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Balloon catheter use for cervical ripening in women with term pre-labor rupture of membranes; a five-year cohort study

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Conflict of interest

None

ABSTRACT

Introduction: To investigate safety of balloon catheter for cervical ripening in women with term pre-labor rupture of membranes (PROM), and to compare the incidence of maternal and neonatal infections in women with PROM and women with intact membranes undergoing cervical ripening with a balloon catheter. **Material and methods:** This retrospective cohort study of 1923 women with term singleton pregnancy and an unfavorable cervix undergoing cervical ripening with a balloon catheter was conducted in Helsinki University Hospital between January 2014 and December 2018. For each case of PROM, two controls were assigned. The main outcome measures were the rates of maternal and neonatal infections. Statistical analyses were performed by SPSS. **Results:** 641 (33.3%) women underwent labor induction following PROM and 1282 (66.6%) women with intact amniotic membranes. The rates of intrapartum infection (3.7% vs. 7.7%; p=0.001) and neonatal infection (1.7% vs. 3.8%; p=0.01) were not increased in women induced by balloon catheter following PROM. Intrapartum infections were associated with nulliparity (OR 3.3, 95% CI 1.6–6.5), history of previous cesarean section (OR 2.8, 95% CI 1.2–6.4), extended gestational age ≥ 41 weeks (OR 1.9, 95% CI 1.2–3.0) and induction to delivery

interval of 48 h or more (OR 2.0, 95% CI 1.2–3.3). The risk of neonatal infection was associated with nulliparity (OR 3.3, 95% CI 1.4-8.0), gestational age ≥ 41 weeks (OR 1.9, 95% CI 1.09–3.36) and induction to delivery interval of 48 h or more (OR 3.4, 95% CI 1.9-6.0). **Conclusions:** Use of balloon catheter in women with term PROM appears safe and was not associated with increased maternal or neonatal infectious morbidity.

Keywords

Term pre-labor rupture of membranes
Induction of labor
Cervical ripening
Balloon catheter
Intrapartum infection
Neonatal infection

Abbreviations

PROM; pre-labor rupture of membranes

IOL; induction of labor

BC; balloon catheter

RCT; randomized controlled trial

GBS; Group B *Streptococcus*

Key message

Cervical ripening by a balloon catheter in women with term pre-labor rupture of membranes appears safe, and was not associated with increased infectious morbidity in a five year cohort study.

INTRODUCTION

Pre-labor rupture of membranes (PROM), defined as rupture of membranes at least one hour prior to onset of regular contractions, occurs in approximately 8 % of term pregnancies. Sixty percent of the women with PROM deliver spontaneously within 24 hours (1). Prolongation of onset of labor for more than 24 hours is associated with an increased incidence of chorioamnionitis and neonatal sepsis (1,2). There are multiple management guidelines for PROM, including expectant management and immediate induction of labor (IOL) with oxytocin or prostaglandins (1,3-5). The recent Cochrane review supports IOL within 24 hours from PROM for lower risk of maternal and neonatal infections without an increase in the rate of cesarean section (6).

An abundance of studies support the efficacy of balloon catheter (BC) for cervical ripening considering the low risk of uterine hyperstimulation, fetal heart rate abnormalities, and adverse maternal outcomes after previous cesarean section (7,8-10). However, most studies include only women with intact amniotic membranes, while the use of BC in women with ruptured amniotic membranes has raised concerns over infectious morbidity. Only a few small studies with limited data exist on the safety of the use of BC in women with PROM. Reassuring results on the use of BC following term PROM have been reported by two relatively small retrospective cohort studies (11,12), a randomized controlled trial (RCT) of 188 women comparing BC and oral misoprostol for cervical ripening following term PROM (13) and a RCT comparing concurrent use of BC and oxytocin with oxytocin only in 128 women (14). On the contrary, another RCT comparing concurrent BC and oxytocin use with oxytocin only in 201 preterm or term women reported increased rates of chorioamnionitis following the use of BC, although infections were associated with longer induction-to-delivery interval (15).

The aim of this five-year cohort study was to assess the safety of use of BC for cervical ripening following PROM, and to compare the incidence of maternal and neonatal infections in women with PROM and women with intact amniotic membranes undergoing cervical ripening with BC.

