



Title	Intrapartum risk factors for neonatal encephalopathy leading to cerebral palsy in women without apparent sentinel events
Author(s)	Yamada, Takahiro; Cho, Kazutoshi; Morikawa, Mamoru; Yamada, Takashi; Minakami, Hisanori
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1 [ORIGINAL ARTICLE] for JOGR

2 **Title: Intrapartum risk factors for neonatal encephalopathy leading to cerebral**
3 **palsy among women without apparent sentinel events**

4

5 Takahiro Yamada,¹ Kazutoshi Cho,¹ Mamoru Morikawa,¹ Takashi Yamada,² Hisanori
6 Minakami¹

7

8 Affiliation

- 9 1. Department of Perinatal Medicine, Hokkaido University Hospital, Sapporo, Japan
10 2. Department of Obstetrics and Gynecology, Japan Community Health care
11 Organization Hokkaido Hospital, Sapporo, Japan

12

13 Correspondence to: Takahiro Yamada, M.D. Ph.D.

14 Department of Obstetrics, Hokkaido University Graduate School of Medicine,

15 Kita-ku N15 W7, Sapporo 060-8638, Japan

16 Phone: +81-11-706-5941; Fax: +81-11-706-7711

17 E-mail: taka0197@med.hokudai.ac.jp

18 **Running foot:** Intrapartum risk factors for CP

19

20 **Abstract**

21 **Aims:** To determine intrapartum factors associated with neonatal encephalopathy
22 leading to cerebral palsy (NE-CP).

23 **Methods:** Analyses of 70 NE-CP cases fulfilling all of the following criteria: cephalic
24 singleton pregnancy attempting vaginal delivery (AVD) at gestational week (GW) \geq 36,
25 intrapartum occurrence of non-reassuring fetal status without apparent causes following
26 reassuring fetal status on admission, and development of NE-CP, in comparison with
27 210 AVD controls with infants with 1- and 5-min Apgar scores \geq 8 matched for GW,
28 maternal parity, and use of uterotonics. Suboptimal care was defined as delayed reaction
29 resulted from misinterpretation of fetal heart rate (FHR) tracing or inappropriate trial of
30 instrumental delivery (TOID). Successful and failed TOID were defined as vaginal and
31 cesarean deliveries after TOID, respectively. The 210 controls were assumed not to have
32 had suboptimal care.

33 **Results:** The rates of successful (34% vs. 12%) and failed TOID (11% vs. 0.0%),
34 cesarean section (34% vs. 14%), suboptimal care (57% vs. 0.0%), pregnancy-induced
35 hypertension (11% vs. 2.4%), birth weight \geq 3800 g (8.6% vs. 1.9%), subgaleal
36 hemorrhage (16% vs. 0.0%) were significantly higher in cases than controls. Selection
37 with the stepwise method and logistic regression analysis identified four independent
38 risk factors for NE-CP: suboptimal intrapartum care (odds ratio [95% confidence
39 interval], 2.21 [1.99 – 2.47]), cesarean section (1.19 [1.08 – 1.31]), successful TOID
40 (1.14 [1.03 – 1.25]), and hypertension (1.20 [1.01 – 1.42]).

41 **Conclusions:** Training programs for improved interpretation of FHR tracing and
42 appropriate TOID are required to prevent NE-CP among healthy and mature fetuses in
43 Japan.

44 (Word count <250)

45 **Key words:** fetal heart rate tracing, instrumental delivery, macrosomia, non-reassuring
46 fetal status, shoulder dystocia, vacuum delivery

47

48 **Introduction**

49 Healthy fetuses based on fetal hear rate (FHR) tracing at the onset of labor pains can
50 develop neonatal encephalopathy (NE) and subsequently develop cerebral palsy (CP).
51 Well-known causative factors for CP derived from hypoxic conditions include placental
52 abruption, uterine rupture, cord prolapse, fetomaternal hemorrhage, or placenta previa
53 [1 - 5]. However, some infants develop NE leading to CP (NE-CP) in the absence of
54 such risk factors.

