

Comparison of neonatal outcome including cerebral palsy between abruptio placentae and placenta previa

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Received 18 December 2001; received in revised form 8 May 2002; accepted 12 June 2002

Abstract

Objective: Our purpose was to evaluate the neonatal prognosis after abruptio placentae and placenta previa during pre-term gestation. **Study design:** A case-control study was performed using a logistic regression model. A poor outcome was defined as neonatal death occurring before hospital discharge or a diagnosis of cerebral palsy. **Results:** A poor outcome was more frequent in cases of abruptio placentae (11/42, 26.2%) than in placenta previa (2/72, 2.8%) and pre-term labor (1/120, 0.8%). The difference was mainly due to the incidence of cerebral palsy. A significant association of abruptio placentae (odds ratio (OR) 61.0, 95% confidence interval (CI) 3.4–1084), delivery at <31 weeks of gestation (OR 19.0, CI 2.8–128.8), and low Apgar score (<7) at 5 min (OR 70.8, CI 16.5–304.9) with increased risk of poor outcome was found in the logistic regression model that controlled for confounding effects. In abruptio placentae, a low Apgar score (<7) at 5 min (OR 19.8, CI 2.0–197.8) was associated with increased risk of poor outcome in the logistic regression model. **Conclusion:** From the standpoint of poor perinatal outcome including cerebral palsy, abruptio placentae was the most significant clinical entity in pre-term gestation.

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Keywords: Abruptio placentae; Placenta previa; Cerebral palsy; Pre-term fetus

1. Introduction

Both abruptio placentae and placenta previa are conditions typically resulting in third-trimester bleeding in pregnancy. The diagnosis and treatment of patients with these conditions have evolved in recent years with the widespread use of ultrasonography and fetal heart rate (FHR) monitoring.

Most of the available data on neonatal consequences are based on neonatal mortality or short-term morbidity rates, such as low Apgar score. Taylor et al. have linked infant neuro-developmental disability to non-specific antepartum bleeding [1]. Data from the National Collaborative Perinatal Project demonstrated that, at least at the uni-variate level, placenta previa was a significant risk factor for the occurrence of cerebral palsy [2]. However, multi-variate analysis of the same data showed that on the whole third-trimester bleeding was associated with increased risk of cerebral palsy only in low-birth-weight infants [3]. Spinillo et al. [4] divided the clinical entity of third-trimester bleeding into abruptio placentae, placenta previa, and unclassified bleeding and demonstrated that infants delivered after abruptio placentae

were 3.9 times more likely than control infants to have a poor outcome, whereas, the odds ratio (OR) for a poor outcome of infants born after placenta previa was 0.9 (not significant). In their analysis, however, the data on perinatal factors, such as FHR patterns, umbilical pH, etc. were insufficient.

The purpose of this study was to evaluate and compare neonatal outcome including cerebral palsy in infants born after abruptio placentae and placenta previa during pre-term gestation.

2. Patients and methods

The approval of the Institutional Review Board was obtained before the start of this retrospective cohort study. The medical records of mothers and neonates were reviewed from all live singleton births between 26 and 36 weeks of gestation at the Perinatal Medical Center, Kagoshima City Hospital, between 1 January 1992 and 31 December 1999. Gestational age was determined based on last menstrual period and standard obstetric ultrasonography.

The diagnosis of abruptio placentae was based on clinical symptoms, such as abdominal pain and vaginal bleeding, usually confirmed by ultrasonographic findings [5] and

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histopathologic examination of the placenta. The classification of abruptio placentae was modified from the three-stage classifications of Page [6] and Knab [7] and defined as either severe or mild. In severe abruptio placentae, more than 50% of the surface area of the placenta was covered by clotting.

Placenta previa was classified according to the results of ultrasound examinations into marginal, partial, and total previa. Since the so-called low-lying placenta is often a transient condition of uncertain diagnostic significance, we excluded this category from the study.

Patients who experienced pre-term labor without intra-uterine infection served as controls. Intra-uterine infection was diagnosed by generally accepted criteria [8], which was confirmed by histopathological examination of placenta [9]. Tocolytic agents, such as ritodrine hydrochloride and/or magnesium sulfate (MgSO_4) were administered to patients with pre-term labor [10] and symptomatic placenta previa [11], but not to those with abruptio placentae, after confirmation of the diagnosis.

