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The frequency of meconium-stained amniotic fluid increases as a function of the duration of labor

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Abstract

Objective—The purpose of this study was to determine whether there is a relationship between the frequency of meconium-stained amniotic fluid (MSAF) and the duration of labor in term singleton gestation.

Methods—The clinical characteristics of women who delivered term singleton live newborns between 2001 and 2006 were examined. The cases involving neonates with major congenital anomalies were excluded.

Results—(1) The frequency of MSAF in term pregnancies was 18.4% (806/4376); (2) MSAF was found in only 2.8% (28/1008) of women who delivered by elective cesarean, but in 23.1% (778/3368) of women who delivered after the onset of labor ($p<0.001$); (3) The longer the duration of labor (first stage, second stage, or total), the higher the frequency of MSAF ($p<0.001$ for each); this remained significant after adjusting for other confounding variables such as parity, duration of rupture of membranes, gestational age at delivery, and mode of delivery ($p<0.001$ for each).

Conclusion—MSAF was found in only 2.8% (28/1008) of women who delivered before the onset of labor, but in 23.1% (778/3368) of women who delivered after the onset of labor. The longer the duration of labor, the higher the risk of MSAF in term singleton gestation.

Keywords

Fetal bowl function; first stage of labor; pregnancy

INTRODUCTION

Meconium-stained amniotic fluid (MSAF) is frequently observed in the labor and delivery unit and is a risk factor for neonatal meconium aspiration syndrome [1–11], sepsis [12], pulmonary disease and death [1,3,5,9,13], subsequent development of cerebral palsy [14], amniotic fluid infection [15], chorioamnionitis [5,9,12,16–18], puerperal endometritis [17], and dehiscence of perineal lacerations [19].

Although the precise etiology of MSAF is still unclear, risk factors for MSAF include advanced gestational age at delivery, mode of delivery, increased duration of rupture of membranes (ROM), prolonged second stage of labor, and intra-amniotic infection

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[8,9,15,17,20,21]. Recently, Cheng et al. [20] demonstrated that the longer the duration of the second stage of labor, the higher the frequency of MSAF (21% when the second stage was less than 1 h, and 28% when it was longer than 3 h). However, there is a paucity of information about the risk of MSAF when the neonate is born before the onset of labor (elective cesarean delivery) or according to the total duration of labor or duration of the first stage of labor. This study was conducted to examine the frequency of MSAF as a function of the duration of labor.

METHODS

The study population consisted of consecutive pregnant women who delivered term (between 37 and 42 weeks of gestational age) singleton live newborns at Seoul National University Hospital between 2001 and 2006. Patients who delivered neonates with a major congenital anomaly were excluded. The presence or absence of meconium was determined at the time of delivery by visual observation. Elective amniotomy is not routine practice in our institution.

Electronic medical records were reviewed for demographics, antenatal and intrapartum characteristics and pregnancy outcomes: maternal age, parity, presence or absence of labor and MSAF at delivery, premature rupture of membranes (PROM), duration of ROM, duration of labor (the first and second stages of labor and total), gestational age at delivery, birth weight, mode of delivery, Apgar scores, umbilical artery pH at birth and admission to the neonatal intensive care unit (NICU). These variables were compared according to the presence of absence of MSAF at the time of delivery. In this study, the women who delivered by elective cesarean section were not in labor. We did an extensive review of medical records and did not include women with regular uterine contractions with or without cervical change. The onset of labor was defined as regular painful uterine contractions based on history taken from the patients. The duration of labor was analyzed only in patients admitted before a cervical dilatation of 4 cm. The duration of the first stage was defined as the length of time elapsed during the progression of cervical dilatation from 4 cm to 10 cm. The duration of the second stage was defined as the length of time elapsed from full cervical dilatation to delivery of the fetus [22]. This study, as well as the use of medical records for research purposes was approved by the Institutional Review Board of the Seoul National University Hospital.

Statistical analysis was performed using SPSS version 12.0 (SPSS Inc., Chicago, IL). Univariate analysis was conducted using Fisher's exact test or Student *t*-test as appropriate. Multiple logistic regression analysis was conducted for the adjustment of confounding variables. A probability value of <0.05 was considered significant.