MATERIAL AND METHODS

This cohort study of women ≥ 37 gestational weeks undergoing IOL and cervical ripening by BC between January 2014 and December 2018 was conducted in the Department of Obstetrics and

Gynecology in Helsinki University Hospital, with approximately 13 500 deliveries annually. All women with PROM, vital singleton pregnancy in cephalic presentation at ≥37 weeks of gestation, and an unfavorable cervix (Bishop score (16) <6) were included in the study. For each case of PROM, two controls of women undergoing cervical ripening by BC for any reason other than PROM were assigned. The controls were selected from the hospital database by including the one woman who had undergone cervical ripening by BC and given birth prior to the case, and the one who had undergone cervical ripening by BC and given birth following the case.

PROM was diagnosed by clinical examination combined with a positive rapid vaginal insulin-like growth factor binding protein-1 dipstick test (ActimProm®, Medix Biochemica, Espoo, Finland). A single 40-80 ml BC (Rüsch 2 way Foley Couvelaire tip catheter size 22 Ch, Teleflex Medical, Athlone, Ireland) was used for cervical ripening in all women. According to the hospital management guidelines, the balloon was retained for a maximum of 8 hours in case of PROM, and 24 hours in women with intact amniotic membranes. If the cervix remained unripe with Bishop score <6 after BC expulsion or removal, induction was continued at the discretion of the treating obstetrician. If Bishop score ≥6 was reached, IOL was continued by amniotomy in case of intact amniotic membranes, and oxytocin in the absence of spontaneous contractions. Oxytocin augmentation and continuous cardiotocography during labor were routinely used.

Group B *Streptococcus* (GBS) was tested in all women by a rapid qualitative in vitro GBS test (Xpert® GBS; Cepheid, Sunnyvale, CA, USA) at the time of admission. Administration of prophylactic antibiotics was started to all GBS-positive women at the time of rupture of membranes or at the time of diagnosing PROM. Benzylpenicillin was routinely used for antibiotic prophylaxis with the first dose of 2.4 g intravenously, followed by 1.5 g every 4 hours until delivery. In case of a penicillin allergy, clindamycin 900 mg or cefuroxime 1.5 g were administered every 8 hours intravenously. Additionally, according to the hospital policy, all women with ruptured membranes received one dose of prophylactic antibiotics during BC retention, regardless of the GBS-result.

The primary outcomes were the rates of maternal and neonatal infections. Maternal infections were categorized as intrapartum (during labor) and postpartum (within one week from delivery). The criteria for intrapartum infection were maternal fever ≥ 38°C during labor and at least one of the following: fetal tachycardia ≥ 160 bpm, uterine tenderness, purulent amniotic fluid or vaginal

discharge, total white cell count > 15E9/L. Postpartum infections included endometritis, cesarean or episiotomy wound infection, sepsis, and puerperal fever of unknown origin. Neonatal infections were categorized into blood culture positive sepsis, clinical sepsis, suspected sepsis, and other suspected infection by a neonatologist. Neonatal clinical sepsis was defined as blood culture negative infection with symptoms and signs consistent with sepsis (respiratory distress, apnea, tachycardia, poor perfusion, low blood pressure, fever, hypoglycemia or hyperglycemia, irritability, feeding problems, lethargy, convulsions) and abnormal blood values (C-reactive protein (>20 mg/l), leukocytosis or leucopenia, increased neutrophil precursors and thrombocytopenia). The cases of suspected sepsis had at least one symptom and at least one abnormal laboratory test value (as listed with clinical sepsis), and a positive response to antibiotic treatment.

The secondary outcomes were the mode of delivery, postpartum hemorrhage, Apgar score, umbilical artery blood gas values, admission to neonatal care, and induction to delivery interval.

The data on baseline characteristics and delivery outcomes were obtained from the hospital database. Late-term pregnancy was defined as gestational age 41^{+0}-41^{+6} weeks and post-term pregnancy was defined as gestational age ≥42 weeks. Gestational diabetes was diagnosed by at least one pathological value in 2-hour oral glucose tolerance test. The BC retention time was defined as an interval from balloon insertion to spontaneous expulsion or removal. The induction to delivery interval was defined as the time from insertion of the BC to delivery. Failed induction was diagnosed after ruptured membranes and 12 hours of oxytocin administration without cervical change (17). Duration of labor was defined as the time from the start of regular contractions with cervical dilation of 6 cm to delivery.

