

Chorionic villous sampling-related complications: a cohort study

Kasemsri Srisupundit, Theera Tongsong, Wirawit Piyamongkol, Supatra Sirichotiyakul, Fuanglada Tongprasert, Suchaya Leuwan, Kuntharee Traisrisilp, Phudit Jatavan & Sirinart Sirilert

To cite this article: Kasemsri Srisupundit, Theera Tongsong, Wirawit Piyamongkol, Supatra Sirichotiyakul, Fuanglada Tongprasert, Suchaya Leuwan, Kuntharee Traisrisilp, Phudit Jatavan & Sirinart Sirilert (2020) Chorionic villous sampling-related complications: a cohort study, The Journal of Maternal-Fetal & Neonatal Medicine, 33:11, 1901-1905, DOI: [10.1080/14767058.2018.1533943](https://doi.org/10.1080/14767058.2018.1533943)

To link to this article: <https://doi.org/10.1080/14767058.2018.1533943>



Published online: 20 Dec 2018.



Submit your article to this journal [↗](#)



Article views: 104



View related articles [↗](#)



View Crossmark data [↗](#)



ORIGINAL ARTICLE



Chorionic villous sampling-related complications: a cohort study

Kasemsri Srisupundit , Theera Tongsong , Wirawit Piyamongkol , Supatra Sirichotiyakul , Fuanglada Tongprasert , Suchaya Leuwan , Kuntharee Trairisilp , Phudit Jatavan and Sirinart Sirilert

Department of Obstetrics and Gynecology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

ABSTRACT

Purpose: To compare the adverse pregnancy outcomes between the pregnant women undergoing chorionic villous sampling (CVS) and those without CVS.

Materials and methods: A cohort study was conducted on low risk pregnancies attending Chiang Mai University Hospital between years 2003 and 2017 and identify the database of women undergoing CVS (study group) and control group. Each case in study group was matched for 10 cases of the control by maternal age and year of procedure.

Results and conclusions: Of 1384 pregnancies undergoing CVS, 776 cases met criteria and were matched with 7760 controls. The gestational age at delivery and actual birth weight were significantly different between two groups (38.02 versus 38.96 weeks, p value $<.001$ and 3025 versus 3092 g, p value $.001$). Moreover, CVS group had significantly higher preterm birth (9.4 versus 7.3%, p value $.037$; RR 1.287, 95% CI 1.017–1.629). However, there was no significant difference in fetal loss rate before 24 weeks (1.16 versus 1.9%, p value $.14$), small for gestational age (SGA); SGA (4 versus 4%, p value $.948$) and low birth weight (LBW); LBW (8.9 versus 8.0%, p value $.41$). Pregnancies undergoing CVS tend to deliver earlier and has significantly higher preterm birth. However, the incidences of fetal loss, SGA and LBW are not significantly increased.

ARTICLE HISTORY

Received 22 June 2018

Revised 25 September 2018

Accepted 5 October 2018

KEYWORDS

Chorionic villous samplings; fetal; loss

Introduction

Chorionic villous sampling (CVS) is a procedure to achieve chorionic villi from placenta under ultrasound guidance, either by puncturing the maternal abdominal wall through needle or using CVS biopsy forceps through uterine cervix, depending on placental accessibility. CVS is a diagnostic procedure suitable for the women who wish to have a definite diagnosis in early gestation. However, the most important information that should be counseled is procedure-related fetal loss and other possible related complications such as preterm birth, small for gestational age (SGA) and low birth weight (LBW). In several previous reports, the risk of fetal loss associated with CVS varies from 0.6 to 3% [1–5]. According to our preliminary report of more than 600 CVS procedures in our center, the fetal loss rate is less than 1% and other minor complications such as vaginal bleeding and amniotic fluid leakage were approximately 1% [6]. However, these numbers were derived from a descriptive study with no control group. Thus, they might not be reflexive of the true CVS-related fetal loss and other complications.