RESULTS

The frequency of MSAF in term pregnancies was 18.4% (806/4376). MSAF was found in only 2.8% (28/1008) of women who delivered by elective cesarean, but in 23.1% (778/3368) of women who delivered after the onset of labor ($p<0.001$).

Table I compares the clinical characteristics and pregnancy outcomes according to the presence of absence of MSAF at birth. Cases with MSAF had significantly higher maternal age, gestational age at birth and birth weight, higher rates of nulliparity, delivery after the onset of labor and umbilical arterial pH less than 7.0, and longer mean duration of ROM and duration of labor (total, first stage or second stage) than those without MSAF ($p<0.05$ for each). In particular, 96.5% (778/806) of the cases with MSAF experienced labor before delivery. The rate of PROM was lower in patients with MSAF than in those without MSAF,

but was not statistically significant ($p>0.1$). Women with MSAF underwent cesarean delivery less frequently than those without MSAF ($p<0.001$) because 74% (1008/1356) of women who delivered by cesarean had no labor before delivery, and the occurrence of MSAF was not frequency under such conditions. Neonates with MSAF had a significantly higher rate of admission to the NICU ($p<0.001$).

Figure 1 shows the frequency of MSAF according to the duration of labor among women who delivered after the onset of labor. The longer the duration of labor (first stage, second stage, or total), the higher the frequency of MSAF ($p<0.001$ for each, see Figure 1). This relationship persisted after adjusting for other confounding variables ($p<0.001$, see Table II).

DISCUSSION

Principal findings of the study

(1) The frequency of MSAF in term pregnancies was 18.4%; (2) MSAF was found in only 2.8% of women who delivered by elective cesarean, but in 23.1% of women who delivered after the onset of labor; and (3) the longer the duration of labor (first stage, second stage, or total), the higher the frequency of MSAF.

MSAF according to the presence or absence of labor

In the current study, MSAF was found in only 2.8% of term pregnant women who delivered before the onset of labor. In contrast, MSAF was identified in approximately 25% of women who delivered after the onset of labor. This frequency is similar to those reported by other investigators [8,17]. Therefore, this finding is consistent with the view that the present of labor is strongly associated with the passage of meconium into the amniotic fluid.

Why is labor a risk factor for MSAF?

Corticotropic-releasing hormone (CRH) derived from the placenta has been suggested to play an important role in the onset of labor [23,24]. Placental CRH may not only modulate myometrial contractility, but also stimulates the production of cortisol from the fetal adrenal gland [23,25]. It has been demonstrated that the cortisol concentration is significantly higher in term newborns delivered after the onset of labor than in those delivered before the onset of labor [26]. Moreover, the umbilical cord blood cortisol concentration is significantly higher in newborns with MSAF than in those without MSAF [25,27]. Term fetal rats and fetal sheep can pass meconium before delivery via CRH, a known mediator of colonic motility [24,28]. Therefore, CRH itself and/or labor might stimulate meconium passage [7,23,25,28]. These observations suggest that MSAF might be a result of labor.

Another explanation of hypoxia. Parasympathetic stimulation of the fetal bowel due to hypoxic events or other stressors may induce premature bowel movements, leading to meconium passage in amniotic fluid [10,29–31]. Many previous studies have demonstrated that there is an association between MSAF and drop in the arterial cord pH value [5,10]. There is a significant inverse relationship in umbilical artery pH with the presence of labor in term newborns [5,32]. Our data also indicate that the umbilical cord pH <7.0 was significantly lower in newborns with MSAF than in those without MSAF (Table I). However, the difference in the mean umbilical cord pH between the two groups was too small to reach significance. Furthermore, after adjusting for confounding variables, an umbilical arterial pH less than 7.0 was not an independent risk factor for MSAF (Table II).

Gestational age at MSAF

The frequency of MSAF increased with advance gestational age at delivery independent of the presence or absence of labor in the current study. This finding is consistent with the

results of previous studies and gives support to the view that MSAF could be a physiologic event that represent normal gastrointestinal tract maturation under the fetal autonomic nervous system [7,9,33–35].

