Thai Journal of Obstetrics and Gynaecology
March 2023, Vol. 31, No. 2, pp. 89-98.

OBSTETRICS

Adverse Neonatal Outcomes in Relation to Modes of Delivery in Thick Meconium-stained Amniotic Fluid with NICHD Category I Fetal Heart Rate Pattern

Pornnapas Chaowanasai, M.D.*,
Pakprapa Chaipakdi, M.D.*

** Department of Obstetrics and Gynecology, Hatyai Hospital, Songkhla, Thailand*

ABSTRACT

Objectives: This work studied the association between adverse neonatal outcomes and modes of delivery in thick meconium-stained amniotic fluid pregnant women with normal fetal heart rate (FHR) patterns and the key factors affecting the adverse neonatal outcomes.

Materials and Methods: This research was a retrospective cohort study. The investigation was conducted by collecting the data of 271 singleton pregnant women who had 37-42 weeks of gestation, were diagnosed with thick meconium-stained amniotic fluid and a normal FHR pattern was determined, according to the National Institute of Child Health and Human Development (NICHD) classification and were admitted to Hatyai Hospital during January 2015 to December 2020. Multivariate analysis was used to determine the association between mode of delivery and neonatal outcomes.

Results: Modes of delivery were not associated with adverse neonatal outcomes. The important factor that was associated with adverse neonatal outcome was oxytocin use > 3 h (adjusted odds ratio (OR) 3.07, $p = 0.01$). Risk factors of meconium aspiration syndrome (MAS) were the patients who did not receive antenatal care (adjusted OR 31.13, $p = 0.04$) and the induction of labor (adjusted OR 3.91, $p = 0.04$). However, increasing the Apgar score could reduce the risk of MAS (adjusted OR 0.61, $p < 0.001$). A risk factor of neonatal intensive care (NICU) admission was preeclampsia (adjusted OR 6.15, $p = 0.02$) but increasing the Apgar score at 1 min could reduce the risk of NICU admission (adjusted OR 0.49, $p < 0.001$).

Conclusion: Modes of delivery were not associated with adverse neonatal outcomes. The significant factor associated with an adverse neonatal outcome was oxytocin use > 3 h.

Keywords: thick meconium-stained amniotic fluid, adverse neonatal outcome, mode of delivery.

Correspondence to: *Pornnapas Chaowanasai, M.D., Department of Obstetrics and Gynecology, Hatyai Hospital, Hatyai, Songkhla 90110, Thailand, Email: pornnapaschaowanasai@gmail.com*

Received: 20 August 2021, **Revised:** 23 December 2021, **Accepted:** 7 January 2022

ความสัมพันธ์ระหว่างผลลัพธ์การคลอดของทารกที่ไม่พึงประสงค์กับวิธีการคลอดในทารกที่มีภาวะขี้เทาข้นปนในน้ำคร่ำและมีหัวใจเต้นปกติ

พรนภัส เชาวนาสัย, พักตร์ประภา ไชยภักดี

บทคัดย่อ

วัตถุประสงค์: *เพื่อหาความสัมพันธ์ระหว่างผลลัพธ์การคลอดของทารกที่ไม่พึงประสงค์กับวิธีการคลอดในภาวะขี้ เทาข้นปนในน้ำคร่ำในกลุ่มทารกที่มีหัวใจเต้นปกติและศึกษาปัจจัยที่มีผลต่อการคลอดของทารกที่ไม่พึงประสงค์*

วัสดุและวิธีการ: *เป็นการศึกษาย้อนหลังของสตรีตั้งครรภ์เดี่ยวช่วงอายุครรภ์ตั้งแต่ 37 ถึง 42 สัปดาห์ ที่ได้รับการวินิจฉัยว่ามีภาวะขี้เทาข้นปนในน้ำคร่ำและทารกหัวใจเต้นปกติตามการแบ่งกลุ่มของ NICHD จำนวน 271 คน ที่มาคลอดบุตร ณ โรงพยาบาลหาดใหญ่ ระหว่างเดือนมกราคม พ.ศ.2558 ถึงเดือนธันวาคม พ.ศ.2563 และวิเคราะห์หาความสัมพันธ์ระหว่างวิธีการคลอดกับผลลัพธ์การคลอดของทารกที่ไม่พึงประสงค์โดยใช้สถิติชนิด multivariate analysis*