The FHR was monitored for at least 2 h before delivery using a Corometrics 116 Fetal Monitor (Atom Medical, Tokyo, Japan). The FHR patterns were defined as non-reassuring when one of the following patterns was detected: persistent late deceleration; recurrent severe variable deceleration; prolonged deceleration; or loss of variability [12]. Those patterns indicate non-reassuring status in full-term fetuses and are also used for the assessment of pre-term fetuses [13].

The fetuses were delivered because of the onset of active labor, non-reassuring fetal status, and maternal indications, such as massive vaginal bleeding. At delivery, the umbilical cord was isolated by double clamping. Then 0.2 ml of

arterial blood was collected on ice for blood–gas analysis with a Radiometer ABL-2 blood gas analyzer (Radiometer Co., Copenhagen, Denmark). An abnormal umbilical arterial pH (fetal acidemia) was defined as a value of <7.0 [14].

A poor outcome was defined as the occurrence of death before hospital discharge or a diagnosis of cerebral palsy. Cerebral palsy was defined as a chronic disorder of central nervous system origin, characterized by aberrant control of movement or posture, appearing early in life and not resulting from progressive disease [15]. A child had to be at least 2 years of age at the most recent diagnosis to be considered a confirmed case of cerebral palsy. All physical findings in presumed cerebral palsy cases were reviewed by a developmental pediatrician.

The results are expressed as mean \pm S.D. Statistical analysis was carried out using the χ^2 -test, Fisher's exact probability test, and the Mann–Whitney test. *P*-values of <0.05 were considered significant. The OR and 95% of confidence interval (CI) were calculated to estimate the relative risk between patients and controls with regard to risk factors for cerebral palsy. They were compared in both uni- and multi-variate analyses. Logistic regression models were used to assess confounding effects.

3. Results

A total of 42 cases of abruptio placentae and 72 cases of placenta previa born at 26–36 weeks of gestation were analyzed, along with 120 cases of pre-term labor (controls). The maternal clinical demographics of these three groups are given in Table 1. Patients with abruptio placentae and

Table 1
Maternal demographics and perinatal events

	Abruptio placentae (Group 1)		Placenta previa (Group 2)		Control (Group 3)		Statistical analysis		
	<i>n</i> = 42	%	<i>n</i> = 72	%	<i>n</i> = 120	%	Group 1 vs. 3	Group 2 vs. 3	Group 1 vs. 2
Age (years)	31.5 \pm 5.1 ^a		30.6 \pm 4.7 ^a		28.7 \pm 4.4 ^a		0.0024	0.006	0.3693
Gestational age (weeks) on admission	31.2 \pm 3.4 ^a		30.7 \pm 3.5 ^a		30.5 \pm 3.8 ^a		0.3528	0.9581	0.445
Multipara	18	42.9	19	26.4	36	30	0.1337	0.6245	0.0928
Maternal transport	33	78.6	59	81.9	71	59.2	0.0258	0.0013	0.8061
Classification	Severe: 7 Mild: 35	16.7 83.3	Total: 27 Partial: 30 Marginal: 15	37.5 41.7 20.8					
Tocolysis							<0.0001	>0.999	<0.0001
None	30	71.4	22	30.6	36	30			
Ritodrine	1	2.4	7	9.7	32	26.7			
Magnesium	5	11.9	18	25	2	1.7			
Ritodrine + magnesium	6	14.3	25	34.7	50	41.6			
Corticosteroids	2	4.8	26	36.1	21	17.5	0.0428	0.0053	<0.0001
Non-reassuring FHR patterns	38	90.4	6	8.3	9	7.5	<0.0001	>0.999	<0.0001
Mode of delivery							<0.0001	<0.0001	0.0168
Vaginal delivery	4	9.6	0	0	63	52.5			
Cesarean delivery	38	90.4	72	100	57	47.5			

^a Mean \pm S.D.

placenta previa were older than control patients. Maternal transport was more common in patients with abruptio placentae and placenta previa than in control patients. There were nine cases (21%) of pre-eclampsia in abruptio placentae. Tocolytic agents and corticosteroids were administered less frequently in patients with abruptio placentae compared with patients with placenta previa and controls. However, non-reassuring FHR patterns were observed more frequently in patients with abruptio placentae. Cesarean section was performed more often in patients with abruptio placentae and placenta previa than in controls.

There was no difference in the incidence of poor outcome between maternal transport cases and in our hospital cases in abruptio placentae (8/33 versus 3/9, $P = 0.676$).

