Vasa previa and placenta associated complications
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CHAPTER 6

Incidence and recurrence rate of placental abruption: a longitudinal linked national cohort study in the Netherlands

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Chapter 6

ABSTRACT

Objective Women who have experienced a placental abruption have a risk of recurrence, but exact information to quantify this risk is currently not available. We studied the incidence and recurrence rate of placental abruption in a subsequent pregnancy and the influence of hypertensive disorders.

Study design We conducted a retrospective national cohort study of all singleton pregnancies that ended between 1999 and 2007 in the Netherlands. A longitudinal linked national cohort of these women with information on a subsequent singleton delivery was used. We calculated and compared incidence and recurrence rates of placental abruption for women in total, stratified by gestational age of first placental abruption and by the presence of a hypertensive disorder in their first pregnancy.

Results We studied 1,570,635 women of which 3,496 (0.22%) experienced a placental abruption. Information was available on a subsequent singleton delivery for 264,424 deliveries. Of these, 521 women (0.20%) had a placental abruption in the first pregnancy versus 214 (0.08%) in the second pregnancy. The risk of placental abruption in a subsequent pregnancy was significantly higher in women with a previous placental abruption compared with women without (5.8% vs 0.06%; adjusted odds ratio (aOR) 93; 95% confidence interval (CI) 62-139). Women with a placental abruption that occurred at term in their first pregnancy were more at risk for recurrence (aOR 188; 95% CI 116-306) than women with a preterm (aOR 52; 95% CI 25-111) or early preterm (< 32 weeks) placental abruption in their first pregnancy (aOR 39; 95% CI 13-116). Placental abruption was more frequent among women with a hypertensive disorder compared with normotensive women (0.44% versus 0.16%, OR 2.7; 95%CI 2.3 – 3.3). Women with a hypertensive disorder were less at risk for recurrence than were normotensive women (aOR 0.68; 95% CI 0.27-1.6). No interaction between a hypertensive disorder in the first pregnancy and the recurrence risk was found.

Conclusion Women with a placental abruption in their first pregnancy have a greatly increased risk of placental abruption in a subsequent pregnancy. Hypertensive disorders increase the risk of placental abruption but do not increase the recurrence rate in a subsequent pregnancy. We suggest elective induction from 37 weeks for women with a history of placental abruption at term in a previous pregnancy.
INTRODUCTION

Placental abruption, the premature dehiscence of a normally inserted placenta from the uterine wall, is associated with significant perinatal morbidity and accounts for 12% of all perinatal deaths in the United States.\(^1\)

Early diagnosis of placental abruption potentially can improve the outcome of the children involved in these pregnancies by closely monitoring women at risk.\(^2\) Advanced maternal age, multiparity\(^3\), chronic hypertension\(^3\), smoking\(^4,5\), cocaine use\(^6\), previous cesarean delivery\(^5,7\), uterine surgery\(^5\) and short interpregnancy interval\(^7\) are reported risk factors for placental abruption. In patients who experienced a placental abruption in a previous pregnancy, there seems to be a tendency for recurrence, although most studies on the incidence and recurrence rate of placental abruption are dated or include relatively small samples of patients.\(^8,9\) Knowledge of these subjects potentially can help in providing specialized prenatal care for women who are at risk for placental abruption for the reason of beneficial outcome.\(^10\)

Our objective was to investigate the incidence and recurrence rate of placental abruption in a retrospective study of two subsequent deliveries in the Netherlands between 1999 and 2007. Moreover, we assessed the influence of hypertensive disorders on the incidence and recurrence rate.

MATERIALS AND METHODS

This study was performed in a retrospective nationwide cohort with the use of the Netherlands Perinatal Registry (PRN). The PRN consists of prospectively collected population-based data that contain information on pregnancies, deliveries and (re)admissions until 28 days after birth. The database is obtained by a validated linkage of three different registries: the midwifery registry (LVR1), the obstetrics registry (LVR2), and the neonatology registry (LNR) of hospital admissions of newborn infants.\(^11,12\)

The coverage of the PRN registry is approximately 96% of all deliveries in the Netherlands and it contains all pregnancies that ended in live births and stillbirths at > 22 weeks of gestation and a birthweight of at least 500 g. Furthermore, all admissions to the neonatology care unit are registered until 28 days after birth. It is used primarily for annual assessment of the quality indicators of obstetric care.