Additionally, though several studies on CVS-related fetal loss have been published, long-term or late consequences like fetal growth restriction or preterm birth which might be associated with CVS have been rarely explored. Therefore, we conducted this retrospective cohort study to evaluate the rates of various complications related to CVS procedure.

Materials and methods

A retrospective cohort study was conducted at Maharaj Nakorn Chiang Mai Hospital, Chiang Mai University, with ethical approval of the local Institute Review Boards. Cases in the study group were retrieved from our computerized prospective database of CVS at the Maternal Fetal Medicine (MFM) Unit, Faculty of Medicine, Chiang Mai University, between January 2003 and February 2017. The inclusion criteria for the study group consisted of (1) singleton pregnancies, (2) undergoing CVS at gestational age of 11–14 weeks, (3) CVS performed by experienced operators, defined as MFM specialist or the second year in-

training fellowship in MFM, and (4) complete follow-up with availability of the final outcomes. The exclusion criteria were (1) the cases that had repeated prenatal diagnostic procedure such as amniocenteses or cordocenteses in the same pregnancy and (2) pregnancies which resulted in termination of pregnancy because of fetal disorders such as severe fetal thalassemia disease, structural anomalies or chromosomal abnormalities.

The control group was recruited from our MFM database of low-risk pregnancies during the same study period. The inclusion criteria consisted of (1) singleton pregnancies with no any invasive prenatal diagnostic procedure, (2) attending antenatal care clinic in the first trimester, (3) low-risk pregnancies without underlying medical diseases, and (4) complete follow-up with availability of the final outcomes. The pregnancies with fetal anomalies or chromosomal abnormalities were excluded. The records of the pregnancies meeting the inclusion criteria were stratified into subgroups by maternal age of 5-year-intervals and the year of delivery. The controls were randomly selected from the records with the same age strata as the study group on the basis of matching ratio 10:1.

CVS procedures were performed under real-time ultrasound guidance using transabdominal 3.5-MHz curvilinear transducer equipped with machine either model SSD 620, 680EX, SSD 1700; SSD 5000 (Tokyo, Japan) or E8GE medical system (Wauwatosa, WI). Detailed ultrasound scan was done to determine the number of fetuses, viability, gestational age, and placental location. CVS was done under aseptic, freehand technique and carried out as outpatient setting. In case of transabdominal CVS, after local anesthesia was infiltrated, a 20-Ga spinal needle was inserted at the area of placenta under ultrasound guidance with back and forth movement technique to obtain chorionic villi under vacuum condition of the syringes. In case of transcervical approach, a Rodeck CVS biopsy forceps was used to access the placenta via uterine cervix under transabdominal ultrasound guidance and then grasp some chorionic villi. Chorionic villi were dissected under microscope to separate from maternal decidua, then the villi were transferred into the specific media and sent to the laboratory for the pertinent tests. After the needle or CVS forceps were removed, the fetal heart rate was assessed. After 20 minutes of bed rest, the patients were discharged home without any tocolysis or antibiotics. All continuing pregnancies were followed with standard antenatal care. Outcomes of CVS were prospectively recorded in the database of the MFM Unit.

The main outcome measures for comparison between CVS and control group were rates of fetal loss (delivery before 24 weeks), gestational age at delivery, birth weight, incidence of SGA, LBW, and preterm birth.

Statistical analysis

The analyses were performed using IBM SPSS version 21.0 (IBM SPSS Statistics for Windows, released 2012, IBM Corp, Armonk, NY). The rates of pregnancy adverse outcomes were compared using McNemar's chi-square test, paired *t*-test and Cox regression analysis as appropriate. A *p* value <.05 was considered statistically significant.

Results

During the study period, a total of 1384 pregnancies underwent CVS. Of them, 608 cases were excluded from analysis, including twin pregnancies (12), subsequent invasive prenatal diagnostic procedure (36), intentional termination of pregnancies due to either fetal severe thalassemia disease or aneuploidy (313), and incomplete data for analysis (247). The remaining 776 pregnancies undergoing CVS and meeting the inclusion criteria were available for analysis as the study group, as presented in [Figure 1](#). A total of 7760 normal pregnancies were included into the control group.

