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# The Effect of Chorionic Villus Sampling on Fetal Heart Rate

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**Key Words**
Chorionic villus sampling · Fetal heart rate · Prenatal diagnosis

**Abstract**
***Objective:*** Fetal heart rate (FHR) variation during chorionic villus sampling (CVS) is a controversial topic. Limited studies have been published on this subject. Our study intended to evaluate the effects of CVS on the FHR. ***Method:*** One hundred and sixty-five patients undergoing first-trimester elective CVS for prenatal diagnosis of β-thalassemia were entered into a prospective study. M-mode FHR was obtained before and immediately after CVS in the patients. Potentially confounding variables also recorded included: gestational age, number of needle passes and placental location. ***Results:*** FHR values before and after CVS were compared using the paired t test and showed no statistically significant differences by 95% confidence. No differences were found in data analyzing gestational age, number of needle passes or placental location. ***Conclusion:*** We were unable to detect any significant change in FHR after performing CVS. It seems that FHR is generally not altered by CVS.



## Introduction

Chorionic villus sampling (CVS) has been proposed as a safe alternative to amniocentesis in patients at an increased risk of aneuploidy or several hereditary disorders [1, 2]. Possibility of fetal heart rate (FHR) alteration by CVS has been considered from two points of view: Bradycardia could be a cause of ischemia and subsequent side effects such as limb defect [3]. FHR alteration could be considered as an indicator for fetal hypoxia [4] or distress [5, 6]. Limited studies with almost controversial results have been published. Post-CVS bradycardia, tachycardia and no alteration have been reported [7, 8]. Measuring the FHR before CVS is also proposed as an indicator for subsequent fetal loss [9, 10].

This study was designated to evaluate the effect of CVS on FHR and the possible fetal heart responses following the procedure.

## Materials and Methods

We prospectively evaluated 165 patients undergoing CVS from November 2000 to February 2001 (65 cases) and September 2002 to December 2002 (100 cases). After the first time study (65 cases), a second study was also preformed (100 cases) due to expert reviewer's comment that the number of cases was not enough to rely on results of the first study. We kept all the parameters the same to be able to add the second study data to the first one. Both period studies were done by a single operator, same technique, same population at risk and similar equipments and conditions.

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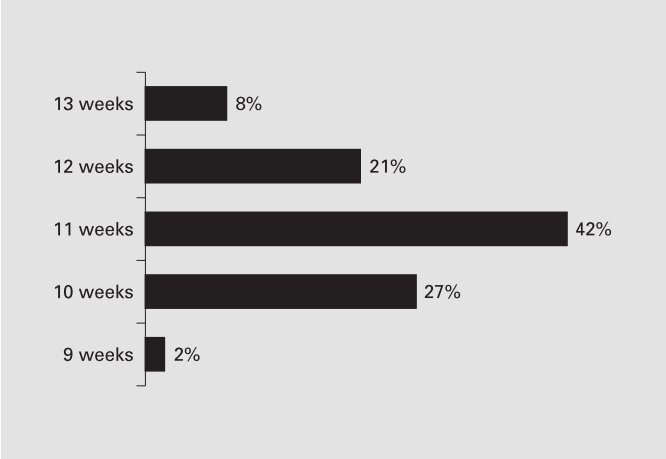



**Fig. 1.** The 169 cases were distributed as follow: 3 (9 weeks), 44 (10 weeks), 69 (11 weeks), 35 (12 weeks) and 13 (13weeks). From this figure, it is determined that 90% of the patients are between 10 and 12 GSA and this shows that in practice most of the cases for prenatal diagnosis of β-thalassemia are within this range in our center.