The records included in the PRN registry are entered at child’s level. There is no unique maternal identifier available in the registry to follow-up on outcomes of subsequent pregnancies of the same mother. Previously, a longitudinal probabilistic-linkage procedure in which records of children of the same mother are linked was performed to create a mother identifier. This resulted in a cohort of 272,551 women with complete data on first and second
deliveries of the same mother. Details on this linkage procedure are described elsewhere.\textsuperscript{13} The data in the PRN database are anonymous, the Dutch Perinatal Registry gave their approval for the use of the data for this study (approval no. 12.71).

**Inclusion and exclusion criteria**

We selected all women who delivered in The Netherlands between Jan. 1, 1999 and Dec. 31, 2007. We excluded women with a multiple gestation (n = 7,472) and women with a gestational age at delivery of > 42 + 6 weeks (n = 655).

**Outcome measures**

Our primary outcome was placental abruption. We identified all women with a placental abruption that had been registered in the PRN registry with a code for placental abruption. Codes are assigned by midwives, residents and obstetricians based on information in the patients’ medical record. A clinical diagnosis of placental abruption is made based on a combination of the following clinical symptoms: vaginal bleeding, abdominal pain or fetal distress and further supported by ultrasonographic findings as retro placental bleeding. After delivery, the diagnosis may be confirmed by a couvelaire uterus, gory amniotic fluid, or examination of the placenta that reveals a clot.\textsuperscript{14} Placental abruption is primarily documented by one of the care providers after delivery; there is no stratification in severity in the PRN database. In addition, all women with a positive history of placental abruption at the start of the second pregnancy were labelled as cases of placental abruption in the first pregnancy. The gestational age at delivery of the fetus was used as the gestational age of placental abruption.

**Characteristics**

We extracted demographic and obstetric baseline characteristics from the PRN registry as ethnicity, maternal age, socioeconomic status, pregnancy interval, hypertension, and neonatal sex. All characteristics were primarily documented by the care providers. Ethnicity was categorized into white (native Dutch and other Caucasian women) and non-white (different ethnic groups as African/Surinamese, South Asian, Moroccan and Turkish) for this study. The continuous socioeconomic status score (based on mean income level, the percentage of households with a low income, inhabitants without a paid job, and households with, on average, a low education in a postal code area) was categorized into a high, middle, and low group based on percentile ranges (≤ 25th percentile, middle, > 75th percentile). Gestational age was based on last menstrual period or ultrasound measurements at < 20 weeks. If the estimation by ultrasound measurement differed > 6 days from the last menstrual period, then the ultrasound measurement was considered the dominant measurement. Hypertensive disorders (HTD) included chronic hypertension, pregnancy-induced hypertension, and
preeclampsia. The clinical diagnosis of hypertension was made with a systolic blood pressure of ≥ 140 mm Hg and/or a diastolic blood pressure of ≥ 90 mm Hg. Preeclampsia was diagnosed with hypertension and proteinuria.\textsuperscript{15}

Cases of placental abruption were analyzed in total and stratified into three groups based on the gestational age at the time of placental abruption in the first pregnancy; early preterm (22\textsuperscript{0}-31\textsuperscript{6} weeks of gestation), late preterm (32\textsuperscript{0}-36\textsuperscript{6} weeks of gestation) and term (37\textsuperscript{0}-42\textsuperscript{6} weeks of gestation).

In addition, we stratified the analysis by HTD in the first pregnancy: women with an HTD in their first pregnancy and women without an HTD in their first pregnancy.

**Analysis**

We calculated the incidence of placental abruption in our cohort of 1,570,635 singleton deliveries by dividing the number of placental abruptions by the total number of deliveries. We calculated the incidence per gestational week by dividing the number of placental abruptions in a particular week by the total number of deliveries in that given week.