The mean ($\pm$ SD) maternal age of pregnancies who underwent CVS was 31.49 ± 5.7 (16–46) years. Fetal loss rate before 24 weeks and other possible CVS-related complications of both groups are presented in [Table 1](#). There was no statistically significant difference of the fetal loss rate between the two groups (1.16 versus 1.9%, *p* value .14). After the cases of fetal loss were excluded, the gestational age at delivery and birth weight were slightly but significantly lower in the study group (38.02 versus 38.96 weeks, *p* value <.001 and 3025.47 versus 3092.65 g, *p* value .001, respectively). Although the incidences of SGA and LBW were not significantly different (4 versus 4%, *p* value .948; and 8.9 versus 8.0%, *p* value .41, respectively), the rates of preterm birth in the study group were significantly higher than that in the control group (9.4 versus 7.3%, *p* value .037, RR 1.287 with 95% CI: 1.017–1.629).

Cox regression analysis was done for gestational age at delivery and other parameters which are maternal age, parity, neonatal gender and groups of the patients (case versus control). All parameters except for neonatal gender significantly affected the gestational age at delivery with *p* value <.001.

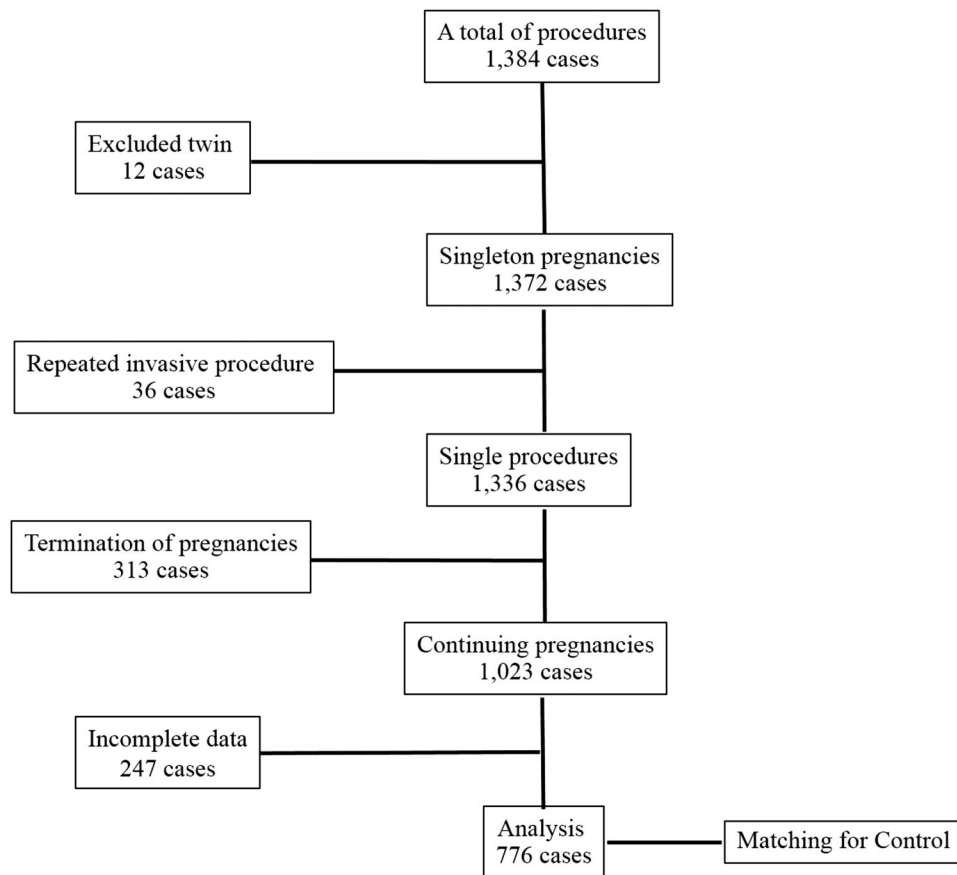


Figure 1. Chart of the patient flow in recruitment.