Statistical analyses were performed by using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA). Categorical variables were analyzed for odds ratios (OR) with 95% confidence interval (CI). Categorical variables were compared by the chi-square test and Fisher's exact test when appropriate. Data with continuous variables were performed by T-test when the data followed normal distribution and by a Mann-Whitney U test if the data did not follow normal distribution. Univariate and multivariate logistic regression analyses were performed to assess relative risk for intrapartum infection. Variables used in the multivariate analyses were parity, maternal age, height, IOL indication, in-vitro fertilization, smoking, body

mass index, previous cesarean section, Bishop score, gestational age, gestational diabetes, need of oxytocin induction, epidural/spinal analgesia, and the induction to delivery interval ≥ 48 h. Adjusted OR with 95% CI were calculated by modelling the data to control for possible confounding factors. A p-value <0.05 was considered statistically significant.

Ethical approval

The study was approved by the Institutional Review Board of the hospital region (Helsinki and Uusimaa Hospital District Committee for Obstetrics and Gynecology), (nr. HUS/3172/2018, HUS/54/2019 and HUS/6/2015). Due to the retrospective nature of the study, written informed consent was waived by the Institutional Review Board according to national legislation (Medical Research Act 488/1999, chapter 2 a (23.4.2004/295), section 5 and 10a).

RESULTS

A total of 1923 women were included in the study. Of these, 641 (33.3 %) underwent labor induction and cervical ripening by BC following PROM and 1282 (66.6 %) with intact amniotic membranes. The characteristics of the study population are presented in Table 1. The mean age of the women was 31.5 (5.3 SD) years, the mean body mass index 25.4 (5.4 SD) and the mean gestational age 40.4 (1.4 SD) weeks. The women induced for reasons other than PROM were more obese, more often were smokers, and more often had gestational diabetes and late-term or post-term pregnancy (Table 1). The most common indications for labor induction in the non-PROM group were post-date pregnancy (41 %), gestational diabetes (12.9 %), hypertensive disorders (11.0 %), maternal request for psychosocial reasons (8.0 %), intrahepatic cholestasis of pregnancy (7.2 %), oligohydramnios (5.1 %) and intrauterine growth restriction (4.7 %).

Table 2 presents the delivery outcomes. The median time from PROM to start of IOL was 27.3 h (range 1.7 – 328 h). The median BC retention time was 4.0 (range 0.1 – 18.0) h in women with PROM and 6.4 (range 0.1 – 28.5) h in women with intact amniotic membranes (p<0.001). There were no significant difference in the rates of cesarean section between the groups (23.7 vs. 23.7 %; p=0.82) (Table 2). Induction to delivery interval was longer in women with intact amniotic membranes (26.2 [3.1-164] h vs. 17.4 [2.6 – 75.7] h; p< 0.001), but the duration of labor was longer in women with PROM (6.7 [0.4 – 31.3] h vs. 7.7 [0.9 – 36.5] h; p<0.001) (Table 2). The

rates of low Apgar scores and low umbilical artery pH-values did not differ between the groups, but there were more admissions to NICU among the women with intact amniotic membranes (Table 2).

The total rate of intrapartum infection was 6.4 % (n=123). The rate of intrapartum infection was lower in women induced for PROM compared to women induced with intact amniotic membranes (3.7 % vs. 7.7 %; p=0.001, OR 0.5, 95% CI 0.3-0.7) (Table 3). After adjustment with cofounding factors, intrapartum infections were associated with nulliparity (OR 3.3, 95% CI 1.6–6.5; p=001), history of previous cesarean section (OR 2.8, 95% CI 1.2–6.4; p=0.02), extended gestational age ≥ 41 weeks (OR 1.9, 95% CI 1.2–3.0; p=0.003) and induction to delivery interval of 48 h or more (OR 2.0, 95% CI 1.2–3.3; p=0.005) (Table 4A).