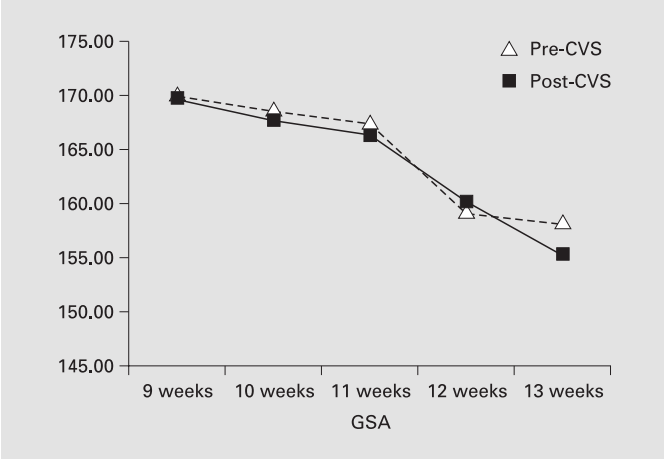



**Fig. 2.** This graph clearly showed that as we expected the FHR declined with increasing the gestational age in our cases. This decline is measurable and should always be taken into account when a wide range of gestational ages are analyzed for FHR.

The indication for prenatal diagnosis was to rule out β-thalassemia in fetuses. All procedures were performed after 9 weeks' gestation on the basis of CRL and or BPD measurements obtained immediately before the procedure.

We routinely performed CVS after 10th week, but if there was some exception due to patient condition where we found it mandatory to perform the CVS before 10 weeks, this took up 2% of our patients.

Trans-abdominal CVS was performed in all cases. After the initial ultrasonographic assessment, trans-abdominal CVS was started. A 20-gauge Chiba needle (Bards, USA) was used under continuous ultrasound guidance. The samples were immediately evacuated into a disposable sterile plastic dish and flushed with normal saline and were then evaluated by the author for adequate amount of villi on bright yellow light without any inverted microscope or loop. If the sample was not sufficient, the procedure was repeated up to 3 times. Immediately after the sampling, FHR measurements were obtained within 1 min following needle extraction. In case of two or three needle passes the measurements were obtained after the last sampling. FHR measurements were obtained trans-abdominally using the Hitachi EUB 405 (Hitachi, Japan) and Toshiba Justvision (Toshiba, Japan) scanners. M-mode measurements were recorded during a period of absent fetal movement from direct investigation of the fetal heart. Comparisons of mean values for various parameters before and after CVS were performed using paired t test by Microsoft Excel spreadsheet.

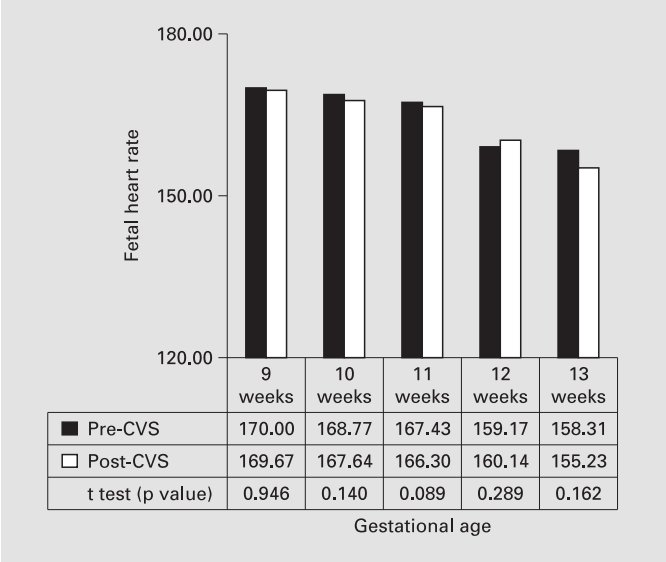
## Results

All patients (n = 165) had successful CVS performed between 9 and 13 weeks' gestational age. Patients were classified according to gestational age. Ninety percent of the patients were between 10 and 12 weeks, 2% were 9 weeks and 8% were 14 weeks of gestational age (fig. 1).