We selected all women with a subsequent singleton delivery and compared incidence of placental abruption in a subsequent pregnancy in women with and without a placental abruption in their first pregnancy. In addition, we compared their demographic and obstetric baseline characteristics. Comparison of the baseline characteristics was by univariate analysis that was performed with the unpaired t-test for normally distributed continuous variables and with the χ\textsuperscript{2} test for categoric variables. All tests were two-sided with a probability value of .05 as threshold for statistical significance.

To estimate the effect of a history of placental abruption on the occurrence of placental abruption in a subsequent pregnancy, logistic regression modeling was used and was expressed as odds ratio (OR) with a 95% confidence interval (CI). In addition, the effect of gestational age at placental abruption in the first pregnancy was estimated and expressed as odds ratio with 95% CI. To account for the effect of potential confounders, we used a multivariate logistic regression analysis to adjust for variables that were unequally distributed in the baseline characteristics. When a low incidence of placental abruption was found, Firths’ penalized likelihood approach was performed to minimize small sample size bias. Kaplan-Meier curves by gestational age of first placental abruption were constructed for the recurrent placental abruptions.

We tested for an association between placental abruption and HTD in the first pregnancy. When statistically significant, analyses were also performed separately for HTD and non-HTD cases per three strata of gestational age of first placental abruption. In addition, we tested for interaction between HTD in the first pregnancy and the recurrence of placental abruption in a subsequent pregnancy by adding an interaction term to our logistic regression model.

The data were analyzed with the SAS statistical software package (version 9.3; SAS Institute Inc, Cary, NC, USA).
RESULTS

Between Jan. 1, 1999 and Dec. 31, 2007, a total of 1,570,635 singleton pregnancies were identified, 3,496 pregnancies (0.22%) were complicated by a placental abruption. The overall incidence was highest between 28 and 31 weeks of gestation; 40.8 per 1000 deliveries (4.1%). Between 32 and 34 weeks of gestation, the incidence was 20.5 per 1000 deliveries (2.1%); between 39 and 42 weeks of gestation the incidence was 0.8 per 1000 (0.08%). (Figure 1).

Figure 1. Incidence of placental abruption among singletons per 1000 deliveries by gestational age

This figure shows the incidence of placental abruption per 1000 deliveries per gestational week of pregnancy.

A total of 264,424 women (528,848 deliveries) were available for the analysis of the recurrence rate and incidence of placental abruption in a subsequent pregnancy. Baseline characteristics of our linked cohort are listed in Table 1. In the first pregnancy, 521 women (0.20%) had a placental abruption, among these women an age < 25 years, non-white ethnicity, low socioeconomic status and HTDs were more prevalent.

Of the 521 women with a placental abruption in the first pregnancy, 30 women (5.8%) had a recurrent placental abruption in the subsequent pregnancy. Placental abruption in a subsequent pregnancy occurred in 184 parous women (0.07%) without a history of placental abruption. Figure 2 shows all women with a placental abruption in the first pregnancy and their time to a recurrent placental abruption stratified by gestational age of the first placental abruption.
Table 1. Baseline characteristics of the linked cohort

<table>
<thead>
<tr>
<th>Characteristics of the first pregnancy</th>
<th>Placental abruption in first pregnancy (n = 521)</th>
<th>No placental abruption in first pregnancy (n = 263,903)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal characteristics</td>
<td>n</td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>Mean maternal age, years&lt;sup&gt;a&lt;/sup&gt;</td>
<td>28.0 ± 4.6</td>
<td>28.6 ± 4.2</td>
<td>0.0001</td>
</tr>
<tr>
<td>Maternal age &lt; 25 years</td>
<td>115</td>
<td>22.1</td>
<td>42,784</td>
</tr>
<tr>
<td>Mean gestational age, weeks&lt;sup&gt;a&lt;/sup&gt;</td>
<td>34.6 ± 4.3</td>
<td>39.2 ± 2.2</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Non-white maternal ethnicity (n)</td>
<td>74</td>
<td>14.2</td>
<td>28,826</td>
</tr>
<tr>
<td>Low socio-economic status (n)</td>
<td>149</td>
<td>28.6</td>
<td>57,732</td>
</tr>
<tr>
<td>Hypertensive disorder</td>
<td>147</td>
<td>28.2</td>
<td>33,186</td>
</tr>
<tr>
<td>Fetal characteristics, male (n)</td>
<td>283</td>
<td>54.3</td>
<td>135,887</td>
</tr>
</tbody>
</table>

