of genetic disorders especially thalassemia[9,10], it has only been recently started in Khyber Pakhtunkhwa (KP)[11]. High rate of consanguineous marriage in KP is one of the main reasons of high incidence of genetic disorder seen in the province[12]. Timely diagnosis and

treatment of these diseases are important if we desire a healthy generation. In the present study, the outcomes of first 70 samples were compared with national and international studies after starting the procedure. So via this study we share our experience of the procedure and this makes a start of generating our local statistics as well.

## METHODOLOGY

This was a descriptive study with non-probability consecutive sampling, conducted in the Department of Obstetrics and Gynaecology from July 2017 till December 2018. Couples who were carriers of genetic disorder like thalassemia, spinal muscular atrophy, history of children with Down syndrome and who demanded prenatal diagnosis were recruited in the study. Using proportion of thalassemia carriers in Pakistan as 5%[13], confidence interval 95%, margin of error 5%, the estimated sample size of 70 was calculated. Exclusion criteria were diseases for which prenatal diagnosis is not available or is very costly, unaffordable for the couple, gestational age more than 16 weeks and if consent was not given.

At the time of appointment, couples were counselled regarding the genetic risk, the technique and complexity of fetal sampling, diagnostic flaws and termination of pregnancy as well as its Islamic connotations. Written informed consent was taken from all the couples before the procedure. To determine the fetal viability, gestation age, number and placenta position, a preliminary ultrasound scan was performed. CVS was carried out with the gestation age between 12-14 weeks. Outcomes of the procedure including miscarriage, pain hypogastrium requiring intramuscular analgesia, infection and failure to retrieve chorionic villi following suction and vaginal bleeding were noted. The ethical review board of the hospital approved the study.

The subject were placed in the supine position and the placenta was localized by transabdominal ultrasonography (USG). Lower abdomen was painted with pyodine solution, 10 ml of 1% xylocaine was injected through 10ml disposable syringe in the skin just above the rectus sheath. Then CVS needle with trocar & cannula was introduced in the placenta under ultrasound guidance. Once needle location in the placenta was confirmed, the trocar was removed and suction needle was introduced through a cannula. After that suction was created with a 20cc disposable syringe. The sample was then withdrawn under negative pressure. Villi were placed in normal saline and then transferred to the Eppendorf bottle after confirmation under the microscope and transferred to laboratory for genetic analysis or required testing.

The patients were allowed home 30-60 minutes after the procedure with instruction to take bed rest for 24 hours. In case of pain, two tablets paracetamol was advised. Patient's confidentiality was ensured at each step.

Data were analyzed using IBM SPSS, Version 23.0. Descriptive statistics were used. Continuous variables like age was reported as mean and standard deviation and categorical variables like parity, education status and outcome as well as indications of CVS as frequency and number (percent).

## RESULTS

Mean age of study population was 29.54 ±4.65years. Demographic data is shown in table 1. There were 55 (78.5%) anteriorly placed placentae.

Aspiration in the majority of patients was smooth and facile, whereas, it was complex in 10 (14.28%). Posterior placenta n=6(8.57%), nervous patients n=1(1.42%), thick anterior abdominal wall n=3(4.28%) were some of the aspects related to complicated aspiration. Aspiration was successfully done in the first attempt in most of the patients (90%). Whereas, in the rest of the patients, it was done in 2nd or barely 3rd attempt with the same cannula left in place. Miscarriage due to the procedure occurred in 1/70 (1.42%). Significant pain requiring intramuscular analgesia occurred in 40 patients (57%) and there were no reported cases of infection. Failure to retrieve sample occurred in 4 (5.7%) patients requiring repeat procedure after 10 days. 3 (4.2%) patients reported vaginal bleeding within a week after the procedure.

Indications for CVS are shown in Figure 2. Fetal blood group was rhesus positive in both 2 cases and 3 males and 1 female fetal sex was diagnosed

After DNA analysis of the submitted samples, it showed thalassemia major 15 (21.42%) and thalassemia minor 20 (28.57%)(%), Figure 3.