Table 1. Maternal characteristics and chorionic villous sampling (CVS)-related complications.

	Case (CVS) 776 cases	Control 7760 cases	p Value	RR (95% CI)
Maternal age (mean $\pm$ SD)	$N = 749$ 31.49 ± 5.7	$N = 7760$ 31.24 ± 5.8	.219 ^a	
Fetal loss (delivery before 24 weeks)	9 cases 9/776 = 1.16%	148 cases 148/7760 = 1.9%	.14 ^b	0.608 (0.31–1.18)
Gestational age at delivery ^c (mean $\pm$ SD)	$N = 758$ 38.02 ± 1.6	$N = 7612$ 38.96 ± 2.3	<.001 ^a	
Birth weight ^c (mean $\pm$ SD)	$N = 767$ 3025.47 ± 439.2	$N = 7612$ 3092.65 ± 551.1	.001 ^a	
SGA ^c	$N = 767$ 31/767 = 4.0%	$N = 7612$ 304/7612 = 4.0%	.948 ^b	1.012 (0.70–1.45)
LBW ^c	$N = 767$ 68/767 = 8.9%	$N = 7612$ 610/7612 = 8.0%	.41 ^b	1.106 (0.87–1.40)
Preterm birth ^c	$N = 758$ 71/758 = 9.4%	$N = 7612$ 554/7612 = 7.3%	.037 ^b	1.287 (1.01–1.62)

^at-test.

^bChi square.

^cExcluded fetal loss.

Kaplan–Meier’s graph of cumulative delivery and gestational age at delivery between group of cases (CVS) and controls is shown in [Figure 2](#).

However, after the actual neonatal birth weight in this study was converted into Z-score of gestational age at delivery, the mean of absolute Z-score between CVS and control groups was not statistically significantly different (0.76 versus 0.79, p value .15 by t -test).

Discussion

The new insight gained from this study is that pregnancies underwent CVS tend to deliver earlier and could be associated with an increased risk of preterm

birth. Accordingly, the mean birth weight is slightly lower than that of the control. Nevertheless, overall risk of CVS performed by experienced hands may be only minimal since the fetal loss rate and other complications were not significantly increased.

Several studies have reported the CVS-related complications [1–5,7–11], including the one from our center [6]. The CVS-related fetal loss rate is relatively low but it is varied from study to study. Mujezinovic and Alfirevic [7] performed a systematic review and found that pregnancy loss within 14 days after CVS was 0.7%, pregnancy loss before 24 weeks was 1.3% and total pregnancy loss was 2%. However, they concluded that in most previous studies, lack of adequate