55 As suboptimal intrapartum care is commonly seen with NE, especially in neonates with
56 metabolic acidemia in Sweden [6], and as NE proceeds to CP in some cases [7],
57 suboptimal intrapartum care may be a risk factor for NE-CP. Instrumental deliveries,
58 including vacuum and forceps deliveries, are widely used in patients requiring
59 facilitated delivery. However, as some trials of instrumental deliveries (TOID) fail to
60 provide successful vaginal delivery, some cases of failed TOID require cesarean section
61 during labor. In such cases with failed TOID for non-reassuring fetal status (NRFS),
62 delay in delivery increases the theoretical risk of NE-CP. Vacuum delivery is associated
63 with serious complications, such as subgaleal hemorrhage (SGH), and some of neonates
64 with SGH die or develop CP later [8, 9]. Thus, TOID may be associated with increased
65 risk of NE-CP. However, as the prevalence of CP is low, approximately 1 per 1000 live
66 births for infants weighing ≥ 2.5 kg [10, 11], and as intrapartum hypoxia accounts for
67 less than 30% of all cases of NE [12, 13], it is unclear whether suboptimal intrapartum
68 care and TOID increase the risk of NE-CP.

69 The present study was conducted to determine the intrapartum factors associated with
70 increased risk of NE-CP.

71

72 **Materials and Methods**

73 This study was conducted after approval by the Ethics Committee of Hokkaido
74 University Hospital.

75 *Selection of 70 cases with NE-CP*

76 The Japan Council for Quality Health Care (JCQHC) launched a new medical insurance
77 system, the Japan Obstetric Compensation System for Cerebral Palsy, on January 1,
78 2009, to compensate for cerebral palsy (CP) derived in principle from intrapartum
79 hypoxia and to improve perinatal care. The details of this system were described
80 previously [4]. In this system, maternal and neonatal records were audited by members
81 of the investigation committee belonging to the JCQHC. One of the authors (HM) was a
82 member of this committee. Each case was clinically assessed for the presence or
83 absence of suboptimal ante- and intrapartum care, which was assigned by consensus.
84 Researchers can gain access to a detailed report made by the committee after approval
85 by the JCQHC. We were provided access by the JCQHC to 244 detailed reports made
86 up to March 31, 2013, in which detailed clinical courses of 244 infants born to 244
87 women, causative factors for NE-CP determined by the investigation committee, and
88 the presence or absence of suboptimal care were recorded. However, personal
89 information regarding the date of birth, including year and month, place of birth,
90 maternal age, and maternal body height and weight, were masked for privacy protection.
91 All of the 244 infants were born in or after January 2009.

92 We reviewed all 244 reports for the 244 cases, focusing on clinical courses, FHR tracing,
93 causative factors for CP, and the presence or absence of misinterpretation of FHR

94 tracing, inappropriate TOID, and neonatal SGH. We identified 70 and 174 cases that did
 95 and did not fulfill all of the following four conditions: (1) cephalic singleton pregnancy
 96 attempting vaginal delivery (AVD) on or after gestational week (GW) 36, (2) reassuring
 97 fetal status at the onset of labor pains based on FHR tracing, (3) intrapartum occurrence
 98 of NRFS on FHR tracing in the absence of placental abruption, uterine rupture, cord
 99 prolapse, fetomaternal hemorrhage, or placenta previa/low lying placenta, and (4)
 100 diagnoses of NE at birth and subsequently CP by neuropsychiatrists. Thus, all 70 cases
 101 were judged to be NE-CP associated with intrapartum factors other than placental
 102 abruption, uterine rupture, cord prolapse, fetomaternal hemorrhage, or placenta
 103 previa/low lying placenta. The 70 neonates exhibited a pH of 6.86 ± 0.78 with base
 104 deficit of 20.1 ± 6.9 mmol/L in the umbilical cord blood or neonatal blood at birth or on
 105 admission to neonatal intensive care unit. In these 70 neonates, Apgar score at 1-min
 106 was < 3 in 50 (71%), < 5 in 64 (91%), and < 7 in 68 (97%) neonates, and that at 5-min
 107 was < 3 in 24 (34%), < 5 in 47 (67%), and < 7 in 64 (91%) neonates. Neither congenital
 108 malformation, inborn error of metabolism, nor infection was detected in the 70 infants.

