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Placenta previa and immediate outcome of the term offspring

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Abstract
Purpose Immediate neonatal outcome in pregnancies complicated by placenta previa is largely dependent on gestational age. We aimed to investigate whether placenta previa increases the risk for perinatal mortality and immediate morbidity of the offspring born at term.
Methods A population-based cohort study included all singleton pregnancies, with and without placenta previa, delivered at term. Maternal and pregnancy characteristics as well as immediate neonatal morbidity and mortality were compared. Deliveries occurred between the years 1991–2013 in a tertiary medical center. Multiple pregnancies, and fetal congenital malformations were excluded.
Results During the study period 233,123 consecutive term deliveries met the inclusion criteria; 0.2 % of the babies were born to mothers diagnosed with placenta previa. Women with placenta previa were significantly older and more likely to have had a previous cesarean section. Pregnancies were more likely to be complicated with pathological presentations and cesarean hysterectomies. Babies born at term following pregnancies with placenta previa were more likely to weigh less than 2500 g (OR 2.78 CI 1.9–3.9, $p < 0.001$). However, 5 min Apgar score and perinatal mortality rates were comparable between the groups. Neonatal outcomes remained comparable between the groups in a sub-analysis of cesarean deliveries only.
Conclusion Although placenta previa pregnancies involve higher maternal morbidity rates, term offsprings are not at an increased risk for immediate adverse outcome.

Keywords Abnormal placentation · Neonatal morbidity · Short-term outcome · Term pregnancy · Perinatal mortality

Introduction

In roughly four of every 1000 deliveries, the placenta covers part or all of the internal os, and is referred to as placenta previa [1, 2]. Well established risk factors for abnormal placentation include: advanced maternal age, maternal smoking, multiparity, previous placenta previa, previous cesarean delivery (CD), and more [2–6]. Some of theses risk factors (advanced maternal age, previous cesarean section) are more common than before. Specifically, one of the consequences of increasing CD rates over the last several decades is an increase in placental implantation abnormalities including placenta previa. The pathogenesis of placenta previa is thought to involve the presence of areas of suboptimal endometrium [1, 3, 6, 7] or reduced placental perfusion. Previous cesarean deliveries may contribute to the development of suboptimal endometrium and the resultant placenta previa.

Pregnancies complicated with placenta previa are prone for bleeding throughout the pregnancy, which in return elevate the risk of preterm delivery to up to 40–50 % [5, 8, 9]. Thus, placental implantation abnormalities are a major cause for indicated preterm delivery, usually in an effort to reduce the risk for the anticipated life threatening complications for both mother and child [8]. Neonates born to

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mothers with placenta previa are at increased risk for perinatal morbidity and mortality and evidently, the principal causes are primarily related to preterm delivery (which is still common), rather than growth restriction, hypoxia or anemia [10].

We therefore sought to investigate whether placenta previa per se, is a risk factor for immediate neonatal morbidity and mortality, excluding pregnancies ending prematurely (<37 completed weeks of gestation). We hypothesize that since placenta previa may represent poor placentation and suboptimal intrauterine environment, it may impact on the child's immediate well-being.

Methods

Included in this population-based cohort study, were all singleton pregnancies of women who delivered between January 1991 and December 2013 at the Soroka University Medical Center. This medical center, is the sole hospital in the Negev (southern Israel), and occupies 60 % of the land of Israel, providing services to the entire population of the region (14.4 % of Israel's population) [11]. Thus, the study is based on non-selective population data.

The institutional review board approved the study that has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments (# SOR-0236-13 approved on November 20, 2013). The primary exposure was a diagnosis of placenta previa during pregnancy. Placenta previa was defined as placenta covering all, or part, of the internal os diagnosed by ultrasound during the second or third trimester. As a routine, placenta previa was confirmed immediately prior to delivery by an ultrasound. Gestational age was determined using menstrual history and first trimester ultrasound. We excluded multiple pregnancies, preterm deliveries (occurring prior to 37 completed weeks of gestation), and fetuses with congenital malformations. A comparison was performed between neonates born at term to women diagnosed with placenta previa and those born at term without such diagnosis. Outcomes assessed included maternal demographic characteristics, obstetrical data, and immediate neonatal outcome.