ผลการศึกษา: *วิธีการคลอดไม่ได้สัมพันธ์กับผลลัพธ์การคลอดของทารกที่ไม่พึงประสงค์แต่ปัจจัยสำคัญที่มีผลต่อผลลัพธ์การคลอดของทารกที่ไม่พึงประสงค์คือ การใช้ยาเร่งคลอด oxytocin นานกว่า 3 ชั่วโมง (adjusted OR 3.07, p = 0.01) ปัจจัยที่มีผลต่อภาวะทารกสำลักขี้เทาเข้าปอด ได้แก่ สตรีที่ไม่ได้ฝากครรภ์ (adjusted OR 31.13, p = 0.04), การชักนำการคลอด (adjusted OR 3.91, p = 0.04) ส่วนทารกที่มีคะแนนประเมินแรกคลอดที่สูงขึ้นจะมีโอกาสเกิดภาวะทารกสำลักขี้เทาเข้าปอดน้อยลง (adjusted OR 0.61, p < 0.001) ปัจจัยที่มีผลต่อการเข้าหออภิบาลทารกแรกเกิดภาวะวิกฤต ได้แก่ มารดาที่มีภาวะครรภ์เป็นพิษ (adjusted OR 6.15, p = 0.02) ส่วนทารกที่มีคะแนนประเมินแรกคลอดที่ 1 นาที สูงขึ้นจะมีโอกาสเข้าหออภิบาลทารกแรกเกิดภาวะวิกฤตน้อยลง (adjusted OR 0.49, p < 0.001).*

สรุป: *วิธีการคลอดไม่ได้สัมพันธ์กับผลลัพธ์การคลอดของทารกที่ไม่พึงประสงค์แต่ปัจจัยสำคัญที่มีผลต่อผลลัพธ์การคลอดของทารกที่ไม่พึงประสงค์คือ การใช้ยาเร่งคลอด oxytocin นานกว่า 3 ชั่วโมง*

คำสำคัญ: *ภาวะขี้เทาข้นปนในน้ำคร่ำ, ผลลัพธ์การคลอดของทารกที่ไม่พึงประสงค์, วิธีการคลอด*

Introduction

Meconium comprises fetal bowel contents consisting of various products of secretion[1]. Thick meconium is a thick dark green amniotic fluid or any meconium-stained amniotic fluid that contains lumps of meconium[2].

The incidence of thick meconium-stained amniotic fluid in Hatyai Hospital is 3.02%, which is less than that in previous studies (5.61%[3] and 5.47%[4]). Meconium staining of the amniotic fluid (MSAF) has been reported more commonly in term (7-22%) and post-term deliveries (23-52%)[5]. This may be explained by three theories regarding the fetal passage of meconium. Firstly, the fetus may pass meconium in response to hypoxia causing fetal compromise. Secondly, meconium may be representative of normal gastrointestinal tract maturation under neural control. The last theory explains that meconium passage follows vagal stimulation due to umbilical cord entrapment causing bowel peristalsis to increase[1].

Meconium-stained amniotic fluid is considered to be a bad predictor of fetal outcomes. The presence of meconium in amniotic fluid is a potentially serious sign of fetal compromise and is associated with poor perinatal outcomes[6]. Meconium aspiration syndrome (MAS) is significantly associated with fetal acidemia at birth[7]. Infants born through meconium-stained amniotic fluid have a five-fold increase in perinatal mortality, compared with low-risk patients with clear amniotic fluid[8]. It is difficult to make the decision whether to continue normal vaginal delivery or to proceed with cesarean delivery for the best neonatal outcome in the thick meconium-stained amniotic fluid pregnant women with a normal fetal heart rate (FHR) pattern, according to the National Institute of Child Health and Human Development (NICHD) classification[9].

There are no previous guidelines on the proper mode of delivery and no studies about the association between neonatal outcomes and modes of delivery in thick meconium-stained amniotic fluid pregnant women who had a normal FHR pattern (NICHD category I) in Thailand. Therefore, the primary objective in this study was to investigate the association between adverse neonatal outcomes and modes of delivery in thick meconium-stained amniotic fluid pregnant women with a normal FHR pattern (NICHD category I). The secondary outcome was to find the key factors affecting the adverse neonatal outcomes in this group. We assumed that the mode of delivery may be associated with adverse neonatal outcomes.

Materials and Methods

This work was a retrospective cohort study. This study was approved by The Institutional Review Board of Hatyai Hospital. The investigation was performed by collecting the data of pregnant women who were diagnosed with thick meconium-stained amniotic fluid and were admitted to the labor ward in Hatyai Hospital during January 2015 to December 2020.