109 *Selection of 210 controls*

110 We used a database provided by the Japan Society of Obstetrics and Gynecology
 111 (JSOG) [14] that included information on 11724 mothers who were registered at the
 112 JSOG Successive Pregnancy Birth Registry System and gave birth during the period
 113 from November 1, 2009, to December 31, 2009. From this database, we abstracted 2809
 114 mothers who fulfilled all three of the following conditions: (1) AVD with cephalic
 115 presentation on and after $GW \geq 36$, (2) no occurrence of placental abruption, uterine
 116 rupture, cord prolapse, fetomaternal hemorrhage, or placenta previa/low lying placenta,
 117 and (3) neonate with both 1- and 5-min Apgar scores of ≥ 8 . Three controls for each
 118 case (3:1) were chosen after matching for GW at delivery, maternal parity (nulliparous

119 or not), and use of uterotonics. Thus, a total of 210 mother–child pairs were chosen
 120 from the database of the JSOG Successive Pregnancy Birth Registry System for
 121 controls. In these 210 neonates, neither congenital malformation, inborn error of
 122 metabolism, SGH, nor infection was detected during a several-day stay at the obstetrical
 123 facilities. Data on the umbilical cord blood pH were not available for these control
 124 infants.

125 *Definitions and predefined assumption in this study*

126 Suboptimal intrapartum care was defined as delayed reaction to NRFS due to
 127 misinterpretation of FHR tracing and or inappropriate TOID not fulfilling two
 128 prerequisite conditions, i.e., “fetal head engagement” and “full dilatation of the uterine
 129 cervix.” The delayed reaction to NRFS due to misinterpretation of FHR tracing was
 130 defined as follows: the investigation committee belonging to the JCQHC pointed out
 131 that an early delivery had not been attempted in the presence of NRFS based on FHR
 132 pattern of level ≥ 4 (according to the Japanese guidelines [14]) lasting for a considerable
 133 time and/or FHR pattern of level 5 lasting more than 120 min until delivery. The
 134 inappropriate TOID was defined as a follow: the investigation committee concluded that
 135 TOID performed before full dilatation of the uterine cervix and/or fetal head
 136 engagement worsened fetal condition. As the 210 control infants left obstetric facilities
 137 several days after birth according to the clinical path of each facility, all of the 210
 138 controls were assumed not to have developed NE and not to have received suboptimal
 139 care. Successful and failed TOID were defined as vaginal and cesarean deliveries after
 140 TOID, respectively, irrespective of the condition of the neonate at birth. Emergent
 141 cesarean section (ECS) was defined as that performed in women during labor.
 142 Hypertensive disorders included preeclampsia and gestational hypertension.
 143 Hypertensive disorders included preeclampsia and gestational hypertension.

144 *Statistical analyses*

145 All of the data are presented as the means \pm SD or frequency. Fisher's exact test was
146 used for comparison of categorical data. Factors that were significantly correlated with
147 NE-CP were determined by univariate and multivariate logistic regression analyses
148 performed using IBM SPSS Statistics 18.0 software (SPSS Inc., Chicago, IL). We used
149 a stepwise method (Wald) to choose independent risk factors for NE-CP and used
150 logistic regression analysis to determine the odds ratio (OR) with 95% confidence
151 interval (95%CI) of independent risk factors. In all analyses, $P < 0.05$ was taken to
152 indicate statistical significance.

153

154 **Results**

155 The suboptimal intrapartum cares were identified in as many as 40 (57%) of the 70
156 cases (Table 1). The delayed reaction to NRFS due to misinterpretation of FHR tracing
157 and the inappropriate TOID occurred in 38 and 4 women, respectively. Thus, both the
158 delayed reaction to NRFS and inappropriate TOID occurred in two women. In three of
159 four women with inappropriate TOID, TOID was performed before full dilatation of the
160 uterine cervix and fetal head engagement. Frequency of low Apgar scores of < 3 , < 5 ,
161 and < 7 did not differ significantly between women with and without suboptimal cares
162 (Table 2).

163 The mean GW at delivery, distribution of GW at delivery, frequencies of nulliparous
164 women, and the rate of uterotronics use did not differ between the 70 cases and 210
165 controls (Table 3). As control subjects were matched for cases with regard to the use of
166 uterotronics, the rate of uterotronics use in controls in the present study (54%) was higher

167 than that of approximately 23% in general pregnant Japanese women [15]. Frequencies
168 of TOID, successful and failed TOID, ECS, suboptimal intrapartum care, hypertensive
169 disorders, birth weight ≥ 3800 g, and SGH were significantly higher in the cases than
170 controls. Of the 11 cases with SGH, 10 (91%) experienced TOID, and four of the 10
171 with TOID and SGH experienced failed TOID. Thus, within the NE-CP cohort, SGH
172 occurred significantly more often in cases with than without TOID (31% [10/32] vs.
173 2.6% [1/38], respectively, $P = 0.0017$).

