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Factors Associated with Meconium Aspiration Syndrome in Cases with Meconium-Stained Amniotic Fluid

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ABSTRACT

Objectives: To determine the factors associated with meconium aspiration syndrome (MAS) in cases with meconium-stained amniotic fluid (MSAF) at Chonburi Hospital.

Materials and Methods: Singleton pregnancies delivered at Chonburi Hospital with vertex presentation with MSAF during the 15 May 2011 – 15 May 2014 period were reviewed. These pregnancies included women who delivered at or beyond 24 weeks of gestation or birth weight at least 700 grams but excluded those who delivered infants with lethal congenital abnormalities. They were divided into 2 groups depending on whether the neonates developed MAS or not. The two groups were compared retrospectively regarding baseline characteristics, and then binary logistic regression analysis was used to identify independent significant factors associated with MAS.

Results: Among 776 pregnancies who met the inclusion criteria, 111 neonates developed MAS, 665 neonates did not. Thick meconium, abnormal external fetal monitoring, non-vigorous newborn, Apgar score at 1 minute less than or equal to 7, and low birth weight were significantly associated with MAS ($p<0.05$). By the binary logistic regression analysis; thick meconium, non-vigorous newborn, and Apgar score at 1 minute less than or equal to 7 remained statistically significant (OR 4.82, 95% CI 2.86-8.14, OR 5.87, 95% CI 2.84-12.13 and OR 3.23, 95% CI 1.60-6.54, respectively).

Conclusion: Thick meconium, non-vigorous newborn and Apgar score at 1 minute less than or equal to 7 were associated with MAS in MSAF

Keywords: Factors, meconium aspiration syndrome, meconium-stained amniotic fluid

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ปัจจัยที่มีความสัมพันธ์ต่อการสูดสำลักขี้เทาของทารกแรกเกิดในรายที่มารดามีขี้เทาปนในน้ำคร่ำ

สิริพร ไตรนาค, ธีระ ศิวะดุลย์

บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาปัจจัยที่เกี่ยวข้องต่อการเกิดภาวะสำลักขี้เทาของทารกแรกเกิดในรายที่มารดามีขี้เทาปนในน้ำคร่ำ*

วิธีการวิจัย: *ศึกษาด้วยวิจัยเชิงวิเคราะห์ ในมารดาที่คลอดบุตรในโรงพยาบาลชลบุรี ในช่วงวันที่ 15 พฤษภาคม 2554 ถึง 15 พฤษภาคม 2557 โดยมารดาที่ศึกษา เป็นมารดาที่คลอดทารกท่าศีรษะครรภ์เดี่ยวที่มีขี้เทาปนในน้ำคร่ำ อายุครรภ์ตั้งแต่ 24 สัปดาห์หรือน้ำหนักแรกคลอด 700 กรัมขึ้นไป และไม่พบความผิดปกติที่ไม่สามารถมีชีวิตหลังคลอดได้ โดยนำปัจจัยที่เกี่ยวข้องมาหาความสัมพันธ์แบบตัวแปรเดี่ยว จากนั้นนำปัจจัยที่มีความสัมพันธ์ต่อการเกิดภาวะสำลักขี้เทาดังกล่าวมาวิเคราะห์การถดถอยโลจิสติกเพื่อควบคุมอิทธิพลจากปัจจัยอื่นอีกครั้ง*

ผลการวิจัย: *ในหญิงตั้งครรภ์ที่มีขี้เทาปนในน้ำคร่ำ 776 ราย แบ่งเป็นกลุ่มที่ทารกเกิดภาวะสำลักขี้เทา 111 ราย และไม่เกิดภาวะสำลักขี้เทา 665 ราย หลังวิเคราะห์ความสัมพันธ์ตัวแปรเดี่ยวพบว่า มารดาที่มีขี้เทาลักษณะเหนียวข้น, ทารกในครรภ์มีการเต้นของหัวใจผิดปกติและไม่ตอบสนองหลังการแก้ไข, ประเมินทารกแรกคลอดพบมีหัวใจเต้นผิดปกติหรือหายใจผิดปกติหรือความตึงตัวลดลงหลังคลอด, ประเมินสภาวะทารกแรกเกิดที่เวลา 1 นาทีแรกได้คะแนนน้อยกว่าหรือเท่ากับ 7 คะแนน, และ น้ำหนักแรกคลอดทารกน้อยกว่า 2500 กรัม มีความสัมพันธ์กับการเกิดภาวะสำลักขี้เทา แต่เมื่อนำปัจจัยทั้ง 5 ข้างต้นมาวิเคราะห์ถดถอยโลจิสติก พบว่ามีสามปัจจัยที่ยังคงมีความสัมพันธ์ต่อการเกิดภาวะสำลักขี้เทาของทารกในรายที่มารดามีขี้เทาปนในน้ำคร่ำ คือ มารดาที่มีขี้เทาลักษณะเหนียวข้น, ประเมินทารกแรกคลอดพบมีหัวใจเต้นผิดปกติหรือหายใจผิดปกติหรือความตึงตัวลดลงหลังคลอด, ประเมินสภาวะทารกแรกเกิดที่เวลา 1 นาทีแรกได้คะแนนน้อยกว่าหรือเท่ากับ 7 คะแนน (OR 4.82, 95% CI 2.86-8.14, OR 5.87, 95% CI 2.84-12.13 และ OR 3.23, 95% CI 1.60-6.54 ตามลำดับ)*