The inclusion criteria were singleton pregnant women at 37-42 weeks of gestation with a normal FHR pattern (NICHD category I) and cephalic presentation. Those pregnant women who had non-cephalic presentation, multifetal pregnancy, abnormal FHR pattern (NICHD category II, III), the need for instrumental delivery (forceps and vacuum extraction), abnormal placenta, intrauterine fetal growth restriction, or fetal anomaly were excluded.

Among the 1,200 pregnant women diagnosed with thick meconium-stained amniotic fluid, 271 patients met the inclusion criteria of this study. Among the 271 patients, 127 patients were in the cesarean section (C-section) group and the rest were in the normal vaginal delivery (NVD) group.

The sample size was calculated using the formula for descriptive study:

$n = (Z_{\alpha/2}+Z_{\beta})^{2*} (p_1 (1 - p_1) + (p_2 (1- p_2)) / (p_1- p_2)^2)$.

Based on a previous study[5], where

$Z_{\alpha/2} = 1.96$, $Z_{\beta} = 0.84$, $p1 = 0.15$ and $p2 = 0.04$. The minimum sample size needed for each group is 126 cases.

After the admission, the management of labor

and delivery were provided according to the institutional guidelines. Continuous electronic fetal monitoring was offered to all pregnant women during labor and delivery and all FHR tracing underwent interpretation by the attending obstetricians. The definition of thick meconium-stained amniotic fluid was dark green in color and containing particulate matter[10] that was diagnosed by two midwives or the attending obstetricians at the time of rupture of the membranes or initial per-vaginal examination during admission when rupture of the membranes occurred before the patient arrived in the labor room. For the patients who needed induction or augmentation of labor, the oxytocin dosage used was about 4-16 mU/min and could be adjusted by uterine contraction. The indication of induction was similar between two groups such as overt diabetes mellitus (DM), preeclampsia and oligohydramnios. In our protocol, the cesarean section was performed in thick meconium-stained amniotic fluid pregnant women with abnormal FHR patterns (NICHD category II and III), but there was no guideline for management of the mode of delivery in patients with normal FHR patterns (NICHD category I).

All data included demographic data (age, gravida, body mass index (BMI), gestational age, antenatal care), medical condition (chronic hypertension, overt DM, human immunodeficiency virus (HIV), hepatitis B, systemic lupus erythematosus (SLE), asthma, hyperthyroid, anemia), obstetric risk factors (gestational hypertension, preeclampsia, GDM, oligohydramnios, chorioamnionitis), intrapartum assessment (onset of labor, duration of oxytocin use, duration of labor, duration rupture of membranes (ROM), cervix dilation at the time of diagnosis of thick meconium), neonatal outcome (neonatal intensive unit (NICU) admission, neonatal medium care unit (NMCU) admission, MAS, respiratory distress syndrome (RDS), persistent pulmonary hypertension of the newborn (PPHN), Apgar score, intubation, cardiopulmonary resuscitation (CPR), transient tachypnea of the newborn (TTNB), sepsis, pneumonia), and maternal complications (postpartum hemorrhage (PPH), uterine atony, uterine segment tear, metritis) were collected from Hatyai Hospital medical records.

Statistical analysis was done by use of R program version 4.0.2. Descriptive statistics including frequencies and cross tabulations were performed. Multiple logistic regression fitted with an odds ratio (OR) with a 95% confidence interval (CI) was calculated. Adjusted OR were calculated by entering the proposed explanatory variables having a significant p value < 0.05. Univariate and multivariate analyses were used to determine the association between neonatal outcomes and modes of delivery.

Results

The study found that the median maternal age and birth weight in the C-section group were greater than in the NVD group ($p = 0.01$ and $p = 0.01$, respectively). The number of patients who completed antenatal care in the C-section group was higher than that in the NVD group ($p = 0.04$). The gestational age, BMI, and medical conditions between the two groups were not significantly different. For the obstetric risk factor data, the number of patients diagnosed with gestational diabetes mellitus (GDM) in the C-section group was higher than those in the NVD group ($p = 0.05$). The patients diagnosed with chorioamnionitis were found in the C-section group only ($p = 0.05$). The other obstetric risk factors such as gestational hypertension, preeclampsia, and oligohydramnios were not statistically different between the two groups.