174 In univariate analysis, the OR (95% CI) for 70 cases compared to 210 controls was 5.96
175 (3.19 – 11.13) for TOID, 3.69 (1.94 – 7.02) for successful TOID, 27.0 (3.31 – 220) for
176 failed TOID, 3.13 (1.67 – 5.86) for ECS, 279 (36.9 – 2103) for suboptimal intrapartum
177 care, 5.29 (1.67 – 16.8) for hypertensive disorders, 2.08 (0.95 – 4.54) for birth weight \geq
178 3500 g, 4.83 (1.32 – 17.6) for birth weight ≥ 3800 g, and 39.0 (4.93 – 308) for SGH. All
179 nine of the above factors were candidates as independent risk factors for NE-CP. After
180 selection with the stepwise method, the following four factors were chosen as
181 independent risk factors for NE-CP (Table 4): suboptimal intrapartum care (OR, 2.21;
182 95%CI, 1.99 – 2.47), hypertensive disorders (1.20; 1.01 – 1.42), ECS (1.19; 1.08 –
183 1.31), and successful TOID (1.14; 1.03 – 1.25). Thus, among the causative factors other
184 than placental abruption, uterine rupture, cord prolapse, fetomaternal hemorrhage, and
185 placenta previa/low lying placenta, suboptimal intrapartum care was the greatest risk
186 factor for NE-CP in fetuses assumed to be healthy at the commencement of labor.

187

188 **Discussion**

189 The present study demonstrated that suboptimal intrapartum care was the greatest risk
190 factor for NE-CP among pregnant Japanese women who attempted vaginal delivery

191 with cephalic presentation of healthy fetuses at GW 36 or later and did not develop
192 placental abruption, uterine rupture, cord prolapse, fetomaternal hemorrhage, or
193 placenta previa/low lying placenta. Other independent risk factors for NE-CP
194 determined in this study included hypertensive disorders, ECS, and successful TOID.

195 Suboptimal intrapartum care, defined as a delayed reaction to NRFS and/or
196 inappropriate TOID not fulfilling prerequisite conditions, was noted in 40 (57%) of the
197 70 cases with NE-CP and increased the risk of NE-CP independently by 2.2-fold
198 compared to women who were not given suboptimal intrapartum care in this study. This
199 was suggested by previous studies in infants without congenital malformation, inborn
200 error of metabolism, or infection [6, 16 - 18]: in a study of 141 term infants with CP
201 born in 1984 – 1987 in the UK, care giver's failure to respond to NRFS occurred more
202 often for CP compared to controls (OR, 4.5; 95%CI, 2.4 – 8.4) [16]; in regional audits
203 of 49 cases with NE born in 1997 in the UK, significant or major episodes of
204 suboptimal care were identified in 64% of NE cases [18]; in regional audits of 52 term
205 infants born with NE in 1997 – 2000 in New Zealand, suboptimal fetal monitoring
206 practice was identified in at least 42% of cases [17]; and in audits of 47 and 22 NE
207 infants with and without metabolic acidemia at birth defined as by umbilical artery pH <
208 7.00 and base deficit \geq 12 mmol/L born in 2003 – 2010 in Sweden, suboptimal care was
209 identified in 47% (22/47) and 20% (6/30) of cases, respectively [6]. Thus, suboptimal
210 intrapartum care is prevalent worldwide among neonates with NE and is a major
211 intrapartum risk factor for NE and/or NE-CP after excluding well-known risk factors,
212 such as placental abruption, uterine rupture, and cord prolapse.

213 TOID was not an independent risk factor for NE-CP in this study. However, both ECS
214 and successful TOID increased the risk of NE-CP independently by 19% and 14%,
215 respectively. As failed TOID inevitably requires ECS and even successful TOID was an

216 independent risk factor for NE-CP, the present study suggested that TOID should be
 217 considered as an independent risk factor for NE-CP.

