

Once We Find Grade III Meconium Stained Amniotic Fluid, Must We Act as Early as Possible?

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Background: Grade III meconium stained amniotic fluid (MSAF) is a common obstetric disease, and has the greatest impact on poor maternal and neonatal outcomes.

Question or Hypothesis or Aim: There is no consensus on treatment, especially on the timing of delivery.

Methods: We collected the medical records of 345 women who gave birth with grade III MSAF and analyzed the difference in baseline characteristics and maternal and neonatal outcomes relative to different labor stage, observation times in the first stage of labor, and the presence or absence of abnormal fetal heart rate (FHR) or thick amniotic fluid.

Findings: Higher rate of cesarean section was observed when grade III MSAF was found in active labor. Intervention occurred at an observation time of 90–120 min, but there were no significant differences in maternal or neonatal outcomes shown when the observation time was greater than 3 or 4 hours. However, a higher rate of admission to the neonatal intensive care unit was demonstrated in cases with grade III MSAF with abnormal FHR either in the first or second stage of labor or in cases with thick MSAF in the second stage of labor.

Discussion: Higher rate of composite adverse neonatal outcomes was found when secondary MSAF (a transition from clear AF to MSAF) was diagnosed >3 h before delivery.

Conclusion: In the first stage of labor, an observation time of greater than 4 hours might be possible after grade III MSAF is found if the labor has progressed and is without abnormal FHR.

Keywords: MSAF, grade III MSAF, observation time, abnormal FHR, thick AF

Statement of Significance

Problem or Issue.

Grade III MSAF has the greatest impact on poor maternal and neonatal outcomes, like higher caesarean section and operative vaginal delivery rates in women, and respiratory complications and higher neonatal intensive care unit admission rates in neonates.

What is Already Known.

No consensus about the treatment algorithms when grade III MSAF was observed before delivery, especially the timing of active intervention.

What this Paper Adds.

It might be feasible that waiting for up to 4 hours once finding grade III MSAF in the first stage of labor if the labor was progressed and without abnormal FHR or without thick AF.

Introduction

Meconium is a thick, dark-green, germ-free, odorless stool, found in the fetal gut from the age of 10 weeks, but it normally passes within the first 24 to 48 h after birth. If meconium is passed into amniotic fluid during pregnancy, it stains the fluid, leading to meconium stained amniotic fluid (MSAF).^{1–3} MSAF is a common obstetric disease, prevalent in approximately 8–38% of pregnancies; the large span in prevalence depends on sample size. Two large studies reported that the incidence was approximately 14.7% (35,897/243,725; 35,609/242,342).^{4,5} Before 37 weeks, MSAF was less common, occurring in approximately 4.3–6.9% of pregnancies, but with increasing gestation week, a higher incidence of MSAF was observed, in approximately 10.0–14.6% of pregnancies (listed in [Table S1](#)),⁶ which was in accordance with previous studies showing that MSAF most commonly occurred from 38–41 weeks of gestation.⁷

According to the standard grading system for meconium, MSAF can be classified into 3 grades: I (translucent, light green or yellow flesh), II (opalescent, deep green and light yellow, brown), and III (opaque and deep green), and it can also be classified as thin or thick based on the different solid contents.⁸ The proportion of grade III MSAF in all MSAF populations is approximately 7.8–10.6% (listed in [Table S1](#)).^{9,10} Grade III MSAF, which results from especially thick meconium, is regarded as posing a higher risk of poor neonatal outcomes than grade I or II MSAF. For example, sepsis, respiratory complications (such as meconium aspiration syndrome, MAS), hypoglycemia, seizures, lower Apgar scores and higher neonatal intensive care unit (NICU) admission rates may occur. For this reason, a higher risk of vaginal operation and cesarean section was also observed.¹¹ There is still no consensus or guidelines on the management of grade III amniotic fluid, a dilemma regarding the timing of active treatment like operative vaginal delivery or cesarean section for either midwife or doctor.

The aims of this study were to collect recent two-year data and analyze the observation times, and maternal and neonatal outcomes in pregnancies with grade III MSAF.