The most common indication of neonatal admission was meconium aspiration syndrome (MAS) followed by neonatal sepsis. Jaundice was found in the NVD group to a greater extent than in the C-section group ($p = 0.04$). Indications of cesarean section delivery were cephalopelvic disproportion (55 cases, 43.31%), previous cesarean section (8 cases, 6.30%), thick meconium-stained amniotic fluid (53 cases, 41.73%), and failed induction (11 cases, 8.66%). The demographic data are shown in Table 1.

Table 1. Demographic data of the studied patients.

Characteristics	C-section (N=127) n (%)	NVD (N=144) n (%)	p value
Age (years)			0.03
≤ 20	19 (14.96%)	34 (23.61%)	
21-25	30 (23.62%)	45 (31.25%)	
26-30	38 (29.92%)	39 (27.08%)	
> 30	40 (31.50%)	26 (18.06%)	
Median (IQR)	28 (23,32)	25 (21,29)	0.01
Gravida			0.06
Primi	72 (56.7%)	64 (44.4%)	
Multi	55 (43.3 %)	80 (55.6%)	
BMI (kg/m^2)			0.34
< 25	71 (55.90%)	93 (64.58%)	
25-29.9	32 (25.20%)	30 (20.84%)	
≥ 30	24 (18.90%)	21 (14.58%)	
Gestational age			0.07
37-38	29 (22.83%)	39 (27.08%)	
39-40	78 (61.42%)	95 (65.98%)	
41-42	20 (15.75%)	10 (6.94%)	
Antenatal care			0.04
Complete	123 (96.86%)	131 (90.96%)	
Incomplete	2 (1.57%)	11 (7.64%)	
No ANC	2 (1.57%)	2 (1.40%)	
Medical condition			
Chronic hypertension	1 (0.79%)	1 (0.69%)	1.00
Overt DM	1 (0.79%)	0 (0.00%)	0.47
HIV	0 (0.00%)	0 (0.00%)	0.30
Hepatitis B	2 (1.57%)	4 (2.78%)	0.69
SLE	0 (0.00%)	0 (0.00%)	0.30
Asthma	3 (2.37%)	0 (0.00%)	0.10
Hyperthyroid	0 (0.00%)	1 (0.69%)	1.00
Anemia	11 (8.69%)	12 (8.28%)	0.48
Obstetric risk factor			
Gestational HT	2 (1.57%)	2 (1.39%)	1.00
Preeclampsia	8 (6.32%)	4 (2.78%)	0.27
GDM	8 (6.32%)	2 (1.39%)	0.05
Oligohydramnios	7 (5.53%)	3 (2.08%)	0.20
Chorioamnionitis	4 (3.16%)	0 (0.00%)	0.05
Birth weight (grams)	3280	3087	0.01
Sex			
Male	67 (52.76%)	78 (54.17%)	
Female	60 (47.24%)	66 (45.83%)	
Indication for NICU and NMCU admission			
MAS	24 (18.90%)	24 (16.67%)	0.75
Neonatal sepsis	16(12.60%)	9 (6.25%)	0.11
Hypoglycemia	2 (1.57%)	0 (0.00%)	0.22
Pneumonia	3 (2.36%)	1 (0.69%)	0.34
Jaundice	9 (7.09%)	23 (15.97%)	0.04
TTNB	7 (5.51%)	2 (1.39%)	0.09
Amphetamine positive	1 (0.79%)	0 (0.00%)	0.47

Values are given as median (interquartile range) and number (%).
C-section: cesarean section, NVD: normal vaginal delivery, IQR: interquartile range, BMI: body mass index, ANC: antenatal care, DM: diabetes mellitus, HIV: human immunodeficiency virus, SLE: systemic lupus erythematosus, HT: hypertension, GDM: gestational diabetes mellitus, NICU: neonatal intensive unit, NMCU: neonatal medium care unit, MAS: meconium aspiration syndrome

According to the study, the number of patients who received induction of labor and the duration of labor in the C-section group were both higher than in the NVD group ($p = 0.02$ and $p < 0.001$, respectively). Most patients in both groups did not receive oxytocin. However, it was observed that the number of patients who received oxytocin > 3 h in the C-section group was greater than those in the NVD group ($p < 0.001$).

The median cervical dilatation at the first instance of thick meconium diagnosis in the NVD group was greater than that in the C-section group. Moreover, most patients in the NVD group had cervical dilatation ≥ 6 cm ($p < 0.001$). Uterine atony and uterine segment tear were found in the C-section group only ($p < 0.001$) and were not found in the NVD group ($p = 0.05$). The intrapartum data are shown in Table 2.