218 Both TOID and ECS are known to be associated with CP in term infants having OR of
 219 1.9 (95% CI, 1.6 - 2.3) and 1.8 (1.6 - 2.0), respectively compared to population with
 220 counterpart characteristics [1]. However, it is uncertain whether TOID is a causative
 221 factor for NE-CP. ECS is used in women with difficult labor irrespective of the use of
 222 TOID, and ECS without TOID accounted for 67% (16/24) of cases and for 100%
 223 (30/30) of controls in this study. In a population-based study on the frequencies of
 224 subdural and cerebral hemorrhage according to delivery mode by Towner et al. [19]
 225 examining 583340 live-born singleton infants born to nulliparous women between 1992
 226 and 1994 and weighing between 2500 and 4000 g in California, OR of subdural or
 227 cerebral hemorrhage compared with spontaneous vaginal delivery was 1.4 (0.8 – 2.6)
 228 for cesarean section without labor, 2.3 (1.7 – 3.2) for ECS without TOID, 2.7 (1.9 – 3.9)
 229 for vaginal delivery with vacuum extraction, 3.4 (1.9 – 5.9) for vaginal delivery with
 230 forceps delivery, 7.3 (2.9 – 17.2) for vaginal delivery with combined use of vacuum and
 231 forceps, and 8.8 (3.9–19.9) for ECS after TOID [19]. The risk of subdural or cerebral
 232 hemorrhage associated with ECS (OR of 0.9 [0.6 – 1.4] compared to vacuum
 233 extraction) did not differ from that associated with vaginal delivery after vacuum
 234 extraction, suggesting that difficult labor requiring cesarean section or vacuum
 235 extraction was causative for subdural or cerebral hemorrhage, although an increased
 236 number of operative interventions, including vacuum extraction, use of forceps, and
 237 ECS, additively increased the risk of subdural or cerebral hemorrhage [19]. Thus, it was
 238 not surprising that both ECS and successful TOID were independent risk factors for
 239 NE-CP in this study.

240 SGH is a rare but potentially lethal medical emergency, and is associated with an

241 increased risk of NE [8, 9, 20, 21] as was confirmed in this study, although not an
242 independent risk factor for NE-CP in this study. Its frequency is estimated to be 4 to 5
243 per 10000 spontaneous deliveries and 40 to 60 per 10000 vacuum-assisted deliveries [8,
244 9]. Ten (91%) of the 11 neonates with both SGH and NE-CP were after TOID in this
245 study. In other studies, the frequency of TOID among neonates with SGH varied from
246 64% (79/123) [8], 77% (32/42) [9], 85% (27/33) [22], and to 97% (36/37) [20]. As the
247 general frequency of TOID was estimated to be less than 20% based on previous studies
248 (instrumental delivery of 7% \pm 4% in 2004 in 124 facilities in the USA [23], the vacuum
249 delivery of 10% in 1982-92 in Western Australia [20], the vacuum delivery rate of 14%
250 in 2012 in Sweden [24] as well as 12% in the 210 control women in this study), it was
251 apparent that TOID increased the risk of SGH. Poor outcome is likely to occur in
252 neonates with SGH; of 42 neonates with SGH in Taiwan, 13 (31%) had poor outcomes,
253 including death in five, epilepsy in four, severe auditory dysfunction in three, CP in two,
254 and renal vein thrombosis in one [9]. In another study in Western Australia [20], of 37
255 neonates with SGH, one died and four of 25 with follow-up developed minor
256 neurological disabilities.

257 Hypertensive disorder in pregnancy was also an independent risk factor for NE-CP in
258 this study. There has been controversy regarding whether preeclampsia is associated
259 with increased risk of CP. Mann et al. [25] conducted a population-based study to
260 address this issue, examining 122476 mother-child pairs, including 337 children
261 (0.28%) with CP and 4226 (3.5%) women with preeclampsia. Children born to mothers
262 with preeclampsia were more likely to have CP compared to those of mothers without
263 preeclampsia (OR of 1.94 [1.25 – 2.97]) [25]. These observations suggested that more
264 intensive monitoring is required at term in women with hypertensive disorders, and this
265 is emphasized in the current Japanese guidelines [26].

266 A major limitation of this study was that control mother–child pairs were assumed not
267 to have had suboptimal intrapartum care. It is possible that suboptimal intrapartum care
268 was given in a very small number of control women, but not leading to NE in the
269 neonate. Therefore, there is the possibility of overestimation in the risk of NE-CP
270 associated with suboptimal intrapartum care in this study.

271 In conclusion, the present study suggested that, among factors other than well-known
272 factors, including placental abruption, uterine rupture, cord prolapse, fetomaternal
273 hemorrhage, and placenta previa/low lying placenta, suboptimal intrapartum care was
274 the greatest risk factor for NE leading to CP among mature and healthy fetuses on
275 admission to facilities for delivery and confirmed that ECS as well as successful TOID,
276 defined as vaginal delivery after TOID, were significant risk factors for NE leading to
277 CP. Training programs for improved interpretation of FHR tracing and appropriate
278 TOID are required to prevent NE-CP.