MSAF and duration of labor and parity

Nulliparity itself may lead to an increased risk of obstetric complications [36]. However, based on the inspection of demographic characteristics of the existing studies, it is not clear whether or not MSAF is associated with nulliparity [10,13,18,37]. The duration of labor of a nulliparous woman is significantly longer than that of a multiparous woman [38,39]. Several investigators have demonstrated that prolonged duration of the second stage of labor is associated with a higher risk of the occurrence of MSAF [20,40]. These observations suggest that the frequency of MSAF is higher among nulliparous women than among multiparous women after the onset of labor because of a longer duration of the second stage of labor in nulliparous women. The results of our study support the view and are consistent with findings of the previous studies [6,8]. Interestingly, these positive relationships between MSAF and the duration of the second stage of labor existed between MSAF and the duration of the first stage and total duration of labor (Figure 1).

MSAF and PROM

PROM is a well-known risk factor for intrauterine infection [41–55]. Several investigators have suggested that MSAF is highly associated with infection, including endometritis and chorioamnionitis [16,17]. Based on these reports, one would expect that the frequency of MSAF would be higher in the PROM group than the group without PROM. Unexpectedly, our study demonstrated that the frequency of PROM in cases with MSAF was similar to that in cases with clear amniotic fluid in the total population, but lower than those without MSAF in the labor group. In addition, two large-scale studies demonstrated that the frequency of PROM was significantly lower in the MSAF group than in the clear amniotic fluid group [18,41]. The mechanisms for this are unknown.

Strength of this study

W confirmed the frequency of MSAF in women not in labor is drastically lower than in women with labor and clarified the association between MSAF and the duration of labor.

Unanswered questions and proposals for future research

Romero et al. [15] demonstrated that the prevalence of a positive amniotic fluid culture was significantly higher in patients with MSAF than in those without MSAF among those who underwent transabdominal amniocentesis because of preterm labor and intact membranes. However, this kind of information is not available in pregnant women at term. We recently demonstrated that the presence and progression of labor are associated with an increased risk of a positive amniotic fluid culture for microorganisms, a more intense intra-amniotic response and histologic chorioamnionitis in term pregnancy with intact membranes [56]. The relationship between the presence of MSAF and intra-amniotic infection or inflammation in term pregnancy should be examined in a large number of term pregnant women with the results of amniotic fluid analysis.