We have classified ultrasonographical findings in abruptio placentae according to the criteria by Jaffe et al. [5]. The abnormal findings were observed in 31 cases. Those results were as follows: placental thickness, 18 cases; retroplacental anechoicity, 3 cases; intra-placental anechoicity, 5 cases; and edge abnormalities, 5 cases, respectively. As a result, five of the seven in severe cases were classified as placental thickness. There was no relationship between severity of placental separation and abnormal ultrasonographical findings in abruptio placentae. (5/7 versus 13/24, $P = 0.667$).

Indications for delivery were non-reassuring FHR pattern with vaginal bleeding (30 cases), non-reassuring FHR pattern without vaginal bleeding (8 cases), and advanced labor (4 cases), respectively. We have analyzed the relationship between the duration of non-reassuring FHR pattern and poor outcome. There was no relationship in the incidence of poor outcome before and after 30 min (8/19 versus 3/19, $P = 0.151$).

We have investigated the relationship between the amount of vaginal bleeding and the prognosis of neonate in placenta previa. As a result, there was no relationship between

massive bleeding ($>500 \text{ cm}^3$) and poor outcome. (2/17 versus 0/55, $P = 0.0532$).

We had four cases with low Apgar score at 5 min (<7) in placenta previa. Two of them were delivered from mothers with massive vaginal bleeding and shock, followed by poor outcome (death before discharge and cerebral palsy). On the other hand, massive bleeding was not observed in other two cases. These babies were well without any long-term sequelae.

Table 2 shows the influence of perinatal events on good or poor outcome in abruptio placentae, placenta previa, and pre-term labor. Poor outcome was more frequent in the abruptio placentae group (11/42, 26.2%) than in the placenta previa (2/72, 2.8%) and pre-term labor (1/120, 0.8%) groups. This difference was mainly due to the incidence of cerebral palsy. In the uni-variate analysis, abruptio placentae, non-reassuring FHR patterns, delivery at <31 weeks of gestation, low Apgar score (<7) at 1 and 5 min, and fetal acidemia had a significant influence on poor outcome. However, in a logistic regression model that controlled for confounding effects, a significant association with risk for poor outcome was found for abruptio placentae (OR 61.0, 95% of CI 3.4–1084), delivery at <31 weeks of gestation (OR 19.0, CI 2.8–128.8), and low Apgar score (<7) at 5 min (OR 70.8, CI 16.5–304.9). Other factors, including the use of corticosteroids, analyzed were not associated with an increased risk of poor outcome.

Table 3 shows the results of comparison of risk factors for good or poor outcome based on the occurrence of perinatal events in abruptio placentae. In the uni-variate analysis, non-reassuring FHR patterns, delivery at <31 weeks of gestation, low Apgar score (<7) at 1 and 5 min, and fetal acidemia were significant risk factors for poor outcome. However, only low Apgar score (<7) at 5 min (OR 19.8, CI 2.0–197.8) was associated with increased risk of poor outcome in the logistic regression model. Other factors were not associated with an increased risk of poor outcome.

Table 2
Perinatal outcome between three groups

	Abruptio placentae (Group 1)		Placenta previa (Group 2)		Control (Group 3)		Statistical analysis		
	<i>n</i> = 42	%	<i>n</i> = 72	%	<i>n</i> = 120	%	Group 1 vs. 3	Group 2 vs. 3	Group 1 vs. 2
Gestational age (week) at delivery	31.5 ± 3.1 ^a		33.4 ± 2.4 ^a		32.7 ± 2.8 ^a		0.0288	0.1629	0.0013
<31 weeks	16	38.1	9	12.5	28	23.3	0.0723	0.0883	0.0022
Birth weight (g)	1670 ± 533 ^a		2117 ± 501 ^a		2010 ± 583 ^a		0.0015	0.2559	<0.0001
<1500 g	15	35.7	8	11.1	28	23.3	0.1546	0.0375	0.003
Apgar score at 1 min (<7)	27	47.6	30	41.7	23	19.2	<0.0001	0.0014	0.0321
Apgar score at 5 min (<7)	11	26.2	4	5.6	1	0.8	0.0089	0.4199	0.003
Fetal acidemia (<7.0)	14	33.3	0	0	1	0.8	<0.0001	>0.999	<0.0001
Poor outcome									
Total	11	26.2	2	2.8	1	0.8	<0.0001	0.5573	0.0003
Death before discharge	3	7.1	1	1.4	0	0	0.0165	0.375	0.1406
Cerebral palsy	8	20.5 ^b	1	1.4 ^b	1	0.8 ^b	<0.0001	>0.999	<0.0001

^a Mean ± S.D.