Table 2. Intrapartum data.

Intrapartum	C-section (N=127) n (%)	NVD (N=144) n (%)	p value
Onset of labor			0.02
Spontaneity	50 (39.37%)	70 (48.61%)	0.16
Augmentation	65 (51.18%)	71 (49.31%)	0.85
Induction	12 (9.45%)	3 (2.08%)	0.02
Duration of oxytocin use (h)			< 0.001
None	64 (50.39%)	90 (62.50%)	
≤ 3	20 (15.75%)	39 (27.08%)	
> 3	43 (33.86%)	15 (10.42%)	
Median duration labor (h)	4 (2,6)	2 (1,4)	< 0.001
Median duration ROM (h)	3 (1.5,6)	2 (1,4)	0.06
Cervix dilation (centimeters)			< 0.001
< 6	96 (75.59%)	61 (42.36%)	
≥ 6	31 (24.41%)	83 (57.64%)	
Median (IQR)	3 (2,5)	6 (4,9.2)	< 0.001
Maternal complication			
(n = 26)	(n = 20)	(n = 6)	
PPH	7 (35.00%)	5 (83.33%)	0.60
Uterine atony	9 (45.00%)	0 (0.00%)	< 0.001
Uterine segment tear	4 (20.00%)	0 (0.00%)	0.05
Metritis	0 (0.00%)	1 (16.67%)	1.00

Values are given as median (interquartile range) and number (%).
C-section: cesarean section, NVD: normal vaginal delivery, ROM: rupture of membranes, IQR: interquartile range, PPH: postpartum hemorrhage

The number of patients who had adverse neonatal outcomes including MAS, RDS, intubation, PPHN, CPR, TTNB, neonatal sepsis, pneumonia, NICU admission, NMCU admission, and Apgar score < 7 at 1 and 5 min in the C-section group was greater than in the NVD group ($p = 0.01$). The median duration of hospital neonatal admission between two groups showed no difference ($p < 0.001$). Transient tachypnea of newborns (TTNB) was found in the C-section group to a greater extent than in the NVD group ($p = 0.01$). Jaundice was found in the NVD group to a greater extent than in the C-section group ($p = 0.04$). These data are shown in Table 3.

Table 4 presents the univariate analysis which found that the factors associated with adverse neonatal outcomes (MAS, RDS, intubation, PPHN, CPR, TTNB, neonatal sepsis, pneumonia, NICU admission, NMCU admission, Apgar score < 7 at 1 and 5 min) were C-section (crude OR 2.07, $p = 0.01$) and duration of oxytocin (crude OR 1.10, $p = 0.02$).

Table 3. Neonatal outcome.

Neonatal outcome	C-section (N=127) n (%)	NVD (N=144) n (%)	p value
Apgar score			
1 min			0.05
< 7	13 (10.24%)	7 (4.86%)	
≥ 7	114 (89.76%)	137 (95.14%)	
5 min			0.66
<7	4 (3.15%)	3 (2.08%)	
≥ 7	123 (96.85%)	141 (97.92%)	
Adverse neonatal outcome	4 (2,6)	2 (1,4)	< 0.001
Admission NICU	3 (1.5,6)	2 (1,4)	0.06
Admission NMCU			< 0.001
Duration of admission (day) (Median (IQR))			
MAS	24 (18.90%)	25 (17.36%)	0.51
RDS	1 (0.79%)	1 (0.69%)	1.00
PPHN	4 (3.15%)	4 (2.78%)	1.00
Intubation	20 (15.75%)	15 (10.42%)	0.26
CPR	2 (1.57%)	0 (0.00%)	0.22
TTNB	11 (8.66%)	2 (1.39%)	0.01
Pneumonia	3 (2.36)	1 (0.69)	0.34
Jaundice	9 (7.09)	23 (15.97)	0.04
Hypoglycemia	2 (1.57)	0 (0.00)	0.22
Neonatal sepsis	16 (12.60)	9 (6.25)	0.11

Values are given as median (interquartile range) and number (%).
C-section: cesarean section, NVD: normal vaginal delivery, NICU: neonatal intensive unit, NMCU: neonatal medium care unit, IQR: interquartile range, MAS: meconium aspiration syndrome, RDS: respiratory distress syndrome, PPHN: persistent pulmonary hypertension of the newborn, CPR: cardiopulmonary resuscitation, TTNB: transient tachypnea of the newborn

Table 4. Univariate analysis of adverse neonatal outcomes.