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REFERENCES

1. Katz VL, Bowes WA Jr. Meconium aspiration syndrome: reflections on a murky subject. Am J Obstet Gynecol. 1992; 166:171–183. [PubMed: 1733193]
2. Blackwell SC, Moldenhauer J, Hassan SS, Redman ME, Refuerzo JS, Berry SM, Sorokin Y. Meconium aspiration syndrome in term neonates with normal acid-base status at delivery: is it different? Am J Obstet Gynecol. 2001; 184:1422–1425. discussion 5–6. [PubMed: 11408862]
3. Vain NE, Szyld EG, Prudent LM, Wiswell TE, Aguilar AM, Vivas NI. Oropharyngeal and nasopharyngeal suctioning of meconium-stained neonates before delivery of their shoulders: multicentre, randomised controlled trial. Lancet. 2004; 364:597–602. [PubMed: 15313360]
4. Fraser WD, Hofmeyr J, Lede R, Faron G, Alexander S, Goffinet F, Ohlsson A, Goulet C, Turcot-Lemay L, Prendiville W, et al. Amnioinfusion for the prevention of the meconium aspiration syndrome. N Engl J Med. 2005; 353:909–917. [PubMed: 16135835]
5. Ziadeh SM, Sunna E. Obstetric and perinatal outcome of pregnancies with term labour and meconium-stained amniotic fluid. Arch Gynecol Obstet. 2000; 264:84–87. [PubMed: 11045329]
6. Greenwood C, Lalchandani S, MacQuillan K, Sheil O, Murphy J, Impey L. Meconium passed in labor: how reassuring is clear amniotic fluid? Obstet Gynecol. 2003; 102:89–93. [PubMed: 12850612]
7. Ahanya SN, Lakshmanan J, Morgan BL, Ross MG. Meconium passage in utero: mechanisms, consequences, and management. Obstet Gynecol Surv. 2005; 60:45–56. quiz 73–74. [PubMed: 15618919]
8. David AN, Njokanma OF, Iroha E. Incidence of and factors associated with meconium staining of the amniotic fluid in a Nigerian University Teaching Hospital. J Obstet Gynaecol. 2006; 26:518–520. [PubMed: 17000496]
9. Oyelese Y, Culin A, Ananth CV, Kaminsky LM, Vintzileos A, Smulian JC. Meconium-stained amniotic fluid across gestation and neonatal acid–base status. Obstet Gynecol. 2006; 108:345–349. [PubMed: 16880305]
10. Becker S, Solomayer E, Dogan C, Wallwiener D, Fehm T. Meconium-stained amniotic fluid – perinatal outcome and obstetrical management in a low-risk suburban population. Eur J Obstet Gynecol Reprod Biol. 2007; 132:46–50. [PubMed: 16837118]
11. de Beaufort AJ. Early human development at the perinatal interface: meconium stained amniotic fluid (MSAF) and meconium aspiration syndrome (MAS). Early Hum Dev. 2009; 85:605. [PubMed: 19822400]
12. Berkus MD, Langer O, Samueloff A, Xenakis EM, Field NT, Ridgway LE. Meconium-stained amniotic fluid: increased risk ror adverse neonatal outcome. Obstet Gynecol. 1994; 84:115–120. [PubMed: 8008304]
13. Alchalabi H, Abu-Heija AT, El-Sunna E, Zayed F, Badria LF, Obeidat A. Meconium-stained amniotic fluid in term pregnancies – a clinical view. J Obstet Gynaecol. 1999; 19:262–264. [PubMed: 15512291]
14. Spinillo A, Fazzi E, Capuzzo E, Stronati M, Piazzi G, Ferrari A. Meconium-stained amniotic fluid and risk for cerebral palsy in preterm infants. Obstet Gynecol. 1997; 90:519–523. [PubMed: 9380308]
15. Romero R, Hanaoka S, Mazor M, Athanassiadis AP, Callahan R, Hsu YC, Avila C, Nores J, Jimenez C. Meconium-stained amniotic fluid: a risk factor for microbial invasion of the amniotic cavity. Am J Obstet Gynecol. 1991; 164:859–862. [PubMed: 1900664]
16. Rao S, Pavlova Z, Incerpi MH, Ramanathan R. Meconiumstained amniotic fluid and neonatal morbidity in near-term and term deliveries with acute histologic chorioamnionitis and/or funisitis. J Perinatol. 2001; 21:537–540. [PubMed: 11774015]
17. Tran SH, Caughey AB, Musci TJ. Meconium-stained amniotic fluid is associated with puerperal infections. Am J Obstet Gynecol. 2003; 189:746–750. [PubMed: 14526306]
18. Maymon E, Chaim W, Furman B, Ghezzi F, Shoham Vardi I, Mazor M. Meconium stained amniotic fluid in very low risk pregnancies at term gestation. Eur J Obstet Gynecol Reprod Biol. 1998; 80:169–173. [PubMed: 9846662]