FHR reduction by increasing the gestational age was seen and plotted (fig. 2). These changes were in the range of 155–170 beats per second from 9 to 13 weeks' gestational age. In each gestational age group, FHR mean and SD were calculated before and after the trans-abdominal CVS procedure. The t test results (for comparing the FHR means showed in fig. 3) showed that the changes were not significant ($p > 0.05$) in 9, 10, 11, 12 and 13 weeks' groups ($p = 0.946$, $p = 0.140$, $p = 0.089$, $p = 0.289$, $p = 0.162$, respectively). When analyzed, pre- and post-CVS FHR apart from the gestational age, the $p = 0.06$ was still larger than 95% confidence ($p > 0.05$) but with very close margin (table 1).

The maximum number of needle passes was three (single 104, two 52 and three 8 patients). The evaluation between the number of the needle passes and FHR also showed that there was no difference ($p > 0.05$) between the single ($p = 0.330$), two ($p = 0.085$) and three ($p = 0.220$) needle passes groups (fig. 4).

The placenta was located anteriorly in 83 (51%) cases, posteriorly in 64 (39%) and fundally in 17 (10%). The statistical analysis between the placental location and FHR also showed no difference ($p > 0.05$) among the anterior ($p = 0.124$), posterior ($p = 0.179$) and fundal ($p = 0.921$) groups (fig. 5).

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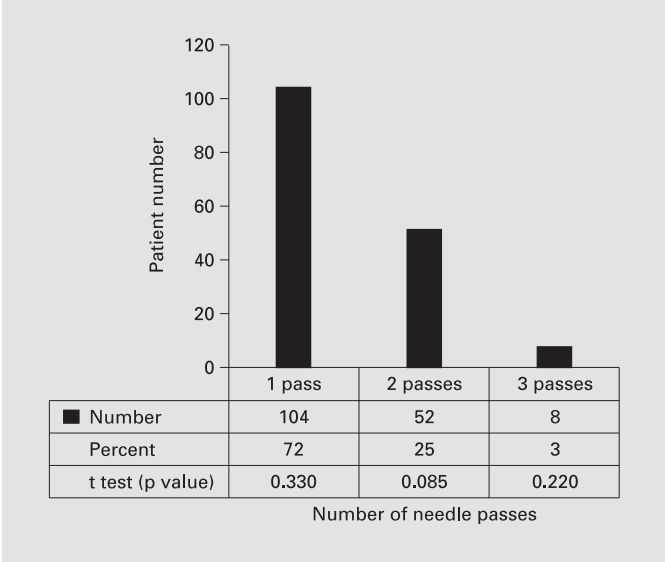


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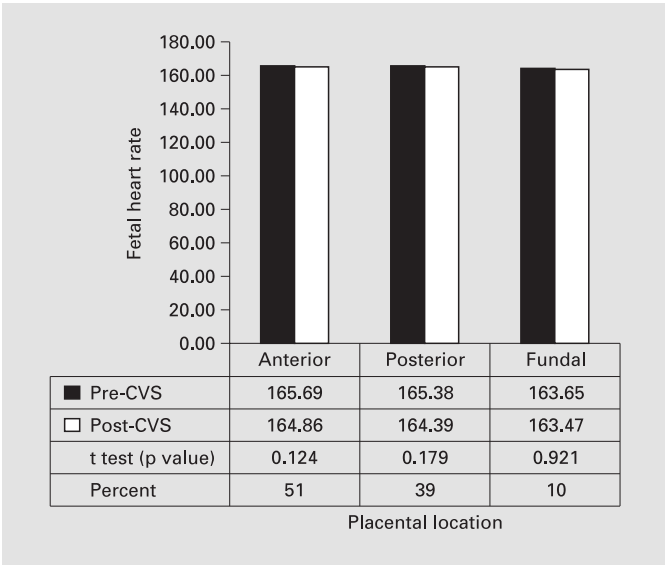


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**Fig. 3.** We had five groups as dividing the cases by gestational ages. In each group, the mean FHR value before and after CVS were calculated and a t test has been carried out. The results clearly showed that there are no significant changes between pre- and post-CVS FHR among each group.