<sup>a</sup> Presented as mean ± SD

Figure 2. Recurrent placental abruption by gestational age of first placental abruption

This figure shows the time to placental abruption in a subsequent pregnancy after an first early preterm, late preterm or term placental abruption.

After adjustment for maternal age, ethnicity, socioeconomic status, and hypertension, a placental abruption in the first pregnancy was associated with a significantly increased risk of placental abruption in a subsequent pregnancy (adjusted odds ratio (aOR) 93, 95%CI 62-139).

Table 2 shows the distribution of placental abruption in a subsequent pregnancy in women with and without a history of placental abruption and the crude and adjusted odds ratios of placental abruption in the first pregnancy on the recurrence rate of placental abruption in
a subsequent pregnancy, stratified by gestational age of first placental abruption. The odds ratio of a history of placental abruption on the recurrence in a subsequent pregnancy was higher for women with a placental abruption in the term period of the first pregnancy than for women with a previous late or early preterm placental abruption.

Table 2. Placental abruption in a subsequent pregnancy in total and by gestational age of placental abruption in the first pregnancy

<table>
<thead>
<tr>
<th>Placental abruption in second pregnancy</th>
<th>Total abruption second pregnancy</th>
<th>Odds ratio and 95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>n</td>
</tr>
<tr>
<td>Complete cohort of women with first term delivery, no placental abruption in first pregnancy (n=243,799)</td>
<td>26</td>
<td>62</td>
</tr>
<tr>
<td>Complete cohort placental abruption first pregnancy (n = 521)</td>
<td>2</td>
<td>13</td>
</tr>
</tbody>
</table>

Gestational age of placental abruption in the first pregnancy:

<table>
<thead>
<tr>
<th></th>
<th>n</th>
<th>n</th>
<th>n</th>
<th>Crude</th>
<th>Adjusted*</th>
</tr>
</thead>
<tbody>
<tr>
<td>22+0 - 31+6 weeks (n=128)</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>2.3%</td>
</tr>
<tr>
<td>32+0 - 36+6 weeks (n=210)</td>
<td>0</td>
<td>4</td>
<td>3</td>
<td>7</td>
<td>3.3%</td>
</tr>
<tr>
<td>37+0 - 42+6 weeks (n=183)</td>
<td>1</td>
<td>8</td>
<td>11</td>
<td>20</td>
<td>11%</td>
</tr>
</tbody>
</table>

*Adjusted for hypertension, maternal age, ethnicity, low SES

Of the 264,424 first singleton pregnancies, a total of 33,333 women (12.6%) had an HTD. In the second pregnancy, 17,378 (6.6%) women had an HTD. In the first pregnancy, placental abruption was more prevalent in the HTD group compared with the non-HTD group (0.44% vs 0.16%; OR 2.73, 95%CI 2.26-3.31). In the second pregnancy, placental abruption was also more prevalent in the HTD group compared to the non-HTD group (0.52% vs 0.17%). Table 3 shows that, in both women with and without HTD in their first pregnancy, the recurrence risk of placental abruption is increased for women with a history of placental abruption compared to women without a history of placental abruption. Table 3 also shows that the odds ratio of a history of placental abruption on the recurrence risk for is lower for women with an HTD in their first pregnancy compared with women who were normotensive in their first pregnancy. Although the initial risk of placental abruption is increased by the
Incidence and recurrence rate of placental abruption

presence of an HTD, the interaction between an HTD in the first pregnancy and the recurrence risk of placental abruption in a subsequent pregnancy was not statistically significant (p = 0.1).