19. Williams MK, Chames MC. Risk factors for the breakdown of perineal laceration repair after vaginal delivery. Am J Obstet Gynecol. 2006; 195:755–759. [PubMed: 16949409]
20. Cheng YW, Hopkins LM, Laros RK Jr, Caughey AB. Duration of the second stage of labor in multiparous women: maternal and neonatal outcomes. Am J Obstet Gynecol. 2007; 196:585 e1–585 e6. [PubMed: 17547906]
21. Burgess AM, Hutchins GM. Inflammation of the lungs, umbilical cord and placenta associated with meconium passage in utero. Review of 123 autopsied cases. Pathol Res Pract. 1996; 192:1121–1128. [PubMed: 9122031]
22. Lee SM, Lee KA, Lee J, Park CW, Yoon BH. 'Early rupture of membranes' after the spontaneous onset of labor as a risk factor for cesarean delivery. Eur J Obstet Gynecol Reprod Biol. 2010; 148:152–157. [PubMed: 20005623]
23. Grammatopoulos DK, Hillhouse EW. Role of corticotropinreleasing hormone in onset of labour. Lancet. 1999; 354:1546–1549. [PubMed: 10551516]
24. Lakshmanan J, Oyachi N, Ahanya SA, Liu G, Mazdak M, Ross MG. Corticotropin-releasing factor inhibition of sheep fetal colonic contractility: mechanisms to prevent meconium passage in utero. Am J Obstet Gynecol. 2007; 196:357 e1–357 e7. [PubMed: 17403421]
25. Miller NM, Fisk NM, Modi N, Glover V. Stress responses at birth: determinants of cord arterial cortisol and links with cortisol response in infancy. BJOG. 2005; 112:921–926. [PubMed: 15957993]
26. Oh SY, Romero R, Shim SS, Park JS, Jun JK, Yoon BH. Fetal plasma cortisol and dehydroepiandrosterone sulfate concentrations in pregnancy and term parturition. J Matern Fetal Neonatal Med. 2006; 19:529–536. [PubMed: 16966120]
27. Mears K, McAuliffe F, Grimes H, Morrison JJ. Fetal cortisol in relation to labour, intrapartum events and mode of delivery. J Obstet Gynaecol. 2004; 24:129–132. [PubMed: 14766445]
28. Lakshmanan J, Ahanya SN, Rehan V, Oyachi N, Ross MG. Elevated plasma corticotrophin release factor levels and in utero meconium passage. Pediatr Res. 2007; 61:176–179. [PubMed: 17237718]
29. Ciftci AO, Tanyel FC, Bingol-Kologlu M, Sahin S, Buyukpamukcu N. Fetal distress does not affect in utero defecation but does impair the clearance of amniotic fluid. J Pediatr Surg. 1999; 34:246–250. [PubMed: 10052797]
30. Gursoy T, Tekinalp G, Yigit S, Kirazli S, Korkmaz A, Gurgey A. Thrombin activatable fibrinolysis inhibitor activity (TAFIa) levels in neonates with meconium-stained amniotic fluid. J Matern Fetal Neonatal Med. 2008; 21:123–128. [PubMed: 18240081]
31. Simsek A, Celen S, Islimye M, Danisman N, Buyukkagnici U. A long-standing incomprehensible matter of obstetrics: meconium-stained amniotic fluid, a new approach to reason. Arch Gynecol Obstet. 2008; 278:559–563. [PubMed: 18343934]
32. Yoon BH, Kim SW. The effect of labor on the normal values of umbilical blood acid-base status. Acta Obstet Gynecol Scand. 1994; 73:555–561. [PubMed: 8079606]
33. Ramon y Cajal CL, Martinez RO. Defecation in utero: a physiologic fetal function. Am J Obstet Gynecol. 2003; 188:153–156. [PubMed: 12548210]
34. Ramon YCCL, Martinez RO. In-utero defecation between weeks 14 and 22 of gestation: stools are whitish. Ultrasound Obstet Gynecol. 2004; 23:94–95. [PubMed: 14971008]
35. Ciftci AO, Tanyel FC, Karnak I, Buyukpamukcu N, Hicsonmez A. In-utero defecation: fact or fiction? Eur J Pediatr Surg. 1999; 9:376–380. [PubMed: 10661847]
36. Malkiel A, Pnina M, Aloni H, Gdansky E, Grisaru-Granovsky S. Primiparity: a traditional intrapartum obstetric risk reconfirmed. Isr Med Assoc J. 2008; 10:508–511. [PubMed: 18751628]
37. Liu BY, Wang CC, Lau TK, Chu CY, Phil M, Pang CP, Rogers MS, Leung TN. Meconium-stained liquor during labor is associated with raised neonatal cord blood 8-isoprostaglandin F2a concentration. Am J Obstet Gynecol. 2005; 192:289–294. [PubMed: 15672038]
38. Myles TD, Santolaya J. Maternal and neonatal outcomes in patients with a prolonged second stage of labor. Obstet Gynecol. 2003; 102:52–58. [PubMed: 12850607]
39. Schiessl B, Janni W, Jundt K, Rammel G, Peschers U, Kainer F. Obstetrical parameters influencing the duration of the second stage of labor. Eur J Obstet Gynecol Reprod Biol. 2005; 118:17–20. [PubMed: 15596266]