The total rate of postpartum infections was 2.5 % (n=49), and the rates of postpartum infections were similar between the women induced for PROM and the women induced for reasons other than PROM (2.0 % vs. 2.8 %; 0.31) (Table 3). Eight cases (0.5 %) of blood culture positive septicemia occurred, two in the PROM group and six in the women with intact amniotic membranes (Table 3). Two of these occurred during labor and six occurred postpartum.

The total rate of neonatal infections was 3.1 % (n=60), being 1.7 % among the women with PROM and 3.8 % among the women with intact membranes (p=0.01). One case of neonatal blood culture positive (Staphylococcus Aureus) sepsis occurred in the non-PROM group following vaginal delivery and no maternal infection. After adjustment, the risk factors for neonatal infection were nulliparity (OR 3.3, 95% CI 1.4-8.0; p=0.01), gestational age ≥ 41 weeks (OR 1.9, 95% CI 1.09–3.36; p=0.03) and induction to delivery interval of 48 h or more (OR 3.4, 95% CI 1.9-6.0; p<0.001) (Table 4B). When including only neonatal blood culture positive or clinical sepsis, the induction to delivery interval > 48 hours remained significant, OR 12.6 (95 % CI 3.5 – 45.2); p<0.001.

DISCUSSION

Our results suggest that use of BC for cervical ripening following PROM is safe and did not increase the incidence of maternal or neonatal infections compared to women undergoing IOL and BC cervical ripening with intact amniotic membranes. On the contrary, the rates of maternal

intrapartum and neonatal infections were higher in the women who underwent BC cervical ripening with intact amniotic membranes. However, this may be partly explained by the prophylactic antibiotic use during BC retention in the PROM group, and by the fact the women with intact membranes more often had risk factors such as obesity, smoking, gestational diabetics, and extended gestational age. The women without PROM also had longer induction to delivery intervals, which is known to be associated with increased rates of maternal and neonatal infection. PROM may represent early onset of labor, and therefore more appropriate comparison group may have been women with PROM who underwent cervical ripening by methods other than BC. We acknowledge another major limitation of the study being the prophylactic antibiotic use. In our study, prophylactic antibiotics were routinely administered during BC retention according to the hospital management policy. The authors are aware that the use of prophylactic antibiotics during BC retention in case of ruptured membranes is controversial and question this policy. On the contrary, the women who received antibiotic had significantly lower rates of infections. Following these encouraging results, we are currently reevaluating the antibiotic regimen policy in our hospital. Another major weakness of the study is the lack of histopathological diagnosis of chorioamnionitis for all women with suspected chorioamnionitis. However, this is so far the largest cohort study on the safety of the use of BC in women with ruptured membranes, and adds to the limited data available. As large proportion of IOL is carried out due to PROM, and an increasing number of women have a history of previous caesarean section, it is important to assess the safety and feasibility on the use of BC in cases of ruptured membranes.

The duration of BC retention in both groups deviated from the hospital guidelines of eight hours in case of ruptured membranes and 24 hours in case of intact membranes. However, the duration of BC retention was not associated with the maternal or neonatal infections. Our results suggest that the BC can safely remain in the cervical canal for at least 8 hours following PROM, when prophylactic antibiotics are used during BC retention. In contrast, a previous study reported an increase in cervical pathogenic microbes, such as GBS, Candida albicans and Candida glabrata, and Gardnerella vaginalis during BC retention (18). In previous studies, BC retention time of 12–24 hours is frequently described (19,20), although a Dutch study used a maximum of 96 hours with BC replacement every 24–48 hours, with no increase in the rates of maternal and neonatal infectious morbidity (21). However, these studies have not detailed whether women with PROM

were included in the management protocol. Furthermore, only few trials were explicit about the inclusion and management GBS-colonized women.