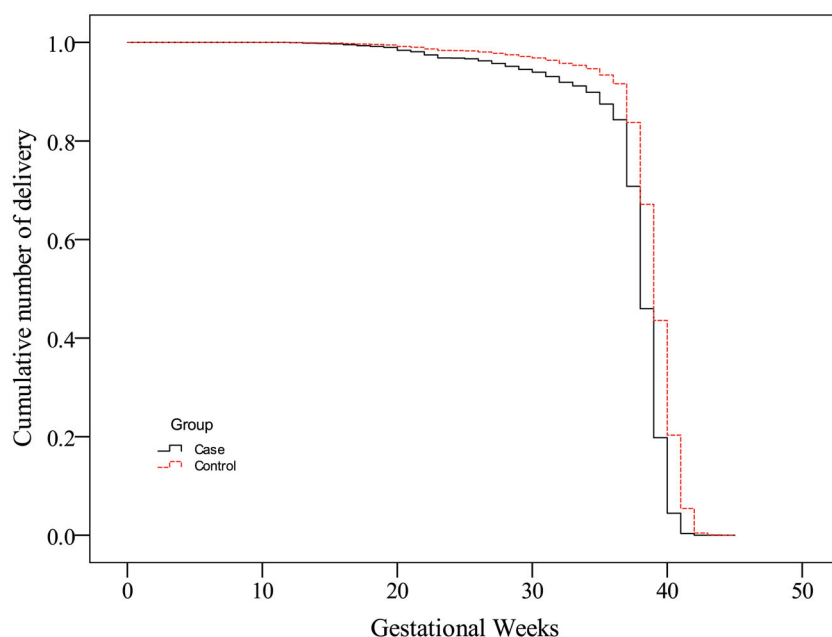


Figure 2. Kaplan–Meier's graph of cumulative delivery and gestational age at delivery between group of cases (CVS) and controls.

controls tends to underestimate the true added risk of CVS. Further, well-controlled studies are still needed. According to the result of this study, the fetal loss rate before 24 weeks of the CVS group is 1.16% which is comparable to previous systematic review [7,12] and did not significantly differ from the control group (p value .14). Nevertheless, the prevalence of fetal loss was a rare event, thus it is possible that the small sample size in this study could not gain enough power to show the small difference, if it existed. However, based on this study and previous publications, it is prudent to conclude that CVS-related fetal loss is relatively low. This information is important for the parents to relieve anxiety about the fetal loss rate secondary to CVS procedure.

Notably, this study showed that the mean gestational age of delivery of the CVS group was slightly but significantly lower than that of the control group. This finding was confirmed by the Kaplan–Meier graph in Figure 2 that the CVS group tends to deliver earlier. Moreover, our study showed that the CVS was significantly associated with a higher rate of preterm birth (9.4 versus 7.3%, p value .037, RR 1.287). This is a novel finding which has not been mentioned elsewhere, though some previous studies showed that CVS might be associated with preeclampsia by mechanism of induced placental disruption [2,13] they never reported about the association of CVS and preterm birth. We hypothesize that the possible mechanism of CVS-related preterm birth may be caused by disruption or minor trauma to placental tissue and this event may induce inflammatory process of the

placenta or activation of some cytokines or inflammatory markers in subtle level and may be one of the precipitating factor of inducing preterm labor and delivery. However, the preterm birth in this study is defined as delivery before 37 weeks which was not subdivided into early and late preterm group. Moreover, it included both spontaneous and induced preterm delivery. Thus, further study is needed to elucidate the association between CVS and preterm delivery.

According to our hypothesis, CVS may traumatize to the placental cotyledon, possibly resulting in some degree of cotyledon dysfunction and possible increasing risk of fetal growth restriction or SGA. Though our result did not show a significant difference in the incidence of SGA or LBW between both groups, if we focused on the birth weight, there was a significant difference. The CVS group tends to have significantly lower neonatal birth weight than controls (p value .001). However, when the actual neonatal birth weight was converted into Z-score of gestational age at delivery, the mean of absolute Z-score between CVS and control groups was not significantly different. Therefore, the findings about the statistically significant difference in neonatal birth weight may be affected by the significant earlier gestational age at delivery in CVS group as mentioned previously.

The limitations of this study are as follows: (1) a large number of the study group were excluded, resulting in too small sample size for comparison of rare events such as fetal loss rate and (2) retrospective

nature of the study leading to missing data in many cases.

The strengths of this study include: (1) the sample size was relative large for comparisons of the most common adverse outcomes such as preterm birth; (2) the control group was large and appropriately selected by matching the potential confounders of adverse outcomes such as maternal age and the year of the procedure. Moreover, we intended to select the control group which had early prenatal visit to reassure that every case in CVS and control groups had equal chance of fetal loss during early gestation that may be reflexive of the natural course of pregnancy; (3) The study population is highly homogenous in terms of single center in which CVS were performed with the same technique by experienced operators.