40. Cheng YW, Hopkins LM, Caughey AB. How long is too long: does a prolonged second stage of labor in nulliparous women affect maternal and neonatal outcomes? Am J Obstet Gynecol. 2004; 191:933–938. [PubMed: 15467567]
41. Burstein E, Sheiner E, Mazor M, Carmel E, Levy A, Hershkovitz R. Identifying risk factors for premature rupture of membranes in small for gestational age neonates: a population-based study. J Matern Fetal Neonatal Med. 2008; 21:816–820. [PubMed: 19031277]
42. Savasan ZA, Romero R, Chaiworapongsa T, Kusanovic JP, Kim SK, Mazaki-Tovi S, Vaisbuch E, Mittal P, Ogge G, Madan I, et al. Evidence in support of a role for antiangiogenic factors in preterm prelabor rupture of membranes. J Matern Fetal Neonatal Med. 2010; 23:828–841. [PubMed: 20158393]
43. Cruciani L, Romero R, Vaisbuch E, Kusanovic JP, Chaiworapongsa T, Mazaki-Tovi S, Mittal P, Ogge G, Gotsch F, Erez O, et al. Pentraxin 3 in amniotic fluid: a novel association with intra-amniotic infection and inflammation. J Perinat Med. 2010; 38:161–171. [PubMed: 19792835]
44. Cruciani L, Romero R, Vaisbuch E, Kusanovic JP, Chaiworapongsa T, Mazaki-Tovi S, Dong Z, Kim SK, Ogge G, Yeo L, et al. Pentraxin 3 in maternal circulation: an association with preterm labor and preterm PROM, but not with intraamniotic infection/inflammation. J Matern Fetal Neonatal Med. 2010; 23:1097–1105. [PubMed: 20121391]
45. Kusanovic JP, Romero R, Jodicke C, Mazaki-Tovi S, Vaisbuch E, Erez O, Mittal P, Gotsch F, Chaiworapongsa T, Edwin SS, et al. Amniotic fluid soluble human leukocyte antigen-G in term and preterm parturition, and intra-amniotic infection/inflammation. J Matern Fetal Neonatal Med. 2009; 22:1151–1166. [PubMed: 19916713]
46. DiGiulio DB, Romero R, Kusanovic JP, Gomez R, Kim CJ, Seok KS, Gotsch F, Mazaki-Tovi S, Vaisbuch E, Sanders K, et al. Prevalence and diversity of microbes in the amniotic fluid, the fetal inflammatory response, and pregnancy outcome in women with preterm pre-labor rupture of membranes. Am J Reprod Immunol. 2010; 64:38–57. [PubMed: 20331587]
47. DiGiulio DB, Romero R, Amogan HP, Kusanovic JP, Bik EM, Gotsch F, Kim CJ, Erez O, Edwin S, Relman DA. Microbial prevalence, diversity and abundance in amniotic fluid during preterm labor: a molecular and culture-based investigation. PLoS One. 2008; 3:e3056. [PubMed: 18725970]
48. Kusanovic JP, Romero R, Chaiworapongsa T, Mittal P, Mazaki-Tovi S, Vaisbuch E, Erez O, Gotsch F, Than NG, Edwin SS, et al. Amniotic fluid sTREM-1 in normal pregnancy, spontaneous parturition at term and preterm, and intra-amniotic infection/inflammation. J Matern Fetal Neonatal Med. 2010; 23:34–47. [PubMed: 19591072]
49. Kim SK, Romero R, Kusanovic JP, Erez O, Vaisbuch E, Mazaki-Tovi S, Gotsch F, Mittal P, Chaiworapongsa T, Pacora P, et al. The prognosis of pregnancy conceived despite the presence of an intrauterine device (IUD). J Perinat Med. 2010; 38:45–53. [PubMed: 19650756]
50. Lee SE, Romero R, Lee SM, Yoon BH. Amniotic fluid volume in intra-amniotic inflammation with and without culture-proven amniotic fluid infection in preterm premature rupture of membranes. J Perinat Med. 2010; 38:39–44. [PubMed: 19708825]
51. Mazaki-Tovi S, Romero R, Vaisbuch E, Chaiworapongsa T, Erez O, Mittal P, Kim SK, Gotsch F, Lamont R, Ogge G, et al. Low circulating maternal adiponectin in patients with pyelonephritis: adiponectin at the crossroads of pregnancy and infection. J Perinat Med. 2010; 38:9–17. [PubMed: 19650757]
52. Mittal P, Romero R, Mazaki-Tovi S, Tromp G, Tarca AL, Kim YM, Chaiworapongsa T, Kusanovic JP, Erez O, Than NG, et al. Fetal membranes as an interface between inflammation and metabolism: increased aquaporin 9 expression in the presence of spontaneous labor at term and chorioamnionitis. J Matern Fetal Neonatal Med. 2009; 22:1167–1175. [PubMed: 19916714]
53. Erez O, Romero R, Tarca AL, Chaiworapongsa T, Kim YM, Than NG, Vaisbuch E, Draghici S, Tromp G. Differential expression pattern of genes encoding for anti-microbial peptides in the fetal membranes of patients with spontaneous preterm labor and intact membranes and those with preterm prelabor rupture of the membranes. J Matern Fetal Neonatal Med. 2009; 22:1103–1115. [PubMed: 19916708]
54. Melamed N, Hadar E, Ben-Haroush A, Kaplan B, Yogev Y. Factors affecting the duration of the latency period in preterm premature rupture of membranes. J Matern Fetal Neonatal Med. 2009; 22:1051–1056. [PubMed: 19900043]