The rates of maternal intrapartum infections and postpartum infections in our study are consistent with the previously shown 7% rate of chorioamnionitis, and the 3.5% rate of postpartum endometritis following labor induction (22,23). Similar reassuring results on the use of BC following PROM at term have previously been reported by a small Swedish pilot study (n=18) (24), an American retrospective cohort study (n=122) (11) and by a Finnish randomized multicenter trial (n=188) (13) that recorded no increase in infections following BC use compared to oral misoprostol. Another retrospective study showed a trend towards a higher rate of chorioamnionitis in 43 women undergoing IOL by BC following PROM, compared with intravaginal misoprostol or intravenous oxytocin use (12). However, after adjustment, the increase was due to nulliparity and intrauterine pressure catheter use (12). Also in our study, nulliparity was associated with an increased risk for intrapartum infections. Increased risk of chorioamnionitis has been demonstrated in nulliparous women remaining in the latent phase for more than 12-15 hours (25,26,), as also seen in our study, in which maternal and neonatal infections were associated with prolonged induction to delivery interval of ≥48 hours. Interestingly, duration of PROM or GBS colonization were not associated with an increased risk for maternal or neonatal infections. In our clinic, GBS colonized women are induced the latest in 12 h following PROM, while the GBS-negative women are managed expectantly for 24 h.

The 1.7 % rate of neonatal infections following IOL in women with PROM was in line with the results of previous studies (22, 27). However, among the women induced for reasons other than PROM, the rate of neonatal infections was more than doubled. This may be partially explained by the longer induction to delivery interval and the higher rate of maternal intrapartum infections in the non-PROM group, as well as the antibiotic prophylaxis protocol which may have led to a reduced rate of infections in the PROM group. One case of blood culture positive neonatal sepsis occurred, which parallels the previously reported global sepsis incidence of approximately 1 per 1000 live births (28, 29). There were more NICU admissions in the women induced for reasons other than PROM, which may have resulted from the higher neonatal infections rate as well as the pregnancy complications that led to labor induction, such as post-term pregnancy, gestational diabetes, hypertensive disorders and intrauterine growth restriction.

A randomized trial comparing 62 women with concurrent use of BC and oxytocin infusion to 66 women with oxytocin infusion alone reported a 10 % rate of chorioamnionitis following the use of BC, although this was not statistically significantly higher compared to the 5 % rate of chorioamnionitis ion the oxytocin only group (15). Another RCT compared 93 women with concurrent use of BC and oxytocin to 108 women with oxytocin induction alone. They recorded 7 % chorionamnionitis rate on the BS group compared to 0 % in the oxytocin group ($p<0.01$) (14). Those with suspected intra-amniotic infection had a 9-hour longer induction to delivery interval than those without suspected infection (14). In this study BC was retained for 12 hours and the use of fetal scalp electrode was significantly more frequent in the BC group, although in their regression model it was not considered significant (14). However, these studies included also cases of preterm premature rupture of membranes, while the current study focused on women with term PROM. Additionally, the two previous studies included oxytocin use in women with unripe cervices, while our study concentrated on cervical ripening with BC and oxytocin was only started when Bishop score of six or more was reached. Contrarily, the Cochrane review suggests similar labor outcomes in women with PROM and an unfavourable cervices when comparing use of oxytocin and prior cervical ripening by prostaglandins (6). In our previous study, BC and misoprostol were as effective in labor induction following prolonged PROM (13). Thus, one may speculate is the use of BC an unnecessary intervention following PROM, and would oxytocin induction without prior cervical ripening be as effectively. Further studies are needed to substantiate the benefits of use of BC in women with prolonged PROM.

CONCLUSION

Our results suggest that with regards to maternal and neonatal infectious morbidity, BC appears a safe method for cervical ripening in women with ruptured membranes when prophylactic antibiotics are used. Intrapartum and neonatal infections in our study were associated with nulliparity, history of previous cesarean section, gestational age of ≥41 weeks, and prolonged induction to delivery interval of 48 hours or more. Further investigations, ideally a randomized trial, are needed to substantiate these findings.

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TABLES

Table 1. The characteristics of the study population (n=1923)

	PROM		non-PROM		p-value
	n	%	n	%	
N	641	33.3	1282	66.7	
Maternal age ≥ 37 years	111	17.3	218	17.0	0.86
Nulliparous	429	66.9	663	51.7	<0.001
Maternal height <164cm[1]	257	40.2	466	36.3	0.10
Late-term	129	20.1	628	49.0	< 0.001
Post-term	136	21.2	856	66.8	< 0.001
IVF	28	4.4	69	5.4	0.34
Smoking	49	7.6	139	10.8	0.03
BMI ≥30 kg/m²	81	12.7	264	20.6	< 0.001
Gestational diabetes[3]	126	20.1	419	32.7	< 0.001
Previous cesarean section	110	17.2	166	12.9	0.01
GBS colonization[4]	131	21.3	310	24.3	0.15

[1]Missing values n= 2 (case).