สรุป: *มารดาที่มีขี้เทาลักษณะเหนียวข้น และ/หรือ ประเมินทารกแรกคลอดพบมีหัวใจเต้นผิดปกติหรือหายใจผิดปกติหรือความตึงตัวลดลงหลังคลอด และ/หรือ ประเมินสภาวะทารกแรกเกิดที่เวลา 1 นาทีแรกได้คะแนนน้อยกว่าหรือเท่ากับ 7 คะแนน มีความสัมพันธ์อย่างมีนัยสำคัญทางสถิติ ต่อการเกิดภาวะสำลักขี้เทาของทารกในรายที่มารดามีขี้เทาปนในน้ำคร่ำ*

Introduction

Meconium is found in amniotic fluid about 12-22% of labors[1, 2]. Three theories have been suggested to explain this condition. First, the fetus excretes meconium due to oxygen deficiency during pregnancy[3]. Second, as physiological mechanism, gastrointestinal tract maturation and neural control of the fetus cause meconium expulsion[4]. Third, vagal stimulation due to transient umbilical cord entrapment causes increasing of the intestine peristalsis[5]. Therefore, the presence of meconium in amniotic fluid could be physiologic or pathologic condition; the latter indicates oxygen deficiency of the fetus.

Aspiration of meconium into the lungs during intrauterine gasping or at the time of first breath must be concerned[6]. About 1.8-18% of meconium-exposed newborns develop meconium aspiration syndrome (MAS) causing respiratory airway obstruction, pulmonary inflammation, surfactant dysfunction, poor gas exchange, and pulmonary hypertension[7]. The consequences of these lung problems and hypoxia lead to increase neonatal morbidity and account for 2% of perinatal death[7, 8].

From existing data, meconium-stained amniotic fluid (MSAF) was found regularly in Chonburi Hospital and occasionally caused MAS. This research work focuses on finding the factors associated with MAS in meconium-complicated labors and epidemiological incidence of MAS in order to initiate better monitoring and develop practice guidelines for taking care of these pregnant women with associated factors.

Materials and Methods

This retrospective analytic study was approved by Institutional Review Board of Chonburi Hospital, Thailand. Medical records of 776 pregnancies with MSAF who delivered at Chonburi Hospital from 15 May 2011 – 15 May 2014 were reviewed. Inclusion criteria were singleton pregnant women who delivered at or beyond 24 weeks of gestation or birth weight at least 700 grams. Exclusion criteria were non-vertex delivery or infants with lethal congenital abnormalities.

MAS neonates, diagnosed based on the presence of respiratory distress and typical chest x-ray findings, were searched from discharge diagnosis on hospital's database.

In our institution, meconium is individually graded by residents in training due to the unavailability of meconium-crit[9]. Meconium in amniotic fluid is graded as thick if the fluid is tenacious, viscous, and opaque and it is graded as thin if it appears to be watery and yellowish to light greenish coloration.

The primary objective was to identify factors associated with MAS in newborns delivered by mothers with MSAF. The secondary objective was to calculate the incidence of MAS in the newborns in Chonburi Hospital.

Sample size in our study was calculated by using the formula from Peduzzi et al[10]. We used the prevalence of MAS in MSAF based on a previous study[11]. We were able to include a total of 776 participants, which was greater than the calculated sample size of 765.

Statistical analysis

Continuous variables were presented as mean with standard deviation, and categorical variables as number with percentage. Chi-square test was used to compare statistical difference among categorical variables, while t-test was used to compare statistical difference among continuous variables. Factors significantly associated with MAS ($P<0.05$) were selected for logistic regression analysis to identify independent factors significantly associated with MAS and to calculate odds ratio (OR) and 95% confidence interval (95%CI). Data were analyzed with SPSS version 18.