Methods

Data Collection

This retrospective study was conducted in the obstetrics department, of Jiangsu Province Hospital, the First Affiliated Hospital of Nanjing Medical University. Clinical data were collected from January 2020 to December 2021. All pregnant women with grade III MSAF (opaque and deep green AF) were included except for cases with elective cesarean section, induction after a stillbirth, incomplete data, and fetal renal abnormalities. Baseline information includes age, body mass index (BMI), gestation, primipara rate, the rate of application of assisted reproductive technology (ART), and complications (including diabetes mellitus (DM), preeclampsia, cord or placental abnormalities, positive Group B Streptococcus (GBS), and premature rupture of membrane (PROM)); Maternal outcomes include observation time (from the discovery of grade III amniotic fluid to the birth of the fetus), thin and thick amniotic fluid (AF) percentages (“thin” or “thick” meconium were defined, respectively, as fluid that was normal except for a greenish or yellowish color, or fluid that was viscous, tenacious and opaque¹²), AF volume (estimated by a midwife or doctor), artificial rupture of membrane rate, the mode of labor, intrapartum regional analgesia rate, intrapartum fever rate (>37.5°C), abnormal fetal heart rate (FHR) (category II and III FHR pattern according to the 3-tier classification system defined by the 2008 National Institute of Child Health and Human Development workshop¹³), delivery mode, vaginal bleeding over 24 hours (estimated by gravimetry; the volume of blood in milliliters is the difference in wet and dry weight in grams approximates), and a routine blood test 24 hours after delivery; Neonatal outcomes include: gender, birth weight, abnormal fetal development rate, Apgar scores at 1 and 5 min, and NICU admission rate. Data analysis is shown in [Figure 1](#). Data acquired from our hospital was approved by the Ethical Board of the First Affiliated Hospital of Nanjing Medical University and were kept anonymized and in confidentiality and complied with the Declaration of Helsinki (IRB-GL1-AF06).

Statistical Analysis

Statistical analysis was performed using the SPSS statistical package (version 26.0, SPSS Inc., Chicago, IL, USA). The normality of continuous variables was analyzed by a Shapiro–Wilk test. The standard normally distributed data are described as the mean ± standard deviation (SD) and were compared by a Student’s *t*-test. Non normally distributed variables are expressed as the median (interquartile range) and were compared by a Mann–Whitney *U*-test. Categorical