[2]missing values n=1 (case) and n=1 (control).

[3]missing values n=15 (case).

[4]missing values n= 26 (case) and n=4 (controls).

PROM, pre-labor rupture of membranes; IVF, in-vitro fertilization; BMI, body mass index; GBS, Group B *Streptococcus*.

Table 2. Maternal and neonatal outcomes

	PROM (n=641)		non-PROM (n=1282)		p-value
	n	%	n	%	
Epidural/spinal analgesia	520	81.1	1028	80.2	0.63
Oxytocin for labor induction	311	57.2	494	50.9	0.02
Oxytocin augmentation	544	84.9	970	75.7	< 0.001
Operative vaginal delivery	77	12.0	151	11.8	0.88
Cesarean section	152	23.7	298	23.7	0.82
Failure to progress[1]	100	15.6	137	10.7	0.002
Fetal distress	38	5.9	120	9.4	0.010
Intrapartum infection	4	0.6	26	2.0	0.02
Other indication[2]	10	1.6	15	1.2	0.48
Post-partum hemorrhage ≥ 1000 ml	99	15.4	190	14.8	0.72
Rupture of membranes to delivery interval ≥ 24 h	584	91,1	162	12,6	<0.001
Duration of labor (h; median [range])	7.7	0.9-36.5	6.7	0.4-31.3	< 0.001
Induction to delivery interval (median; range)	17.4	2.6-75.7	26.2	3.2-163.7	<0.001
Induction to delivery interval ≥ 24 h	184	28.7	691	53.1	< 0.001
Induction to delivery interval ≥ 48 h	17	2.7	192	15.0	< 0.001
Birthweight (g; mean [SD])	3430	440	3560	500	<0.001
5 min Apgar score <7	22	3.4	43	3.4	0.97
Umbilical artery pH ≤ 7.05	12	1.9	20	1.6	0.66
Umbilical artery BE ≤ 12	9	1.4	22	1.8	0.57
NICU	15	2.3	93	7.3	<0.001

[1]Failed vacuum delivery: PROM group n=3; non-PROM group n=9.

[2]PROM group: fetal malpresentation (n=2), maternal request (n=1), placental abruption (n=3), umbilical cord prolapse (n=4); Non-PROM: fetal malpresentation (n=2), maternal request (n=3), placental abruption (n=2), umbilical cord prolapse (n=1), preeclampsia (n=7).

PROM, pre-labor rupture of membranes; BE, blood gas values; NICU, neonatal intensive care unit.

Table 3. Infectious morbidity

	PROM (n=641)		Non-PROM (n=1282)		p-value
	n	%	n	%	
Maternal intrapartum infection	24	3.7	99	7.7	0.001
Blood culture positive sepsis[1]			6	0.5	
Maternal post-partum infection	13	2.0	36	2.8	0.31
Endometritis	5	0.8	20	1.6	0.16
Cesarean section wound infection	2	0.3	9	0.7	0.36
Abdominal/pelvic infection	1	0.2	4	0.3	0.67
Other[2]	3	0.5	3	0.2	0.41
Blood culture positive sepsis[3]	2	0.3			
Neonatal infection	11	1.7	49	3.8	0.01
Blood culture positive sepsis	0		1	0.001	
Clinical sepsis	1	0.2	8	0.6	0.51
Suspected sepsis	9	1.4	35	2.7	0.07
Other suspected infection	1	0.2	5	0.4	

[1]*Stafylococcus epidermoides* n=1, *Stafylococcus anginosus* n=1, Group B *Streptococcus* (GBS) n=1, *Stafylococcus aureus* n=1, *Grannulicatella elegans* n=1, *Enterococcus fecalis* n=1

[2]PROM group: episiotomy wound infection (n=1), urinary tract infection (n=2); Controls: episiotomy wound infection (n=1), urinary tract infection (n=1), pneumonia (n=1)

[3]*Entorococcus faecalis* n=1, *Escherichia coli* with Siprolla n=1

PROM, pre-labor rupture of membranes.