Results

During 15 May 2011 – 15 May 2014, 776 vertex singleton pregnancies with MSAF were enrolled to the study, 111 neonates developed MAS and 665 did not. MAS developed in 14.3% of infants delivered in the presence MSAF at Chonburi Hospital.

Table 1, comprised maternal, labor, and neonatal characteristics, and showed that the majority of the

population was Thai, nulliparous, and 27 years old on average. Most patients had body mass index (BMI) between 25-29.9 kg/m^2. In both groups, more than 85% of the populations were 37^{+0} to 41^{+6} weeks' gestation. The majority of the population gave birth by caesarean section. The average interval of membranes rupture of the non-MAS was 5.37 hours while that of MAS was 5.45 hours. Evidently, there were no significant statistical discrepancies between the groups.

Nevertheless, there were significant statistical differences in five factors. The first factor was the type of meconium. The ratio of thick meconium to thin meconium in the MAS group (68.5%) was clearly larger than that of non-MAS group (18.6%) at P<0.01. The second factor was abnormal external fetal monitoring (EFM). The findings showed that the ratio of abnormal EFM (EFM category II or III that did not turn to EFM category I after intrauterine resuscitation) to normal EFM were more in the MAS group (18.9%) than in non-MAS group (11.6%) at P=0.03. The third factor was low birth weight. The rate of low birth weight was higher in the MAS group (13.5% vs. 6.3%; P<0.01). The fourth factor was the non-vigorous neonates. There were more non-vigorous neonates in the MAS group (56.8% vs. 5.7%; P < 0.01). The fifth factor was the Apgar score at 1 minute. The data showed that there were more cases where 1-minute Apgar score less than or equal to 7 in the MAS group than in the non-MAS group (63.1% vs. 9.9%; P<0.01).

Table 2, binary logistic regression was used to analyze the five factors from Table 1. Three factors were identified as independent associated factors with MAS. These factors included thick meconium (OR 4.82; 95% CI 2.86-8.14), non-vigorous neonates (OR 5.87; 95% CI 2.84-12.13), and the Apgar score at 1 minute less than or equal to 7 (OR 3.23; 95% CI 1.60-6.54).

Table 1. Baseline characteristics of patients with MSAF.

Baseline Characteristics	Non-MAS (n = 665)	MAS (n = 111)	p value
Nationality			0.46
Thai	570 (85.7%)	88 (79.3%)	
Cambodia	37 (5.6%)	9 (8.1%)	
Laos	8 (1.2%)	2 (1.8%)	
Myanmar	42 (6.3%)	11 (9.9%)	
Other	8 (1.2%)	1 (0.9%)	
Age (years)			0.93
Less than 35 years	579 (87.1%)	97 (87.4%)	
35 years or more	86 (12.9%)	14 (12.6%)	
Mean (SD)	27.06 (6.36)	27.08 (6.81)	0.97
BMI (kg/m^2)			0.65
Less than 18.5	5 (0.8%)	1 (0.9%)	
18.5-22.9	53 (8.0%)	11 (9.9%)	
23-24.9	74 (11.1%)	17 (15.3%)	
25-29.9	315 (47.4%)	50 (45.0%)	
30 or more	218 (32.8%)	32 (28.8%)	
Parity			0.92
Nulliparity	470 (70.7%)	79 (71.2%)	
Multiparity	195 (29.3%)	32 (28.8%)	

Table 1. Baseline characteristics of patients with MSAF. (Cont.)

Baseline Characteristics	Non-MAS (n = 665)	MAS (n = 111)	p value
Gestational age (weeks)			0.13
Less than 37^{+0}	30 (4.5%)	7 (6.3%)	
37^{+0} - 41^{+6}	607 (91.3%)	95 (85.6%)	
42^{+0} or more	28 (4.2%)	9 (8.1%)	
Duration of membrane rupture			0.68
Less than 18 hrs	635 (95.5%)	105 (94.6%)	
18 hrs or more	30 (4.5%)	6 (5.4%)	
Mean (SD)	5.37(6.56)	5.45 (6.50)	0.91
Route of delivery			0.44
Vaginal delivery	210 (31.6%)	31 (27.9%)	
Normal labor	5 (2.4%)	1 (3.2%)	
Forceps extraction	13 (6.2%)	4 (12.9%)	
Vacuum extraction	192 (91.4%)	26 (83.9%)	
Cesarean section	455 (68.4%)	80 (72.1%)	
Type of meconium			< 0.01*
Thin Meconium	541 (81.4%)	35 (31.5%)	
Thick Meconium	124 (18.6%)	76 (68.5%)	
External fetal monitoring			0.03*
Normal EFM	588 (88.4%)	90 (81.1%)	
Abnormal EFM	77 (11.6%)	21 (18.9%)	
Vigorous status			< 0.01*
Vigorous	627 (94.3%)	48 (43.2%)	
Non-vigorous	38 (5.7%)	63 (56.8%)	
Apgar score at1 minute			< 0.01*
Less than or equal 7	66 (9.9%)	70 (63.1%)	
More than 7	599 (90.1%)	41 (36.9%)	
Birth weight			
Less than 2,500 gm	42 (6.3%)	15 (13.5%)	
2,500 gm or more	623 (93.7%)	96 (86.5%)	