Table 3. Placental abruption in a subsequent pregnancy by presence of HTD in the first pregnancy

<table>
<thead>
<tr>
<th>HTD in first pregnancy (n = 147)</th>
<th>Placental abruption in second pregnancy</th>
<th>Total abruption second pregnancy</th>
<th>Odds ratio and 95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>n</td>
<td>n</td>
</tr>
<tr>
<td>----------------------------------</td>
<td>-----------</td>
<td>-----------</td>
<td>-----------</td>
</tr>
<tr>
<td>HTD in first pregnancy (n = 147)</td>
<td>2</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>No HTD in first pregnancy (n = 347)</td>
<td>0</td>
<td>11</td>
<td>11</td>
</tr>
</tbody>
</table>

COMMENT

In this study, we investigated the overall incidence and recurrence rate of placental abruption among singleton pregnancies. Moreover, we investigated the influence of HTD on placental abruption. The incidence of placental abruption among singleton pregnancies was 0.22%. The incidence was higher in women with an HTD compared with normotensive women. The risk of placental abruption in a subsequent pregnancy was significantly higher in women with a previous placental abruption, compared with women without a previous placental abruption. Women with a first placental abruption at term were most at risk for recurrence.

Our study has both strengths and limitations. Because placental abruption is a rare, but important, event, large amounts of data are needed to detect differences in populations. Our study was performed with data from a large population-based national registry in which data are collected prospectively. This provides validity of the results because it represents a national outcome, which avoids recall and reporting bias by prospective collection and avoids selection bias that is created potentially by hospital-based studies.

However, this study was a retrospective study, which comes with limitations. We needed to rely on the available information in the PRN; thus, we cannot rule out misclassification bias. It is likely that some cases have been missed, especially the mild or concealed ones. Another limitation is the unavailability of gestational age of abruption. From 32 weeks of gestation, placental abruption will mostly be followed by immediate delivery. Placental abruption can
also be managed expectantly when occurring at <32 weeks of gestation. The gestational age of abruption is then different than the date of delivery. The PRN registry does not provide this information; therefore, the difference in preterm and term incidence of placental abruption may be higher than found in this study. Data on possible confounders as body mass index and tobacco use are also not available in the PRN, and the usage of a linked database comes with restrictions as no linkage because of missing values of the linkage variables.

The incidence of placental abruption described in previous studies is 0.3-1%, which is higher than in our study.\textsuperscript{3-5} There are several potential explanations for this difference, for example missing cases due to the retrospective character of this study as mentioned before, or inconsistencies in diagnostic criteria of placental abruption; there are neither laboratory tests nor diagnostic methods to accurately detect placental abruption. A previous study revealed that inconsistencies in the composition of placental abruption cases lead to differences in incidence.\textsuperscript{3}

Most studies on incidence include singleton and multiple pregnancies. The latter are associated with a higher incidence of placental abruption, thus exclusion of multiple pregnancies from our analysis may have led to a lower incidence.\textsuperscript{16} With the exclusion of subsequent multiple pregnancies we potentially excluded some women with a history of placental abruption as well. Furthermore, the incidence of placental abruption per 1000 deliveries decreases by gestational age. Some studies included pregnancies with a minimum gestational age of 16 weeks, whereas the PRN-registry comprises only pregnancies from a gestational age of 22 weeks.\textsuperscript{17-19}

In general, the incidence of placental abruption seems to be lower in Nordic countries than in the United States, where the population consists of more women from African American ethnicity. These women are more at risk for placental abruption than white women because HTD, smoking, alcohol and cocaine use are more prevalent in this population.\textsuperscript{20-23} Our study population is relatively more homogenous consisting of 90% maternal white ethnicity, thus potentially leading to a lower incidence.