Table 4A. Unadjusted and adjusted risk factors for maternal intrapartum infection

	Unadjusted intrapartum infection			Adjusted intrapartum infection		
	OR	**CI (95 %)**	**p-value**	**OR**	**CI (95 %)**	**p-value**
Nulliparity	2.4	1.6-3.6	<0.001	3.3	1.6–6.5	0.001
Maternal age ≥37	0.6	0.3-1.0	0.047	0.7	0.4–1.3	0.28
Height <160cm	1.1	0.7-1.5	0.743	1.1	0.7–1.6	0.70
PROM	0.5	0.3-0.7	0.001	0.6	0.3–1.1	0.08
IVF	1.1	0.5-2.5	0.735	1.3	0.6–3.0	0.54
Smoking	0.9	0.5-1.7	0.748	0.8	0.4–1.5	0.44
BMI ≥ 30	1.5	1.0–2.4	0.049	1.6	1.0–2.6	0.06
Previous CS	1.1	0.6-1.8	0.722	2.8	1.2–6.4	0.02
Bishop ≤ 3	2.0	1.2–3.1	0.004	1.3.	0.7–2.4	0.40
Gestational age ≥41 weeks	2.1	1.5–3.1	< 0.001	1.9	1.2–3.0	0.003
Need of oxytocin for IOL	1.1	0.7-1.5	0.787	1.0	0.6–1.5	0.91
Epidural/spinal analgesia	2.1	1.2-3.8	0.010	1.3	0.7–2.7	0.42
Gestational diabetes	1.2	0.8-1.7	0.425	1.3	0.8–2.0	0.30
GBS colonization	0.5	0.3-0.9	0.013	0.5	0.3–0.8	0.008
Induction to delivery interval ≥48 h	3.2	2.1-5.0	< 0.001	2.0	1.2–3.3	0.005

PROM, pre-labor rupture of membranes; IVF, in-vitro fertilization; BMI, body mass index; IOL, induction of labor; GBS, Group B *Streptococcus*.

Table 4B. Unadjusted and adjusted risk factors for neonatal infection

	Unadjusted neonatal infection			Adjusted neonatal infection		
	OR	**CI (95 %)**	**p-value**	**OR**	**CI (95 %)**	**p-value**
Nulliparity	3.9	2.2-6.9	<0.001	3.3	1.4–8.0	0.01
Maternal age ≥37	0.8	0.4-1.5	0.543	1.1	0.5-2.3	0.38
Height <160cm	0.7	0.4-1.2	0.172	0.8	0.4-1.3	0.15
PROM	0.5	0.3-0.8	0.007	0.7	0.3-1.7	0.46
IVF	1.8	0.8-4.1	0.140	1.6	0.6-4.2	0.31
Smoking	1.8	1.0–3.3	0.058	1.6	0.7-3.2	0.25
BMI ≥ 30	1.0	0.6-1.8	0.936	0.9	0.4-1.0	0.73
Previous CS	0.5	0.2-1.2	0.124	0.5	0.1-2.6	0.40
Bishop ≤ 3	1.7	1.0–2.9	0.055	1.2	0.6-2.7	0.61
Gestational age ≥41 weeks	2.5	1.6–3.9	< 0.001	1.9	1.1–-3.4	0.03
Need of oxytocin for IOL	1.2	0.7-2.0	0.479	1.1	0.7–1.9	0.69
Epidural/spinal analgesia	1.4	0.8-2.7	0.256	1.1	0.5-2.6	0.77
Gestational diabetes	1.1	0.7-1.9	0.587	1.2	0.7-2.2	0.52
Maternal GBS colonization	0.5	0.3-1.0	0.039	0.4	0.2–0.9	0.03
Induction to delivery interval ≥ 48 h	4.5	2.8-7.3	< 0.001	3.4	1.9–6.0	< 0.001

PROM, pre-labor rupture of membranes; IVF, in-vitro fertilization; BMI, body mass index; IOL, induction of labor; GBS, Group B *Streptococcus*.