## DISCUSSION

Pakistan has a high still birth (53.5/1000 births) and neonatal mortality rate (49.4/1000 live births)[14]. Genetic disorders including hemoglobinopathies add to this burden of perinatal events[15]. Cultural setup including high rate of consanguineous marriages and religious limitations regarding termination of affected pregnancies emphasize the role of chorionic villus sampling in early prenatal diagnosis[16].

Miscarriage as a result of CVS is a main concern. Out of 70 procedures done only one had miscarriage. This is very much similar to miscarriage rates reported in literature. Choudry et al quoted miscarriage figure of 1%[17] and Brun et al 1.64% in their studies[18].

Post procedure pain was a significant finding in our study. Women however also expressed that the procedure was pain free and it was only their fear before the test which made them anxious. This finding is consistent with other studies who also reported transient mild to moderate pain after the procedure[17,19].

**Table 1: Maternal demographics**

| Variables | | Frequency | Percentage |
|---|---|---|---|
| Social class | Middle | 20 | 28.57% |
| | Lower | 50 | 71.42% |
| Background: | Urban | 30 | 42.85% |
| | Rural | 40 | 57.14% |
| Consanguinity: | 1st cousin | 38 | 54.28% |
| | 2nd cousin | 15 | 21.42% |
| | Distant relative | 12 | 17.14% |
| | Unrelated | 05 | 7.14% |
| Education status of mother: | Uneducated | 59 | 84.28% |
| | Primary | 3 | 4.28% |
| | Middle | 1 | 1.42% |
| | Metric | 3 | 4.28% |
| | Intermediate | 1 | 1.42% |
| | Graduate | 2 | 2.85% |
| | Postgraduate | 1 | 1.42% |
| Parity | Para 0 | 2 | 2.85% |
| | 1-2 | 30 | 42.85% |
| | 3 or more | 38 | 54.28% |

Figure 1: Indications of CVS (n=70)

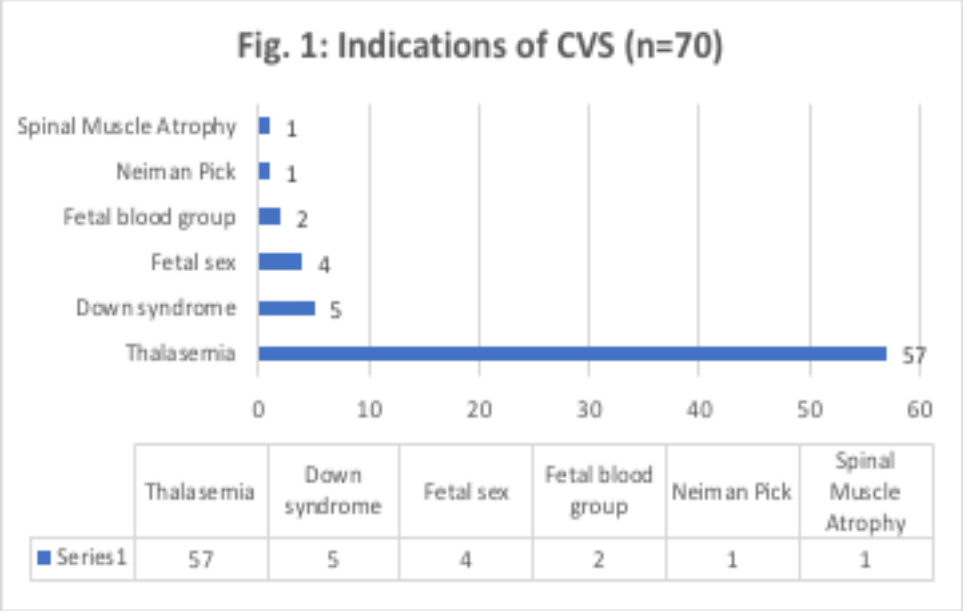
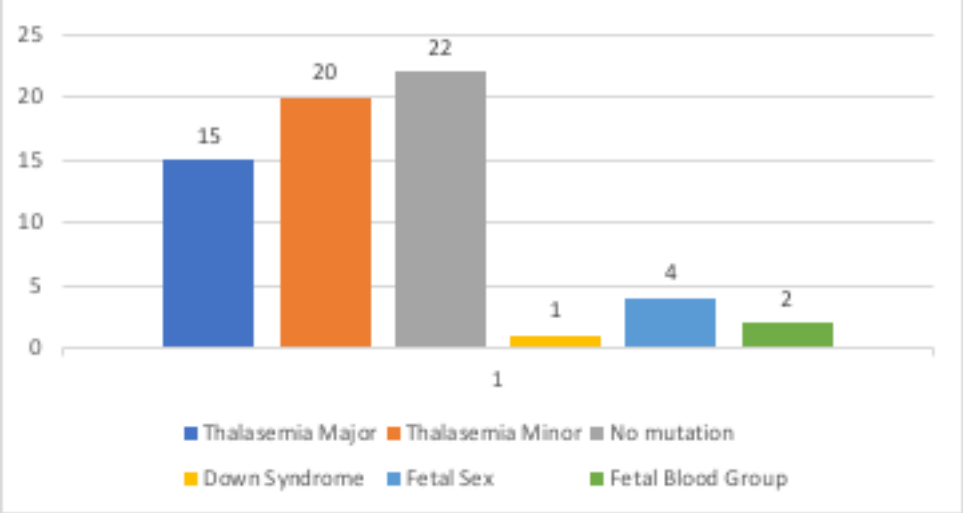