Furthermore, the percentage of Cesarean section and thus the number of women with a history of Cesarean section is significantly lower in our country compared with the United States.\textsuperscript{24}

Studies in the United States found an increasing incidence of placental abruption over time, in contrast to Tikkanen et al.,\textsuperscript{25} who performed a large population-based cohort study in Finland and found a decrease in the incidence of placental abruption from 1980 – 2005. Because we calculated the incidence on a recent cohort in the Netherlands including mainly deliveries in the 21st century, this partially might explain our slightly lower incidence than studies performed from 1980-2000. Also, improvements in prenatal care over the last decades may have contributed. Women with HTD, preeclampsia, or small-for-gestational-age fetuses are diagnosed earlier and delivered before their due date, which potentially could decrease
the risk of a placental abruption. Unfortunately, studies, for example, on medical decision-making in pregnancy-induced hypertension or preeclampsia frequently are underpowered to find significant effects on placental abruption. On the other hand, several risk factors for placental abruption, such as advanced maternal age and a previous cesarean section, are on the rise; therefore the exact development of incidence of placental abruption remains difficult to determine. The decrease in incidence of placental abruption with advancing gestation in our study has been found in previous studies. Our distribution of incidence by gestational age is similar to Tikkanen et al.

The overall recurrence rate of placental abruption in this study was 5.8% (range 2.3-11%). An increased risk for placental abruption after a previous placental abruption is found in previous studies, although in less well defined populations, and data of these studies are dated. The true recurrence rate may even be higher than found in our study because women who have had placental abruption are less likely than women without a history of placental abruption to have another pregnancy. In addition, elective delivery at term before labor in women with a history of placental abruption may also distort the true recurrence rate because, in these women, it is not known whether a placental abruption would have occurred. On the contrary, obstetricians potentially are more likely to diagnose and correctly code a placental abruption in women with a history of placental abruption compared with women without this history, which can amplify the recurrence rate.

To the best of our knowledge, only one previous study investigated the influence of gestational age at first placental abruption on the recurrence rate. Rasmussen et al suggested that women with a history of placental abruption should receive special surveillance six weeks before the gestational age of the first placental abruption to reduce the recurrence risk to the initial risk. This is in line with our results that showed that almost 60% of the second placental abruptions occurred in the same gestational period and that 40% of all women with placental abruption in the term period of the first pregnancy experienced recurrence in the late preterm period. We may add to these results that primarily women with first-term placental abruption are at risk for recurrence (11%). Thus, even though the incidence of a placental abruption in the preterm period is higher than the incidence of placental abruption at term, the consequences for a subsequent pregnancy seem to be lower. However, we must interpret these results with caution because it is likely that term placental abruptions are diagnosed and reported more accurately than early preterm abruptions.

The association between HTD and placental abruption has been found in previous studies. The absent interaction between HTD and the recurrence of placental abruption in a subsequent pregnancy that was found in our study has not been described before. From our results, it seems that placental abruptions in normotensive women are more likely to recur than placental abruptions in women with an HTD. This possibly may be explained partially by the fact that the prevalence of HTD is less in second than in first pregnancies, attenuating
this as a risk factor.\textsuperscript{37, 38} It might also be due to more intensive monitoring of women in subsequent pregnancies after a previous pregnancy-induced hypertension or preeclampsia, leading to earlier diagnosis of complications and delivery. It would be valuable to stratify recurrence risk of placental abruption by type of HTD, because chronic hypertension and severe pre-eclampsia are stronger predictors for placental abruption than pregnancy-induced hypertension and mild pre-eclampsia; however, the design of the PRN registry did not allow us to perform such analysis.\textsuperscript{3, 39}

Furthermore, we would suggest elective induction at 37 weeks of gestation in women with a previous placental abruption in the term period of pregnancy. Although the design of this study cannot provide a clear answer to the question on the best strategy in these women and multiple factors influence delivery timing beyond just the recurrence probability of placental abruption, more than 50\% of the recurrent abruptions occurred after 37 weeks of gestation.

In conclusion, the findings of this study show that women with placental abruption are at increased risk for recurrence, especially when the first placental abruption occurred in the term period. HTDs increase the initial risk of placental abruption. Potentially, normotensive women with a placental abruption in their first pregnancy are more at risk for recurrence than are women with an HTD in their first pregnancy. It is desirable to monitor pregnant women with a history of placental abruption in tertiary centers and to closely monitor them in the gestational period of first placental abruption.

\section*{ACKNOWLEDGEMENTS}

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