Conclusions

In conclusion, this retrospective cohort study showed that pregnancies undergoing CVS tend to deliver earlier and have a significant increase in the incidence of preterm birth with relative risk of 1.3 which is the novel findings never mentioned in previous studies. Likewise, average gestational age at delivery and neonatal birth weight were significantly lower in the study group. These findings are important information about subtle effects of prenatal diagnostic procedure that may need attention besides the obvious complication like fetal loss. However, the incidence of fetal loss before 24 weeks, SGA and LBW are comparable between pregnancies undergoing CVS and the controls.

Disclosure statement

No potential conflict of interest was reported by the authors.

Funding

This work was supported by the Research Fund, Chiang Mai University, Chiang Mai, Thailand.

ORCID

Kasemsri Srisupundit  <http://orcid.org/0000-0001-6554-5050>
Theera Tongsong  <http://orcid.org/0000-0002-3389-6478>
Wirawit Piyamongkol  <http://orcid.org/0000-0003-2199-4625>
Supatra Sirichotiyakul  <http://orcid.org/0000-0002-0413-5581>
Fuanglada Tongprasert  <http://orcid.org/0000-0001-7152-1952>

Suchaya Leuwan  <http://orcid.org/0000-0002-4838-175X>
Kuntharee Traisrisilp  <http://orcid.org/0000-0002-0980-2128>
Phudit Jatavan  <http://orcid.org/0000-0002-4176-3501>

References

- [1] Farina A. Nonabortal pregnancy complications of chorionic villous sampling. *Curr Opin Obstet Gynecol.* 2011;23(2):129–134.
- [2] Basaran A, Topatan B, Basaran M. The association between preeclampsia and placental disruption induced by chorionic villous sampling. Farina A et al. *Prenatal Diagnosis* 2010. *Prenat Diagn.* 2010; 30(12–13):1230–1232; author reply 1233.
- [3] Carlin AJ, Alfirevic Z. Techniques for chorionic villus sampling and amniocentesis: a survey of practice in specialist UK centres. *Prenat Diagn.* 2008;28(10): 914–919.
- [4] Jauniaux E, Rodeck C. Use, risks and complications of amniocentesis and chorionic villous sampling for prenatal diagnosis in early pregnancy. *Early Pregnancy.* 1995;1(4):245–252.
- [5] Ndumbe FM, Navti O, Chilaka VN, et al. Prenatal diagnosis in the first trimester of pregnancy. *Obstet Gynecol Surv.* 2008;63(5):317–328.
- [6] Laksanavilai U, Piyamongkol W, Sirichotiyakul S, et al. Chorionic villous sampling: experience of 636 cases. *J Med Assoc Thai.* 2013;96(4):383–388.
- [7] Mujezinovic F, Alfirevic Z. Procedure-related complications of amniocentesis and chorionic villous sampling: a systematic review. *Obstet Gynecol.* 2007;110(3): 687–694.
- [8] Oloyede OA. Transabdominal chorionic villous sampling in Nigeria: correlation between number of cases and other variables. *West Afr J Med.* 2011;30(1):57–61.
- [9] Alfirevic Z, Sundberg K, Brigham S. Amniocentesis and chorionic villus sampling for prenatal diagnosis. *Cochrane Database Syst Rev.* 2003;(3):CD003252.
- [10] Young C, von Dadelszen P, Alfirevic Z. Instruments for chorionic villus sampling for prenatal diagnosis. *Cochrane Database Syst Rev.* 2013;(1):CD000114.
- [11] Alfirevic Z, Navaratnam K, Mujezinovic F. Amniocentesis and chorionic villus sampling for prenatal diagnosis. *Cochrane Database Syst Rev.* 2017;(9):CD003252.
- [12] 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(1):16–26.
- [13] Farina A, Hasegawa J, Raffaelli S, et al. The association between preeclampsia and placental disruption induced by chorionic villous sampling. *Prenat Diagn.* 2010;30(6):571–574.