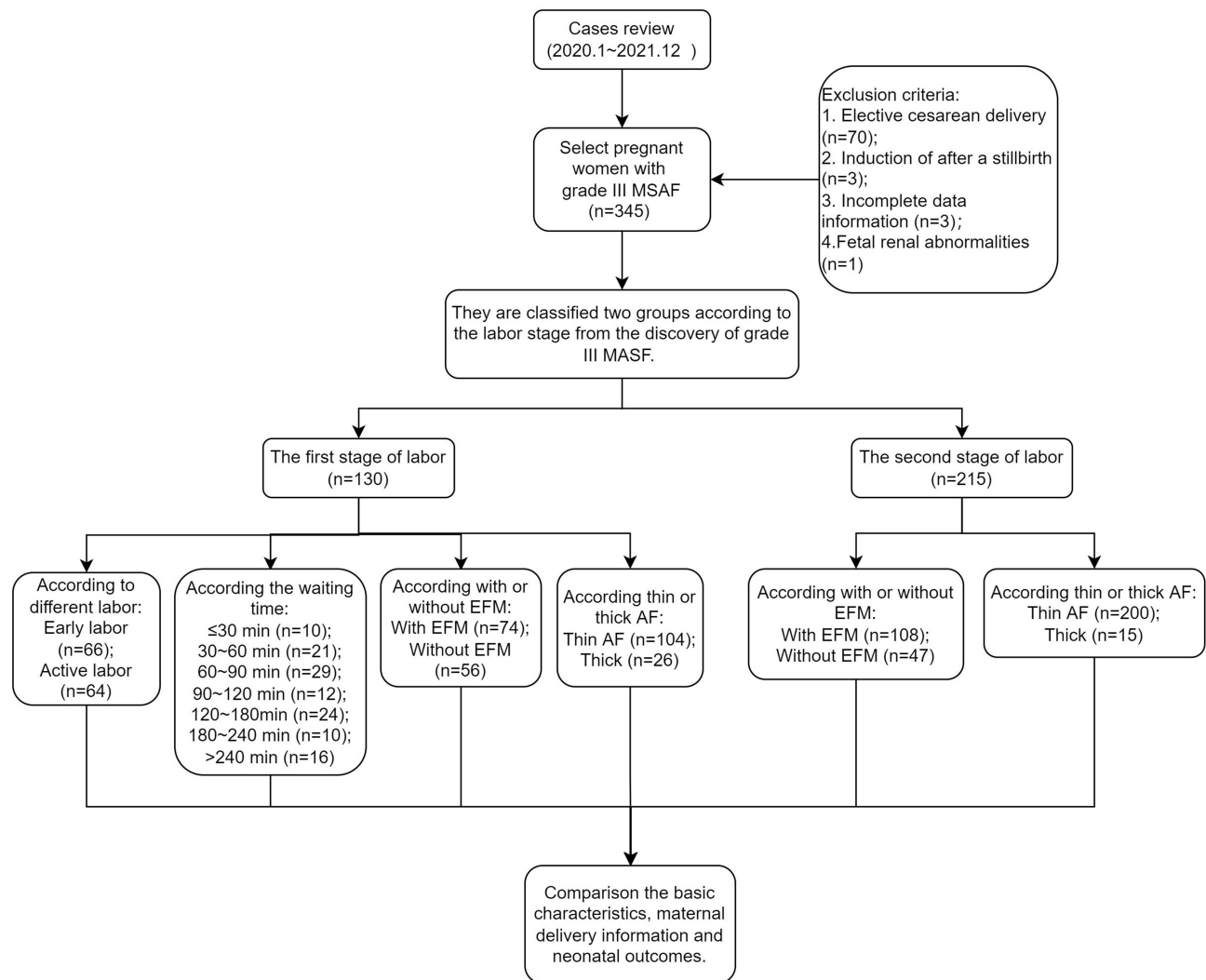


Figure 1 The flow chart of the present study design.

variables were described as concrete cases (percentages) and compared by a chi-square test or Fisher's exact test. A value of $p < 0.05$ was considered statistically significant.

Results

The Higher the Thick Amniotic Fluid Ratio is in the First Stage of Labor, the Higher the Cesarean Delivery Rate

A total of 345 cases were selected in the present retrospective study. Although the age of participants between the first or second stage of labor seemed to be different, when comparing those over 35 years (20 cases vs 22 cases, respectively, in the first or second stage of labor), the P -value was 0.150 (data was not shown). Other baseline characteristics were not significantly different in different stages of labor. There was a significant difference in the cord or placental abnormality ratio between the first and second stages of labor. In the first stage of labor, 1 case had battledore placenta, and 1 case had the cord around the neck. In the second stage of labor, 9 cases of the cord around the neck, 1 case of a true knot of cord, 2 cases of placental adherence, 3 cases of battledore placenta, and 1 case of velamentous placenta were observed. A longer observation time was found in the first stage, and 75% of cases had less than 3 hours of observation time. More cases with thick amniotic fluid were observed in the first stage of labor than in the second stage, and higher rates of cesarean section rates (41.5%) but lower rates of vaginal delivery (25.4%) were observed in the first stage of labor than in the second stage (6.5%, 67.0%). Other maternal and neonatal outcomes were not found to be significantly different between the first and second stages of labor (Table 1).

Table 1 The Differences of Grade III MSAF Between the First and Second Stage of Labor