Maternal factor	Crude OR (95%CI)	p value
Cesarean delivery	2.07 (1.24,3.46)	0.01
Age	1.03 (0.99,1.07)	0.17
Gravidity	1.01 (0.61,1.68)	0.97
BMI	1.03 (0.98,1.08)	0.19
Gestational age	0.95 (0.75,1.21)	0.70
ANC group	3 (2.08%)	
- Incomplete ANC	141 (97.92%)	
- No ANC	2 (1,4)	< 0.001
Hepatitis B	2.05 (0.40,10.35)	0.39
Asthma	4.09 (0.37,45.73)	0.25
Anemia	0.40 (0.13,1.20)	0.10
Gestational HT	2.03 (0.28,14.68)	0.48
Preeclampsia	2.08 (0.65,6.65)	0.22
GDM	2.07 (0.58,7.35)	0.26
Oligohydramnios	3.16 (0.87,11.50)	0.08
Onset of labor	0 (0.00%)	0.22
- Augmentation	2 (1.39%)	0.01
- Induction	1 (0.69)	0.34
Duration of oxytocin	1.10 (1.02,1.2)	0.02
Duration labor	1.02 (0.93,1.12)	0.68
Duration ROM	1.05 (0.99,1.11)	0.13
Cervix dilate	1.05 (0.97,1.14)	0.25

Values are given as odds ratios (95% confidence interval)
OR: odds ratio, CI: confidence interval, BMI: body mass index, ANC: antenatal care, HT: hypertension, GDM: gestational diabetes mellitus, ROM: rupture of membranes

Table 5 presents multivariate analysis of the factors associated with adverse neonatal outcomes (MAS, RDS, intubation, PPHN, CPR, TTNB, neonatal sepsis, pneumonia, NICU admission, NMCU admission, Apgar score < 7 at 1 and 5 min). Although univariate analysis data demonstrated that C-section was associated with adverse outcomes in Table 4, the multivariate analysis showed that C-section was not associated with adverse outcomes (adjusted OR 0.89, p = 0.80). The only factor associated with adverse neonatal outcomes was oxytocin use > 3 h, which increased the risk of adverse neonatal outcomes by 3 times (adjusted OR 3.07, p = 0.01). The cut point of 3 h was from the statistical calculation by using the median and percentile range that results in significantly different adverse neonatal outcomes between the two groups.

Table 5. Multivariate analysis of adverse neonatal outcomes.

Maternal factor	Adverse outcome (case) (n = 90) n (%)	Crude odds ratio (95%CI)	p value	Adjusted odds ratio (95%CI)	p value
Cesarean delivery	54 (60.00%)	2.06 (1.24, 3.44)	0.01	0.89 (0.38, 2.10)	0.80
Duration of oxytocin > 3 h	29 (32.22%)	2.93 (1.34, 6.40)	0.01	3.07 (1.30, 7.23)	0.01

Values are given as odds ratio (95% confidence interval) and number (%).
CI: confidence interval

The study observed that the mode of delivery was not associated with MAS and NICU admission from the univariate analysis (p = 0.42 and p= 0.10, respectively) but the patients who did not receive antenatal care had a 31-fold increase in risk of MAS (adjusted OR 31.13, p = 0.04), and a 3.91-fold increase in risk of induction of labor (adjusted OR 3.91, p = 0.04). Increasing the Apgar score to 1 minute reduced the risk of MAS (adjusted OR 0.61, p < 0.001), as shown in Table 6.

Table 6. Multivariate analysis of MAS.

Factor	Crude OR (95%CI)	Adjusted OR (95%CI)	p value
Anemia	0.18 (0.02,1.33)	0.13 (0.01,1.18)	0.07
Oligohydramnios	4.55 (1.27,16.36)	2.53 (0.56,11.55)	0.23
Augmentation	1.06 (0.56,2.01)	0.92 (0.46,1.86)	0.83
Induction	3.14 (1.01,9.78)	3.91 (0.91,12.47)	0.04
Maternal complication	3.02 (1.28,7.12)	2.37 (0.90,6.26)	0.08
Apgar score at 1 min	0.59 (0.47,0.74)	0.6 (0.47,0.77)	< 0.001
No ANC	14.32 (1.46, 140.88)	31.13 (1.13, 855.94)	0.04

Values are given as odds ratio (95% confidence interval)
MAS: meconium aspiration syndrome, OR: odds ratio, CI: confidence interval, ANC: antenatal care

Moreover, the study revealed that preeclampsia increased the risk of NICU admission by 6 times (adjusted OR 6.15, p = 0.02. Every 1-point increase in the Apgar score at 1 min reduced the risk of NICU admission by 0.49 times (adjusted OR 0.49, p < 0.001) as shown in Table 7.