In addition, we performed a sub analysis in which only cesarean deliveries were included from both groups. Data were collected from the computerized perinatal database and the hospital's computerized charts of the obstetrics and gynecology department. The perinatal database consists of information recorded immediately following delivery by an obstetrician, and is routinely checked for inaccuracies. Medical secretaries routinely review the information prior to entering it into the database to insure its maximal completeness and accuracy. Coding is performed after assessing medical prenatal care records as well as routine hospital documents.

Statistical analysis

Statistical analysis was performed using the SPSS package 17 ed. (SPSS, Chicago, IL). Categorical data are shown in counts and percentages and the differences were assessed by Chi square for general association. The Student t test and Mann–Whitney U test were used for differences in continuous variables. Odds ratios (ORs) and their 95 % confidence intervals (CIs) were computed. A p value of <0.05 was considered statistically significant.

Results

During the study period 233,123 term deliveries met the inclusion criteria. Of those, 0.2 % ($n = 502$) were diagnosed with placenta previa. Table 1 compares maternal demographic and medical characteristics in pregnancies with and without a diagnosis of placenta previa. Pregnancies complicated with placenta previa were characterized by higher maternal age, higher smoking rates, higher parity, and higher likelihood of grandmultiparity (≥5 deliveries). The parturients were more likely to have had a previous CD, and to suffer from repeated pregnancy losses and infertility, compared with the comparison group (i.e. no placenta previa).

Table 2 depicts pregnancy complications and mode of delivery. Transverse lie and pathological presentations were significantly more common in the placenta previa group, as were cesarean deliveries, cesarean hysterectomies, and maternal blood transfusions. Immediate neonatal outcomes are presented in Table 3. Gestational age at delivery was lower. The newborns were more likely to have been diagnosed with low birth weight (<2500 g) but not with very low birth weight (<1500 g) and less likely to weigh over 4000 g at birth. Apgar scores at 5 min were comparable between neonates born to mothers with and without placenta previa. Intra partum death, postpartum death, and total perinatal mortality (including stillbirth, intra partum death, and post partum death in the first week of life) rates were comparable between the groups. Table 4 presents a sub-analysis of the study population in which only cesarean deliveries were included, from both groups, and immediate neonatal outcomes were compared. Similar to the results presented in Table 3, gestational age at delivery was lower, the newborns were more likely to have been diagnosed with low birth weight and less likely to weigh over 4000 g at birth, and Apgar scores at 5 min were comparable. Intra partum death, postpartum death, and

Table 1 Maternal characteristics in pregnancies with and without placenta previa delivered at term

	Placenta previa, $n = 502$	No placenta previa, $n = 232\ 621$	Odds ratio (confidence interval)	P value
Maternal age at index birth (years ± SD)	32.6 ± 5.5	28.1 ± 5.7	–	<0.001
Parity (mean ± SD)	3.8 ± 2.5	3.4 ± 2.4	–	<0.001
Grandmultiparity (%)[a]	29.3	25.4	1.2 (1.001–1.4)	0.048
Previous cesarean delivery (%)	27.3	12.0	2.7 (2.2–3.3)	<0.001
Recurrent pregnancy losses (%)	10.4	4.9	2.2 (1.6–2.9)	<0.001
Infertility treatment (%)	7.4	1.6	4.9 (3.5–6.9)	<0.001
Chronic hypertension (%)	1.6	1.2	1.3 (0.6–2.6)	0.414
Smoking (%)	2.0	1.0	2.0 (1.09–3.8)	0.022