	The First Stage of Labor (n=130)	The Second Stage of Labor (n=215)	P-value
Baseline characteristics			
Age (year), median (IQR)	29 (28~33)	29 (29~31)	0.010
BMI (Kg/m ²), median (IQR)	27.3 (24.8~29.2)	26.9 (25.1~28.8)	0.838
Pregnant gestation (weeks), median (IQR)	40.2 (39.4~40.7)	40.2 (39.5~40.6)	0.517
Primipara, n (%)	29 (22.3)	45 (20.9)	0.763
ART, n (%)			
IVF-ET	9 (6.9)	9 (4.2)	0.208
IUI	0 (0.0)	4 (1.9)	
Ovulation induction	0 (0.0)	2 (0.9)	
Complications, n (%)			
DM	22 (16.9)	35 (16.3)	0.876
Preeclampsia	6 (4.6)	11 (5.1)	0.835
Cord or placental abnormalities	2 (1.5)	16 (7.4)	0.017
With Positive GBS	6 (4.6)	16 (7.4)	0.298
PROM	20 (15.4)	30 (14.0)	0.714
Maternal outcomes			
Observation time (min), median (IQR)	88.5 (50.0~165.50)	2.0 (45)	0.000
Thin/Thick AF, n (%)	104 (80.0) / 26 (20.0)	200 (93.0) / 15 (7.0)	0.000
AF volume (mL), median (IQR)	500 (400~500)	500 (450~500)	0.016
Artificial rupture of membrane, n (%)	58 (44.6)	81 (37.7)	0.203
The mode of labor, n (%)			
Spontaneous	70 (53.8)	115 (53.5)	>1.000
Rupture of membrane	18 (13.8)	13 (6.0)	0.018
Balloon catheter	28 (21.5)	48 (22.3)	>1.000
Oxytocin	5 (3.8)	5 (2.3)	>1.000
Balloon catheter+ Oxytocin	9 (6.9)	34 (15.8)	0.018
With intrapartum regional analgesia, n (%)	87 (66.9)	159 (74.0)	0.162
Intrapartum fever, n (%)	41 (31.5)	54 (25.1)	0.196
With abnormal FHR, n (%)	56 (43.1)	47 (21.9)	0.000
Mode of delivery, n (%)			
Vaginal	33 (25.4)	144 (67.0)	0.000
Operative vaginal	43 (33.1)	57 (26.5)	0.221
Cesarean	54 (41.5)	14 (6.5)	0.000

(Continued)

Table 1 (Continued).

	The First Stage of Labor (n=130)	The Second Stage of Labor (n=215)	P-value
24-hour vaginal bleeding volume (mL), median (IQR)	400 (303.8~512.5)	380 (305~480)	0.295
Routine blood test 24 hours after delivery, median (IQR)			
WBC count ($10^9/l$)	10.5 (8.0~13.9)	10.2 (8.1~13.5)	0.498
CRP (mg/l)	2.7 (0.4~34.4)	1.2 (0.0~5.0)	0.001
N (%)	75.6 (69.8~81.6)	75.2 (69.0~80.9)	0.566
N count ($10^9/l$)	8.0 (5.8~11.2)	7.7 (5.7~10.6)	0.450
Neonatal outcomes			
Male/Female, n (%)	67 (51.5) / 63 (48.5)	114 (53.0) / 101 (47.0)	0.789
Birth weight (g), median (IQR)	3475 (3200~3750)	3500 (3250~3750)	0.680
Abnormal fetal development, n (%)	1 (0.8)	4 (1.9)	0.721
Apgar 1 min (4~7), n (%)	5 (3.8)	9 (4.2)	0.877
Apgar 5 min (4~7), n (%)	1 (0.8)	5 (2.3)	0.518
NICU admission, n (%)	20 (15.4)	48 (22.3)	0.116

Abbreviation: N, neutrophil.

When Grade III MSAF was Found in Active Labor, a Lower Cesarean Delivery Rate, but a Higher NICU Admission Rate Occurred

When we compared the difference between grade III AF found in early labor and active labor, more women had higher BMI and PROM in early labor, and more primipara were in active labor. With the progress of labor, intrapartum regional analgesia rates gradually increased. Higher intrapartum regional analgesia rates were found in active labor. Higher cesarean delivery rates occurred in early labor as well as higher operative vaginal delivery rates (vacuum extraction was used in 2 cases). Higher NICU admission rates were observed in active labor (21.9%) than in early labor (9.1%). Other baseline characteristics, and maternal and neonatal outcomes did not demonstrate a significant difference between early and active labor (Table 2).

If Grade III MSAF was Found in the First Stage of Labor, Waiting for Vaginal Delivery Not Less Than 4 Hours was Possible if Clinically Indicated

When we grouped comparisons according to observation time from the discovery of grade III MSAF to the final delivery, with a wait of more than 30 or 60 min, a higher WBC count and neutrophil count were observed. In addition, over 60 min, the C-reactive protein expression level rose, but the neutrophil percentage and intrapartum fever did not show a significant difference. If a wait of more than 60 min occurred, the 24-hour vaginal bleeding volume showed a slight increase. For waits of more than 90 and 120 min, significantly lower cesarean rates but higher operative vaginal delivery rates occurred than for waits of less than 90 or 120 min. For waits of more than 180 or 240 min, a nonstatistical difference in either baseline characteristics or maternal and neonatal outcomes was observed (Table 3).