**Figure 2: Outcome of chorionic villous sampling**




Patients in our study were followed for 4 weeks after the procedure. However, none of them complained of pain hypogastrium, fever and vaginal bleeding. Choudry et al also reported no cases of chorioamnionitis[17] while Ahmed et al had 0.37% post procedure infection rate[16].

Another essential technical aspect of the procedure noticed was ease or difficulty of insertion and aspiration. Main contributing factors to this in our study were noted to be posterior placenta, anxious patients and thick anterior abdominal wall. Same factors have been described in other studies[17]. We had 2 patients with previous caesarean section but we did not encounter any difficulty in insertion and aspiration. The reason may be that both were slim ladies with easily approachable anterior placentae. This finding is in contrast to Aaron et al who reported previous cesarean section as a predictor of difficult procedure[20]. 90% of aspirations were done in first attempt with adequate sample. Most of the studies also favour this finding [21].

Our majority cases were indicated for prenatal diagnosis of thalassemia. Local studies on chorionic villus sampling also reveal that main indication for prenatal diagnosis in Pakistan is Beta thalassemia. The reason being that Beta thalassemia is the commonest inherited disorder in Pakistan with carrier frequency over 5%[22]. This is a different situation from developed countries where most of invasive prenatal diagnosis is done for detection of aneuploidies and other genetic disorders[18].

We did all sampling between 12 to 14 weeks of pregnancy and results were available within 10 working days. Most of the studies also support the same duration to be the best time for carrying out the procedure. This also helps for timely termination of affected pregnancies before 17 completed weeks according to Islamic shariat law[17].

## CONCLUSION

Chorionic villus sampling was found to be a safe procedure for prenatal diagnosis of inherited disorders. Pain requiring intramuscular analgesia occurred in a significant number of patients (57%). Thalassemias were main indication and diagnosis on CVS.

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## CONTRIBUTORS

IK conceived the idea and drafted the manuscript. IK and BS collected the data, did statistical analysis and interpretation of the data. BS did critical revision of the article. ZAA supervised the study and carried out final proofreading. All authors contributed significantly to the submitted manuscript.