* $p < 0.05$ was considered statistically significant.

Table 2. Binary logistic regression analysis for associated factors of meconium aspiration syndrome.

Characteristics	Adjusted OR	95% CI	P
Thick meconium	4.82	2.86 - 8.14	< 0.01*
Abnormal EFM	0.59	0.29 - 1.19	0.14
Non-vigorous neonates	5.87	2.84 - 12.13	< 0.01*
Apgar score at 1 minute less than or equal 7	3.23	1.60 - 6.54	< 0.01*
Birth weight less than 2,500 gm	1.85	0.82 - 4.20	0.14

* $p < 0.05$ was considered statistically significant.

Discussion

Previous studies showed that the incidence of MAS in cases with MSAF varies greatly (from 1.8 to 18%)[7], while this study yielded the value of 14.3%. Although the value fell in the range, it exceeded that of the study by Uthaithani Hospital[11], which was 6.54%. The possible reason is that Chonburi Hospital is the center hospital of the eastern region of Thailand, which means it has more chance of admitting transferred patients. Anyway, the data strongly suggested that we have to put in more effort into handling MAS and MSAF both in terms of prevention and cure.

This study showed three independent associated factors which could assist the doctors in forecasting MAS in MSAF in order to prepare proper management for patients. The factors were thick meconium, non-vigorous neonates, and the Apgar score at 1 minute less than or equal to 7. In addition, these factors were the same results as previous studies[12-14].

Correlation between the presence of thick meconium during labor and increasing meconium aspiration, neonatal asphyxia, and other adverse neonatal outcomes was expected. Close monitoring of the fetus, clinically, or with EFM, becomes imperative after thick intrapartum meconium is identified. To achieve a positive outcome, thick meconium should indicate need for immediate intervention, skilled pediatric attention at the time of delivery, and more intensive care during the neonatal period.

Non-vigorous physical activities were occasionally found in neonates born through MSAF. This study revealed explicit correlation of MAS occurrence in pregnant women with MSAF. Therefore, if MSAF is present, monitoring is required. If a newborn is non-vigorous, proper management especially neonatal resuscitation and endotracheal suction must be employed in order to improve the perinatal outcome.

Regarding the Apgar scores, Starks had reported that newborns with thick meconium had significantly lower Apgar scores at 1 minute while babies with thin meconium had no increased risk. That means, it can be inferred that thick meconium as a single variable is the most significant factor affecting the fetal outcome. In this study, 1-minute Apgar scores were investigated as a measure of neonatal outcome. It was found that, compared to the group of infants with thin meconium, significant numbers of cases in the group of infants with thick meconium had lower Apgar scores. Many research groups have reported corresponding results[15, 16]. The low Apgar scores might be resulted from direct vasoconstrictor effect of meconium on the umbilical vein, leading to vasospasm and, consequently, impaired placental blood flow[17].

Nevertheless, these works could not confirm that the risk factors reported earlier[18-21], e.g., nulliparity, gender, postdates, and low birth weight, have any correlation with MAS.

Thick meconium, among three independent associated factors, is the only factor obstetricians can perceive before delivery. Future studies regarding antepartum management of patients with thick meconium should be conducted, and this may possibly lead to more effective patient care and minimize MAS. Unfortunately, some other variables were not studied due to unavailability of some information in Chonburi Hospital's database. Anyway, the strength of this research work is the use of logistic regression analysis which keeps any undesired effects from confounding factors to a minimum.

Conclusion

It is a common knowledge that MAS causes serious respiratory problems in neonates. This work urges doctors to be more aware of the association of MSAF and MAS. Neonates with MSAF with at least one of the aforementioned risk factors (thick MSAF, non-vigorous neonates, Apgar score at 1 minute less than or equal to 7) need intensive care due to the higher risk to develop MAS

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Potential conflcts of interest

The authors declare no conflct of interest.

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