Table 2 The Differences of Grade III MSAF Between Early and Active Labor

	Early Labor (n=66)	Active Labor (n=64)	P-value
Baseline characteristics			
Age (year), median (IQR)	29 (28~33)	29 (28~33)	0.641
BMI (Kg/m ²), mean ± SD	27.7 ± 3.2	26.4 ± 3.4	0.037
Pregnant gestation (weeks), median (IQR)	40.2 (39.3~41.0)	40.2 (39.4~40.6)	0.600
Primipara, n (%)	9 (13.6)	20 (31.3)	0.016
ART, n (%)			
IVF-ET	62 (93.9)	59 (92.2)	0.962
IUI	4 (6.1)	5 (7.8)	
Complications, n (%)			
DM	12 (18.2)	10 (15.6)	0.698
Preeclampsia	4 (6.1)	2 (3.1)	0.704
Cord or placental abnormalities	1 (1.5)	1 (1.6)	1.000
With Positive GBS	5 (7.6)	1 (1.6)	0.224
PROM	15 (22.7)	5 (7.8)	0.018
Maternal outcomes			
Observation time, median (IQR)	85 (46.5~173.0)	96 (50.5~159.5)	0.841
Thin/Thick amniotic fluid, n (%)	48 (72.7) / 18 (27.3)	56 (87.5) / 8 (12.5)	0.035
Amniotic fluid volume (mL), median (IQR)	500 (300~500)	500 (400~500)	0.082
Artificial rupture of membrane, n (%)	28 (42.4)	30 (46.9)	0.610
The mode of labor, n (%)			
Spontaneous	31 (47.0)	39 (60.9)	0.429
Rupture of membrane	12 (18.2)	6 (9.4)	
Balloon catheter	16 (24.2)	12 (18.8)	
Oxytocin	2 (3.0)	3 (4.7)	
Balloon catheter+ Oxytocin	5 (7.6)	4 (6.3)	
With intrapartum regional analgesia, n (%)	37 (56.1)	50 (78.1)	0.008
Intrapartum fever, n (%)	18 (27.3)	23 (35.9)	0.288
With abnormal FHR, n (%)	31 (47.0)	25 (39.1)	0.363
Mode of delivery, n (%)			
Vaginal	13 (19.7)	20 (31.3)	0.160
Operative vaginal	12 (18.2)	31 (48.4)	0.000
Cesarean	41 (62.1)	13 (20.3)	0.000
24-hour vaginal bleeding volume (mL), median (IQR)	405 (303.8~531.3)	382.5 (301.8~500.0)	0.210

(Continued)

Table 2 (Continued).

	Early Labor (n=66)	Active Labor (n=64)	P-value
Routine blood test 24 hours after delivery			
WBC count ($10^9/l$), median (IQR)	10.9 (8.0~14.2)	10.2 (8.0~13.6)	0.713
CRP (mg/l), median (IQR)	10.0 (0.0~62.3)	1.8 (0.5~6.8)	0.023
N (%), median (IQR)	76.7 (70.5~82.6)	75.0 (68.2~80.3)	0.348
N count ($10^9/l$), median (IQR)	8.1 (5.8~11.2)	7.8 (5.8~11.2)	0.998
Neonatal outcome			
Male/ Female, n (%)	34 (51.5) / 32 (48.5)	33 (51.6) / 31 (48.4)	0.996
Birth weight (g), median (IQR)	3500 (3200~3750)	3425 (3200~3750)	0.442
Abnormal fetal development, n (%)	1 (1.5)	0 (0.0)	1.000
Apgar 1 min (4~7), n (%)	2 (3.0)	3 (4.7)	0.972
Apgar 5 min (4~7), n (%)	1 (1.5)	0 (0.0)	1.000
NICU admission, n (%)	6 (9.1)	14 (21.9)	0.043

Abbreviation: N, neutrophil.