[a] Defined as five or more deliveries

Table 2 Pregnancy characteristics in mothers with and without placenta previa

	Placenta previa, $n = 502$	No placenta previa, $n = 232\ 621$	Odds ratio (confidence interval)	P value
Preeclampsia				
Without severe features	2.6	2.9	0.89 (0.5–1.5)	0.695
With severe features	0.6	0.5	1.1 (0.38–3.6)	0.767
Gestational DM	6.0	4.9	1.2 (0.8–1.7)	0.266
Polyhydramnion (%)	4	3.3	1.2 (0.7–1.2)	0.404
Oligohydramnion (%)	1.2	2.0	0.6 (0.2–1.3)	0.200
Transversr lie (%)	7.4	0.4	21.9 (15.6–30.8)	<0.001
Pathological presentation (%)[a]	13.7	4.4	3.5 (2.7–4.5)	<0.001
Meconium stained amniotic fluid (%)	6.2	15.4	0.36 (0.25–0.52)	<0.001
Mode of delivery				
Cesarean delivery	92.8	12.1	93.64 (67.131)	<0.001
Cesarean hysterectomy	1.2	0.02	54.1 (23.1–126)	<0.001
Blood transfusion	15.9	1.2	15.1 (11.8–19.2)	<0.001

DM diabetes mellitus

[a] Including any presentation other than vertex

total perinatal mortality rates were comparable between the groups.

Discussion

In this population-based study, we have shown that pregnancies with placenta previa reaching term are not associated with increased perinatal mortality or a low 5-min Apgar score. These findings are complementary to studies evaluating perinatal outcome in placenta previa pregnancies in general.

In 2003, Salihu et al. [10] sought to determine the level of neonatal mortality rates that are associated with placenta previa pregnancies, and to explore the likely pathway for death among these neonates. In their large population based cohort study the authors observed the hazard of neonatal death among placenta previa neonates to be three times that among non–placenta previa neonates. Even more striking was the fact that neonatal death among babies of placenta previa pregnancies was mediated through preterm birth rather than low birthweight or other causes. According to a recent meta-analysis, patients with placenta previa have a 5-fold increase in prematurity rates, NICU admissions, and perinatal/neonatal death compared to patients without placenta previa [12].

These data supports the concept that neonatal mortality and immediate morbidity in placenta previa pregnancies is a function of gestational age per se. It also suggests that

Table 3 Delivery outcomes of children born at term to mothers with and without placenta previa

	Placenta previa, $n = 502$	No placenta previa, $n = 232\,621$	Odds ratio (confidence interval)	P value
Mean gestational age at delivery (weeks ± SD)	38.07 ± 1.2	39.4 ± 1.2	–	<0.001
Gender (%)				
Male	51.0	51.1	0.995 (0.83-1.1)	0.955
Female	49.0	48.9		
Birthweight (grams, mean ± SD)	3069.9 ± 403	3273.8 ± 438	–	<0.001
Birthweight				
<2500 g (%SGA)	7.2	2.7	2.78 (1.9–3.9)	
2500–3999 g (%)	90.8	92.1		<0.001
≥4000 g (%)	2.0	5.2	0.38 (0.2–0.7)	
Very low birth weight[a]	0	0.01	–	0.775
Apgar score <7 at 5 min (%)	1.6	2.0	0.8 (0.34–1.6)	0.535
Perinatal	0.8	0.4	2.2 (0.8–5.9)	0.103
mortality[b] (%)	0	0.02	–	0.730
Post partum death[c] (%)	0.2	0.1	1.6 (0.2–11.1)	0.654

SD standard deviation, *SGA* small for gestational age

[a] Defined as birthweight <1500 g

[b] Including: stillbirth, intrapartum death, and postpartum death in the first week of life

[c] Defined as death in the first week of life

Table 4 Delivery outcomes of children born via cesarean delivery at term to mothers with and without placenta previa