**Fig. 4.** Number of needle passes for obtaining the sample was also considered as a possible confounding factor that may change the FHR. However statistical results showed that there is no significant change between the single, two and three needle passes in pre- and post-CVS conditions.

**Fig. 5.** Location of placenta was also described among the cases and is shown in percentages in this figure. Again statistical analysis showed that no differences were seen among the different groups by placental locations. This evaluation was not considered by previous published articles.

**Table 1.** The mean values, standard deviations obtained from 165 patients prior to and immediately after CVS for FHR and subsequent p value calculation. This p value (0.06) is very close to the 0.05 that is considered for 95% confidence. Nonetheless, this value is not statistically significant too ($p > 0.05$), but care should be taken when analyzing the wide range of gestational ages (9–13 weeks). This was caused by not taking into consideration that FHR is reduced by increasing the gestational age

| | FHR | | p value |
|---|---|---|---|
| | mean | SD | |
| Pre-CVS | 165.35 | 7.66 | 0.06 |
| Post-CVS | 164.53 | 8.15 | |

## Discussion

Previous studies have shown that FHR measurements are reproducible and reliable [11, 12]. Embryonic heartbeat can be detected as early as the 5th week of gestation. Normal development shows an increasing of FHR from 80 to 90 beats per minute at the 5th week to 170–180 beats per minute at the end of 9–10 weeks. Thereafter as pregnancy progresses, the baseline FHR declines to 145–155 beats per min with the appearance of beat-to-beat variation [11–13]. Our result showed this decline and has been demonstrated in the figure 2. This finding is important from a statistical point of view. When a wide range of

the gestational age is considered (i.e. 9–13 weeks), difference in FHR will cause a wide range of SD which could affect the analysis. So in our opinion, separating the data according to the gestational age is mandatory for FHR evaluation. We did not find any statistical difference between mean FHR values in pre- and post-CVS groups based on gestational ages (fig. 3). However, when we analyzed all data together, the p value ($p = 0.06$) is more close to the 95% confidence value. Even if 90% confidence is measured, the differences become significant ($p < 0.1$). These results showed that the data should be separated in each gestational age to have more accurate results.

CVS has been used successfully for first trimester diagnosis of genetic disorders for over 18 years. When performed between 10 and 14 weeks' gestation, it is both safe and effective in the diagnosis of fetal chromosomal, biochemical, and molecular disorders, with risks comparable to those of second trimester amniocentesis [14].

However, CVS-induced limb defect is also an old history [15–18]. The available clinical evidence indicates that these defects occur primarily in pregnancies subjected to trans-cervical or trans-abdominal CVS prior to 9.5 weeks' gestation (66 days).

Wapner et al. [19] recently reported 1–2% risk of limb defect in CVS before 63 days of gestation to obtain an early diagnosis in Orthodox Jewish cases. The etiology of transverse limb reduction defects has not been completely understood. Two major theories prevail [20–22]: amnion disruption and placental vascular disruption. Second one is a more complex mechanism, involving vasospasm and possible embolization [16]. Vascular injury during CVS causes a cascade of events that can lead to fetal limb ischemia and limb resorption. Firth et al. [3] suggested fetal bradycardia from the procedure inciting hypoperfusion to be a plausible mechanism to explain their findings. Our results do not support the Firth theory (i.e. post-CVS bradycardia) for limb defect. Also, earlier concerns about procedure-induced limb defects have been reduced with the CVS registry data analysis 2 and accumulation of additional data, showing minimal to no risk when CVS is performed after 70 days of gestation [14].