Table 7. Multivariate analysis of NICU admission.

Factor	Crude OR (95%CI)	Adjusted OR (95%CI)	p value
BMI (kg/m2)	1.05 (0.99,1.12)	1.04 (0. 96,1.12)	0.35
Preeclampsia	7.35 (2.23,24.23)	6.15 (1.39,27.15)	0.02
Duration of oxytocin use	1.10 (1.00,1.21)	1.10 (0.98,1.23)	0.11
Apgar score at 1 min	0.45 (0.35,0.60)	0.49 (0.35,0.67)	< 0.001
Apgar score at 5 min	0.35 (0.20,0.59)	0.73 (0.47,1.14)	0.17

Values are given as odds ratio (95% confidence interval)
NICU: neonatal intensive unit, OR: odds ratio, CI: confidence interval, BMI: body mass index

Discussion

This study observed that the adverse neonatal outcomes (MAS, RDS, intubation, PPHN, CPR, TTNB, neonatal sepsis, pneumonia, NICU admission, NMCU admission, and Apgar score < 7 at 1 and 5 min) in the C-section and NVD groups were not significantly different. This finding was slightly different from those in previous studies which found that intubation, RDS and NICU admission were higher in NVD groups; however, MAS and asphyxia were not different between groups[5]. The difference in outcomes may be due to this study had smaller sample size than the previous study.

Although univariate analysis of this study showed that C-section was associated with adverse neonatal outcomes ($p = 0.01$), multivariate analysis observed that C-section was not associated with adverse neonatal outcomes ($p = 0.80$). Furthermore, oxytocin use > 3 h was a significant confounding factor because the number of patients who received induction of labor and oxytocin use > 3 h in the C-section group was higher than in the NVD group. Therefore, the significant factor affecting adverse neonatal outcomes was oxytocin use > 3 h, not C-section. This finding correlated with a previous study[11]. This could be explained by oxytocin transiently compromising fetal circulation by increasing the duration, frequency, and strength of uterine contractions. The uterine and umbilical artery flow resistance increased significantly during uterine contractions reflecting a rapid and exaggerated increase of vascular resistance in both arteries which affects neonatal outcomes[12].

Overall, many significantly serious outcomes are associated with thick meconium-stained amniotic fluid, such as MAS and NICU admission. This study demonstrated that significant risk factors of MAS were patients not receiving antenatal care, receiving induction of labor, and having low Apgar scores for the newborn. This corresponded with previous studies describing the risk of MAS as significantly greater in the presence of fetal distress and a low Apgar score[13-16]. The induction of labor was a risk factor of MAS which could be explained by the tendency of induction to take a long time for labor, and prolonged labor caused an increase in the production of fetal cortisol which increased colonic contractions leading to passage meconium[17]. Additionally, a lower Apgar score of 1 min and preeclampsia significantly increased the risk of NICU admission, which agreed with the study of Duhan et al[18].

Additionally, this study showed that modes of delivery are not associated with adverse neonatal outcomes. Hence, the pregnant women who had thick meconium-stained amniotic fluid with normal FHR patterns (NICHD category I) did not necessarily require cesarean delivery. The results of the study can be applied in counseling the patients and guiding proper management about the mode of delivery in this patient group. For the patients who need oxytocin for induction should avoid long durations of oxytocin use and closed fetal heart rate monitoring, especially in oxytocin use > 3 h. Because these factors were associated with adverse neonatal outcomes.

The strength of our study was that there were no previous studies about mode of delivery and neonatal outcomes in pregnant women with thick meconium-stained amniotic fluid with NICHD category I FHR patterns in Thailand. This research was presented as the first investigation in Southern Thailand. However, there were some limitations of this study such as incomplete clinical data due to the retrospective study, and the selective bias cannot totally be excluded because this study population (thick meconium-stained amniotic fluid with NICHD category I FHR pattern) may have benefitted from the creation of the new institutional protocol. This study cannot totally exclude fetal growth restriction (FGR) due to non-available data such as prenatal fetal Doppler, amount of atrial fibrillation (AF), and Ballard score in some cases. The duration after the diagnosis of thick meconium-stained AF until delivery may affect the outcomes of this study. However, this data was not available in our center, so should be

interpreted with caution when assessing the correlation between modes of delivery and neonatal outcomes. We suggest that future study should include this factor for data analysis.