	Placenta previa, $n = 466$	No placenta previa, $n = 28251$	Odds ratio (confidence interval)	P value
Mean gestational age at delivery (weeks ± SD)	37.99 ± 1.2	39.02 ± 1.4	–	<0.001
Gender (%)				
Male	52.1	53.7	0.94 (0.78–1.1)	0.51
Female	47.9	46.3		
Birthweight (grams, mean ± SD)	3059 ± 403	508 ± 3307	–	<0.001
Birthweight				
<2500 g (%SGA)	7.5	3.6	2.1 (1.5–3.1)	
2500–3999 g (%)	90.3	86.5	–	<0.001
≥4000 g (%)	2.1	9.6	0.2 (0.11–0.4)	
Very low birth weight[a]	0	0	–	0.82
Apgar score <7 at 5 min (%)	1.1	1.5	0.7 (0.29–1.7)	0.44
Perinatal mortality[b] (%)	0.4	0.5	0.86 (0.2–3.5)	0.84
Intrapartum death (%)	0	0.1	–	0.59
Post partum death[c] (%)	0.2	0.3	0.77 (0.1–5.5)	0.79

SD standard deviation, *SGA* small for gestational age

[a] Defined as birthweight <1500 g

[b] Including: stillbirth, intrapartum death, and postpartum death in the first week of life

[c] Defined as death in the first week of life

preterm delivery is an intermediary (and not a confounding) characteristic through which death that is associated with placenta previa occurs.

Since the vast majority of placenta previa pregnancies end with a cesarean delivery and only 12 % of the control group underwent a CD, we performed a sub-analysis in

which only pregnancies ending via a cesarean section were included from both groups (Table 4). Our results show that neonatal outcome remained comparable between the groups regardless of delivery mode. Combined with the reassuring results of the present cohort, we reinforce the understanding that neonatal immediate prognosis, in placenta previa pregnancies, is primarily influenced by gestational age and prematurity. Thus, pregnancies delivered at term are expected to follow the normal neonatal course. We believe that perinatal mortality rates observed in our cohort were not significantly different between the groups for the same reason; the fact that we included only term pregnancies.

We observed a relatively low incidence of placenta previa in our term pregnancies cohort of 0.2 %. This is lower than the reported general incidence of approximately 0.4–0.5 % [2, 3]. The reason for this is the fact that preterm deliveries (spontaneous and indicated combined) constitute roughly 45 % of placenta previa pregnancies leaving our cohort with half the general rate [12].

The expected associations with pathological presentations, blood transfusion and cesarean hysterectomy were significantly present in the term placenta previa group as a result of the large cohort presented. With regards to fetal weight, we found higher rates of low birth weight (<2500 g) but not of very low birthweight (<1500 g) and lower rates of macrosomia (>4000 g). An increased risk of intrauterine growth restriction has been reported by several [2, 13–18], but not all [19, 20] investigators, and remains controversial in this setting. If a reduction in fetal growth occurs, it is likely to be mild or due to confounding factors.

Our study's main strength is the fact that our hospital is the only tertiary hospital serving the entire population of southern Israel and thus, is population-based. As the hospital provides both maternity and pediatric services, as long as patients live in the area, they would probably be diagnosed and treated in this hospital.

Inherent faults of database studies should not be overlooked and the possibility of misclassification of the exposure (i.e. placenta previa) exists. The fact that the placenta previa population in our study was significantly older, with higher parity and grandmultiparity, and more likely to have had previous cesarean section, recurrent pregnancy loss and fertility treatments, reduces the likelihood that such misclassification was significant.

We conclude that pregnancies diagnosed with placenta previa and delivered at term do not appear to elevate the risk for perinatal mortality and immediate morbidity. These results reinforce the importance of timing of delivery (preterm vs. term) as the probable major predictor of neonatal survival and outcome in placenta previa pregnancies.

Compliance with ethical standards

Conflict of interest The authors report no conflict of interests.

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