55. Deutsch A, Deutsch E, Totten C, Downes K, Haubner L, Belogolovkin V. Maternal and neonatal outcomes based on the gestational age of midtrimester preterm premature rupture of membranes. J Matern Fetal Neonatal Med. 2010; 23:1429–1434. [PubMed: 20233131]

56. Seong HS, Lee SE, Kang JH, Romero R, Yoon BH. The frequency of microbial invasion of the amniotic cavity and histologic chorioamnionitis in women at term with intact membranes in the presence or absence of labor. Am J Obstet Gynecol. 2008; 199:375 e1–375 e5. [PubMed: 18928978]

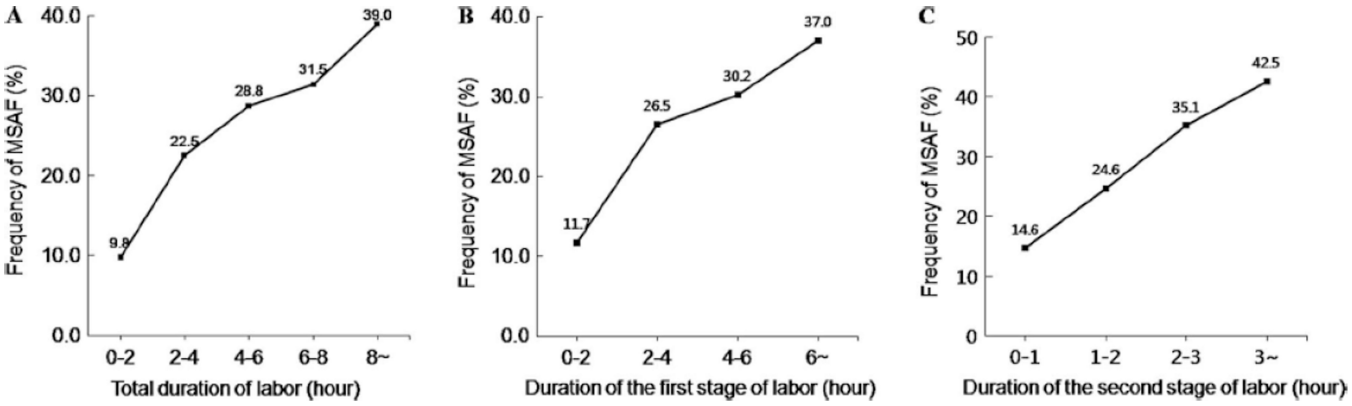

Figure 1.

The frequency of meconium-stained amniotic fluid (MSAF) according to the duration of labor. The longer the duration of labor (first stage, second stage, or total), the higher frequency of MSAF (p<0.001). **A**: The frequency of MSAF according to the total duration of labor. **B**: The frequency of MSAF according to the duration of the first stage of labor. **C**: The frequency of MSAF according to the duration of the second stage of labor.

Table I

PROM, premature or prelabor rupture of membranes; ROM, rupture of membranes; NICU, neonatal intensive care unit