There is not enough and also controversial published data regarding the FHR alteration due to CVS and amniocentesis. Even Ron et al. [5] reported alteration of FHR following the amniocentesis and suggested that lack of alteration or pathological response should be considered as severity of fetal distress. However, this study was carried out in the 3rd trimester and their results can hardly be extrapolated to the 1st trimester. But from this point of view, it is important that alteration is considered as a constant feature of the procedure and lack of it will be pathological. Our results show that FHR alteration is not a feature similar to Ron et al.'s [5] assumption. Four hundred and seventeen pregnancies were evaluated by Wilson et al. [8]. Their results indicated that the heart rate before the procedure was similar for both male and female fetuses. Significant procedure-related changes in FHR occurred only with male fetuses undergoing the trans-abdominal CVS technique. FHR decelerations following CVS were more common than accelerations. Our results were similar to those of Zoppini et al. [23] and Martinez et al. [17], which showed no differences in the FHR after the procedure, but all the studies found a significant variance around the mean FHR. Moreover, Martinez et al. [7] by studying 279 consecutive singleton pregnancies, between 10 and 13 weeks, who underwent trans-cervical CVS has shown no significant decrease in FHR (mean 1.04 beats, $p = 0.94$) and a significant elevation of umbilical artery pulsatility index (PI) post-CVS (mean 0.12, $t = -6.51$, $p < 0.001$). This difference was only significant in procedures performed at less than 11 weeks' gestation, since there was no significant change for those procedures performed thereafter. These preliminary data suggest that acute fetal hemodynamic changes are induced by CVS and may have clinical effects. This means that there is another reason for increasing the umbilical artery PI. Therefore, lack of FHR alteration alone will not exclude the possibility of hemodynamic changes in fetal circulation.

In this study we also took notice of some other possible confounding parameters. Location of the placenta, number of needle passes and gestational age are considered.

Earlier gestations did not differ in results from older gestations, nor was there a difference when two or three passes of needle were performed. As one may see, our second (25%) and third passes (3%) are higher than expected. The reason is, if we consider the positive result from the first needle pass (positive villi), our result will be 94% for single pass. On the other hand our referral genetic laboratories for evaluation of β-thalassemia request large amount of villi, so, we should take more villi by the second or third pass. However regardless to the causes, increased number of second and third passes are a positive point for this study to be able to have more data for evaluating the role of increased needle passes on FHR. Our results were also similar for all three groups classified according to the placental location. We conclude that FHR alteration is not a constant feature of CVS. FHR does not appear to be compromised by CVS and no measurable change in FHR occurs when CVS is routinely preformed.

Evaluation of the FHR per se is also important and has been taken into consideration by several investigators. Fetal bradycardia and fetal tachycardia are associated with a high rate of miscarriage [24]. Yagel et al. [9] demonstrated better correlation between FHR and CRL rather than gestational age. They proposed that before performing invasive procedure in the first trimester, FHR be measured and correlated with CRL. This should assist in predicting a miscarriage, which will not be ascribed erroneously to procedure-related fetal loss [9]. Abnormally, low or high FHR during early pregnancy mainly has been associated with an increased risk of subsequent abortion [12, 25]. The detection of a relative fetal tachycardia (>95th percentile) before carrying out an invasive procedure (such as CVS) should alert to an increased risk for later miscarriage [10]. Therefore, it will be important to evaluate the FHR before CVS due to results of several mentioned studies. In our opinion the evaluation of FHR before CVS should be a routine procedure and recorded for any possible fetal loss.

Assessment of FHR after CVS is another additional entity and this could also be measured as a predictive factor. According to results of our study and the other similar studies that are mentioned above, we accept that FHR should not alter following the CVS. It seems that if FHR is altered by CVS and this alteration remains constant, this could also be of similar value for possible higher risk of fetal loss. However this hypothesis should be evaluated more and a further dedicated study will be necessary.

Our studies show that FHR is not altered following trans-abdominal CVS at the gestational age of 9–14 weeks. This feature is useful information as CVS is the better prenatal invasive test in weeks 10–14 and may become more in demand with increased use of first trimester biochemical and ultrasound screening.

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