279

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283

284 **Conflict of Interest**

285 All authors declare that they have no financial relationships with biotechnology
286 manufacturers, pharmaceutical companies, or other commercial entities with an interest
287 in the subject matter or materials discussed in this manuscript.

288

289

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Table 1. Suboptimal intrapartum cares seen in 40 cases

1. Delayed reaction to NRFS due to misinterpretation of FHR tracing	n=38
1) FHR pattern of level ≥ 4 lasting for a considerable time	n=35
2) FHR pattern of level 5 lasting for ≥ 120 min	n=5
Sentinel events (FHR patterns) seen in the 38 women	
Decreased FHR baseline variability	n=23
with recurrent late deceleration	n=17
with recurrent variable deceleration	n=15
with prolonged deceleration	n=20
Normal FHR baseline variability	n=15
with recurrent late deceleration	n=9
with recurrent variable deceleration	n=11
with prolonged deceleration	n=15
2. Inappropriate TOID	n=4
1) Before full dilatation of the uterine cervix	n=4
2) Before fetal head engagement	n=3

Table 2. Apgar scores in 40 and 30 cases with and without suboptimal cares

	1 min Apgar score			5 min Apgar score		
	<3	<5	<7	<3	<5	<7
Suboptimal care (n=40)	29 (73%)	37 (93%)	39 (98%)	14 (35%)	27 (68%)	38 (95%)
No suboptimal care (n=30)	21 (70%)	27 (90%)	29 (97%)	10 (33%)	20 (67%)	26 (87%)
Overall (n=70)	50 (71%)	64 (91%)	68 (97%)	24 (34%)	47 (67%)	64 (91%)

No significant differences in frequency of low Apgar scores between two groups with and without suboptimal care

Table 3. Demographic characteristics of study subjects

	Case (n=70)	Control (n=210)	P-value
Gestational week at delivery	39.4±1.2	39.4±1.2	>0.9999
36	2 (2.9%)	6 (2.9%)	>0.9999
37 - 38	10 (14.3%)	30 (14.3%)	>0.9999
39 - 40	45 (64.3%)	137 (65.25)	0.8852
41	13 (18.6%)	37 (17.6%)	0.8570
≥42	0 (0.0%)	0 (0.0%)	>0.9999
Nulliparous women	53 (75.7%)	160 (76.2%)	>0.9999
Use of uterotonics	38 (54.3%)	114 (54.3%)	>0.9999
Oxytocin alone	25 (35.7%)	82 (39.0%)	0.6714
Prostaglandins alone	6 (8.6%)	9 (4.3%)	0.2168
Both	7 (10%)	23 (11.0%)	0.8238
Rupture of fetal membranes*	24 (34.3%)	54 (25.7%)	0.1659
Trial of instrumental delivery (TOID)	32 (45.7%)	26 (12.4%)	<0.0001
Successful TOID	24 (34.3%)	26 (12.4%)	<0.0001
Failed TOID	8 (11.4%)	0 (0.0%)	<0.0001
Emergent caesarean section	24 (34.3%)	30 (14.3%)	0.0002
Suboptimal intrapartum cares	40 (57%)	0 (0.0%)	<0.0001
Hyperglycemia†	3 (4.3%)	5 (2.4%)	0.4076
Hypertensive disorders¶	8 (11%)	5 (2.4%)	0.0018
Birth-weight (g)	3099 ± 404	3031 ± 355	0.1809
≥ 3200	25 (35.7%)	66 (31.4%)	0.5073
≥ 3500	12 (17.1%)	19 (9.0%)	0.0616
≥ 3800	6 (8.6%)	4 (1.9%)	0.0092
≥ 4000g	1 (1.4%)	1 (0.5%)	0.4382
Subgaleal hemorrhage (SGH)	11 (15.7%)	0 (0.0%)	<0.0001

*, Rupture of fetal membranes was found on admission to hospital for delivery.

†, Including gestational diabetes mellitus and diabetes mellitus.

¶, Including gestational hypertension and preeclampsia.

Table 4. Independent risk factors for cerebral palsy following neonatal encephalopathy

	B	SE	OR (95%CI)	P-value
Suboptimal intrapartum care	0.795	0.055	2.21 (1.99 – 2.47)	<0.001
Hypertensive disorders	0.182	0.086	1.20 (1.01 – 1.42)	0.035
Emergent cesarean section	0.175	0.048	1.19 (1.08 – 1.31)	<0.001
Successful TOID	0.127	0.050	1.14 (1.03 – 1.25)	0.012

B₀ (SE) was 0.072 (0.023) in this analysis.