^b Percent among survivors.

Table 3

Comparison of perinatal outcome in abruptio placentae

	Poor outcome (<i>n</i> = 11)		Good outcome (<i>n</i> = 31)		OR (95% CI) ^a Uni-variate analysis	OR (95% CI) ^a Multi-variate analysis
	<i>n</i>	(%)	<i>n</i>	(%)		
Gestational age (week) at delivery <31 weeks	7	64	9	29	4.3 (1.0–18.3)	2.2 (0.2–20.9)
Apgar score at 1 min (<7)	10	91	17	55	8.3 (0.9–72.7)	0.9 (0.06–11.6)
Apgar score at 5 min (<7)	8	73	3	10	24.9 (4.2–148.1)	19.8 (2.0–197.8)
Fetal acidemia (pH <7.00)	7	69	7	23	11.8 (2.4–58.9)	1.5 (0.1–21.8)
Severity of separation (>50%)	4	36	3	10	5.3 (0.9–29.3)	4.8 (0.3–70.0)

^a OR, odds ratio; CI, confidence interval.

4. Comment

The purpose of this study was to evaluate the neonatal outcome after the occurrence of third-trimester bleeding. The selection of an appropriate control group is important in case-control studies. Since it has recently been reported that intrauterine infection is a main etiologic factor in the development of pre-term cerebral palsy [15,16], we chose patients with pre-term labor without infection to serve as the control group to minimize the influence of other risk factors.

Nelson and Ellenberg [2] reported that placenta previa was a significant risk factor for the occurrence of cerebral palsy. However, the mortality rate from complications of pre-term birth did not increase in comparison with infants of similar gestational age born to women without placenta previa [11]. In the present study, placenta previa was not a risk factor for cerebral palsy. The sudden interruption of maternal–fetal circulation may result in hypoxic insult to the fetus. Uteroplacental insufficiency is the mechanism of fetal hypoxia in placenta previa, late decelerations are the characteristic FHR pattern, and prolonged decelerations may occur in severe cases [17]. In our study, non-reassuring FHR patterns were observed less frequently in patients with placenta previa, which may have contributed to the better outcome in this group.

The association between abruptio placentae and the occurrence of infant neuro-developmental disorders has been confirmed by several epidemiological studies [1,2]. These studies are important from an epidemiological viewpoint but are of limited clinical value. Spinillo et al. [18] first reported that low-birth-weight infants delivered after abruptio placentae were more likely than controls to have a poor outcome after adjustment for confounding variables (gestational age, birth weight, social class and educational level of the mother). However, the two latter variables form part of the epidemiologic profile. In addition, unlike our present study, Spinillo et al. [18] did not clearly define non-reassuring FHR patterns or fetal acidemia.

In the present study, pathologic fetal acidemia was not an independent risk factor for poor outcome. There are several limitations to consider in the correct interpretation of this finding. First, the major limitation of our study is that it was based on a relatively small number of patients. Although the

incidence of abruptio placentae is very low, this result should be confirmed in a larger series using the same protocol. Second, the effects of fetal acidemia on neonatal outcome might be offset by those of a low Apgar score at 5 min in multi-variate analyses.

It has been reported that a low 5 min Apgar score alone does not demonstrate that subsequent development of cerebral palsy was due to perinatal asphyxia [19]. Topp et al. [20] studied the influence of pre-natal and birth-related risk factors on the development of cerebral palsy in pre-term infants. They concluded that delivery by cesarean section was a prognostic factor for cerebral palsy and that Apgar scores had limited predictive value in multi-variate analyses. On the other hand, Beeby et al. [21] examined the relationship between umbilical artery pH, Apgar scores, perinatal events, and outcome in pre-term infants. Their results showed that umbilical artery pH was not significantly associated with any outcome, although a low Apgar score remained a significant risk factor, with an OR of 2.7 for neonatal death and of 3.8 for cerebral palsy. Spinillo et al. [4] also speculated that the high prevalence of low Apgar scores in these infants could easily explain the increased risk of poor outcome.

In summary, the results of this study show that abruptio placentae is the worst clinical entity among causes of third-trimester bleeding in pre-term gestation. The high prevalence of low Apgar scores at 5 min among pre-term infants born to mothers with abruptio placentae may contribute to the poor outcome.

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