Conclusion

Modes of delivery were not associated with adverse neonatal outcomes in pregnant women who had thick meconium stained amniotic fluid with anormal FHR pattern (NICHD category I). The significant factor affecting the adverse neonatal outcomes was oxytocin use > 3 h.

Potential conflicts of interest

The authors declare no conflicts of interest.

References

1. Cunningham FG, Leveno KJ, Bloom SL, Dashe JS, Hoffman LB, Casey BM, et al. Williams Obstetrics. 25th ed. New York: McGraw-Hill 2018:135.
2. Panicker R, Win LL, Moopil J. Meconium-stained amniotic fluid revisited: a holistic perspective. J South Asian Feder Obst Gynae 2019;11:131-3.
3. Kavyashree HS, Suma KB. Study on effect of nature of meconium stained amniotic fluid on perinatal outcome. JMSCR 2015;3:6317-24.
4. Patra S, Shruthi SS, Puri M, Nangia S, Trivedi SS. Meconium-stained liquor in labour and mode of delivery: a time for reappraisal. Int J Reprod Contracept Obstet Gynecol 2020;9:4016-20.
5. Ouladsahebmadarek E, Hoseinian MH, Hamdi K, Ghojazadeh M. Perinatal outcome in relation to mode of delivery in meconium-stained neonates. Pak J Med Sci 2012;28:13-6.
6. Vaghela HP, Deliwala K, Shah P. Fetal outcome in deliveries with meconium-stained liquor. Int J Reprod Contracept Obstet Gynecol 2014;3:909-12.
7. Monfredini C, Cavallin F, Villani PE, Paterlini G, Allais B, Trevisanuto D. Meconium aspiration syndrome: a narrative review. Children 2021;8:230.
8. Mundhra R, Agarwal M. Fetal outcome in meconium-stained deliveries. J Clin Diagn Res 2013;7:2874-6.
9. Macones GA, Hankins GD, Spong CY, Hauth J, Moore T. The 2008 National Institute of Child Health and Human Development workshop report on electronic fetal monitoring: update on definitions, interpretation, and research guidelines. Obstet Gynecol 2008;112:661-6.
10. Samiyappa DP, Ghose S, John LB, Samal R. Maternal and perinatal outcome in meconium stained amniotic fluid at term: a case control study. Int J Reprod Contracept Obstet Gynecol 2016;5:3404-10.
11. Morel MI, Anyaegbunam AM, Mikhail MS, Legorreta A, Whitty JE. Oxytocin augmentation in arrest disorders in the presence of thick meconium: Influence on neonatal outcome. Gynecol Obstet Invest 1994;37:21-4.
12. Olofsson P, Thuring-Jonsson A, Marsál K. Uterine and umbilical circulation during the oxytocin challenge test. Ultrasound Obstet Gynecol 1996;8:247-51.
13. Rovas L, Razbadauskas A, Boguziene E. Risk factors that can lead to development of meconium aspiration syndrome. Obstet Gynecol Int J. 2018;9:208-12.
14. Dargaville PA, Copnell B. The epidemiology of meconium aspiration syndrome: incidence, risk factors, therapies, and outcome. Pediatrics 2006;117:1712-21.
15. Sori DA, Belete A, Wolde M. Meconium stained amniotic fluid: factors affecting maternal and perinatal outcomes at Jimma university specialized teaching hospital, South West Ethiopia. Gynecol Obstet (Sunnyvale) 2016;6:1-6.
16. Khazardoost S, Hantoushzadeh S, Khooshideh M, Borna S. Risk factors for meconium aspiration in meconium-stained amniotic fluid. J Obstet Gynaecol2007; 27:577-9.
17. Halle-EkaneGE, Fon PN, Koki PN, Tazinya AA, Ekollo R, Mboudou E. Maternal and perinatal outcomes in childbirths with meconium-stained amniotic fluid in a low-resource setting: a prospective cohort study. ACRI 2019;17:1-11.
18. Duhan N, Paul A, Duhan U, Anjali. Meconium staining of amniotic fluid-a poor indicator of fetal compromise. JK Science 2010;12:184-6.