Characteristics	No meconium (*N* = 3570)	Meconium (*N* = 806)	*p*-value
Maternal age (years) †	31.5 ± 3.8	30.9 ± 3.8	<0.01
Nulliparity	1740 (48.7%)	567 (70.3%)	<0.001
PROM	33 (9.5%)	63 (7.9%)	NS
Duration of ROM (hours) †, ‡	4.7 ± 11.5	7.7 ± 13.7	<0.001
Presence of labor	2590 (72.5%)	778 (96.5%)	<0.001
Total duration of labor (hours) *,§, ¶	2.1 ± 3.0	4.3 ± 4.2	<0.001 **
Duration of 1st stage of labor (hours) †,§, ††	1.6 ± 2.5	3.3 ± 3.9	<0.001 **
Duration of 2nd stage of labor (hours) ††,§,‡‡	0.5 ± 0.9	1.0 ± 1.2	<0.001 **
Pregnancy outcomes			
Gestational age at delivery (weeks) †	39.3 ± 1.2	40.2 ± 1.0	<0.001
Birth weight (g) †	3281.5 ± 415.8	3358.8 ± 428.4	<0.001
Cesarean delivery	1207 (33.8%)	149 (18.5%)	<0.001
Cesarean before the onset of labor §§	980 (81.2%)	28 (18.8%)	<0.001
Apgar score <7			
1-minute	108 (3.0%)	51 (6.3%)	<0.001
5-minute	21 (0.6%)	16 (2.0%)	<0.001
Umbilical arterial pH †	7.28 ± 0.06	7.25 ± 0.07	<0.001
pH <7.00 ¶¶	13 (0.4%)	9 (1.1%)	<0.05
NICU admission	60 (1.7%)	44 (5.5%)	<0.001

* Proportions were compared with Fisher's exact test and comparisons of continuous variables between groups were performed with Student *t*-test.

† Values are given at mean ± standard deviation.

‡ Denominator is 3521 for the non-meconium group and 794 for the meconium group

§ Duration of labor was analyzed only in cases who admitted before cervical dilatation of 4cm; duration of 1st stage was defined as duration of cervical dilatation from 4 cm to 10 cm; duration of 2nd stage was defined as duration between full cervical dilatation and fetal delivery.

¶ Denominator is 3077 for the non-meconium group and 637 for the meconium group.

** Significant after adjustment for nulliparity, duration of ROM, gestational age at delivery, mode of delivery and umbilical arterial pH less than 7.0.

†† Denominator is 3066 for the non-meconium group and 629 for the meconium group.

‡‡ Denominator is 3364 for the non-meconium group and 727 for the meconium group.

§§ Denominator is 1207 for the non-meconium group and 149 for the meconium group.

¶¶ Denominator is 3487 for the non-meconium group and 802 for the meconium group.

Table II

Relationship of various independent variables of meconium staining of amniotic fluid at delivery by multiple logistic regression analysis.

	Adjusted odds ratio	95% CI	Adjusted *p*-value*
Total population			
Maternal age	1.007	0.982–1.034	NS
Nulliparity	1.455	1.161–1.822	<0.01
PROM	0.708	0.488–1.027	NS
Duration of ROM (per 2-h increase)	1.027	0.997–1.058	NS
Total duration of labor (per 2-h increase)†	1.291	1.198–1.392	<0.001
Gestational age at delivery (per 1-week increase)	1.607	1.471–1.755	<0.001
Cesarean delivery	0.774	0.608–0.983	<0.05
Umbilical arterial pH <7.0	2.674	0.889–8.048	NS
In women who delivered after the onset of labor			
Maternal age	1.011	0.984–1.039	NS
Nulliparity	1.388	1.096–1.757	<0.01
PROM	0.633	0.436–0.919	<0.05
Duration of ROM (per 2-h increase)	1.012	0.983–1.043	NS
Total duration of labor (per 2-h increase)‡	1.216	1.126–1.312	<0.001
Gestational age at delivery (per 1-week increase)	1.468	1.342–1.607	<0.001
Cesarean delivery	1.694	1.266–2.267	<0.001
Umbilical arterial pH <7.0	2.089	0.590–7.393	NS

PROM, premature rupture of membranes; ROM, rupture of membranes; NS, not significant; CI, confidence interval.

*Adjusted for maternal age, nulliparity, PROM, duration of ROM, gestational age at delivery, mode of delivery and umbilical arterial pH less than 7.0.

†Adjusted odds ratio is 1.314 (95% CI, 1.198–1.441, $p<0.001$) for duration of the first stage of labor (per 2-h increase) and 1.304 (95% CI, 1.173–1.450, $p<0.001$) for duration of the second stage of labor (per 1-h increase).

‡Adjusted odds ratio is 1.240 (95% CI, 1.129–1.360, $p<0.001$) for duration of the first stage of labor (per 2-h increase) and 1.222 (95% CI, 1.098–1.359, $p<0.001$) for duration of the second stage of labor (per 1-h increase).