In Both the First and Second Stages of Labor, NICU Admission Rates Increased with the Occurrence of Abnormal FHR

In the first stage of labor, the artificial rupture of membrane ratio was higher in pregnancies with an abnormal FHR than in those without. A higher cesarean rate (55.4%) occurred in pregnancies with an abnormal FHR than in those without (31.1%), and the vaginal delivery rate (16.1%) among those with an abnormal FHR was lower than that among those without (32.4%). In the second stage of labor, the thick MSAF ratio was higher in pregnancies with an abnormal FHR (21.3%) than in pregnancies without (3.0%). In either the first or second stage of labor, the morbidity of pregnancies with an intrapartum fever was higher in pregnancies with an abnormal FHR (44.7%, 40.4%) than in those without (21.6%, 20.8%). In the first stage of labor, only the WBC count showed a significant difference between pregnancies with and without an abnormal FHR. In the second stage of labor, neutrophil percentage and count were higher in pregnancies with an abnormal FHR in addition to WBC count. In addition, NICU admission rates were higher in pregnancies with an abnormal FHR, whether women were the first stage of labor or the second stage of labor. However, only in the second stage of labor, was the percentage of 1-minute Apgar scores of 4 to 7 was higher in pregnancies with FHR abnormalities than in those without (Table 4).

In the Second Stage of Labor, NICU Admission Rates Increased with the Occurrence of Thick Grade III MSAF

In the first stage of labor, a longer gestation week and a larger AF volume were observed in the thick AF group than in the thin AF group. In addition, thick MSAF was found more frequently in early labor than in active labor. Vaginal bleeding volume was greater in women with thick MSAF than in those with thin AF. The rate of cesarean section was significantly higher in women with thick MSAF than in women with thin AF (73.1% vs 33.7%), but there was a lower vaginal operation rate (7.7% vs 39.4%). A higher incidence of intrapartum fever occurred in women with thick AF, in either the first or second stage of labor. Only in the second stage of labor, the neutrophil percentage was higher in thick AF than in thin AF, and more neonates with Apgar scores of 4~7 at 1 or 5 min were in the thick AF group. Similarly, a higher NICU admission rate was shown in women with thick AF (60.0%) than in thin AF (19.5%) (Table 5).

Table 3 The Maternal and Neonatal Differences of Grade III MSAF Among Different Observation Times

	30 Min (18 vs 112)		60 Min (39 vs 91)		90 Min (68 vs 62)		120 Min (80 vs 50)		180 Min (104 vs 26)		240 Min (114 vs 16)	
		P-value		P-value		P-value		P-value		P-value		P-value
Baseline characteristics												
Age (year), median (IQR) or mean \pm SD	32 (28–35) vs 29 (28–33)	0.118	32 \pm 4.2 vs 30 \pm 4.0	0.038	30 (28–33) vs 29 (28–33)	0.715	29 (28–32) vs 30 (28–33)	0.354	29 (28–33) vs 31 (28–35)	0.408	29 (28–33) vs 30 (28–31)	0.912
BMI (Kg/m²), median (IQR) or mean \pm SD	27.1 \pm 3.4 vs 27.1 \pm 3.3	0.980	27.5 (24.7–29.9) vs 27.2 (24.8–29.1)	0.865	27.3 \pm 3.4 vs 26.8 \pm 3.3	0.394	27.4 \pm 3.4 vs 26.6 \pm 3.2	0.199	27.5 \pm 4.4 vs 26.5 \pm 4.4	0.145	27.1 \pm 3.4 vs 26.4 \pm 3.2	0.403
Pregnant gestation (weeks), median (IQR)	40.2 (39.0–40.4) vs 40.2 (39.4–41.0)	0.302	40.1 (39.5–41.0) vs 40.2 (39.5–41.0)	0.254	40.3 (39.4–41.0) vs 40.1 (39.3–40.6)	0.326	40.2 (39.3–41.0) vs 40.2 (39.4–40.6)	0.564	40.2 (39.4–40.6) vs 40.1 (39.1–41.0)	0.631	40.2 (39.4–40.6) vs 40.1 (39.2–41.1)	0.972
Primipara, n (%)	5 (27.8) vs 24 (21.4)	0.768	10 (25.6) vs 19 (20.9)	0.550	15 (22.1) vs 14 (22.6)	0.943	18 (22.5) vs 11 (17.7)	0.947	24 (23.1) vs 5 (19.2)	0.796	28 (24.6) vs 1 (6.3)	0.185
IVF-ET, n (%)	1 (5.6) vs 8 (7.1)	1.000	2 (5.1) vs 7 (7.7)	0.598	5 (7.4) vs 4 (6.5)	1.000	5 (7.4) vs 4 (6.5)	0.978	8 (7.7) vs 1 (3.8)	0.796	9 (7.9) vs 0 (0.0)	0.523
Complications, n (%)												
DM	5 (27.8) vs 17 (15.2)	0.325	8 (20.5) vs 14 (15.4)	0.475	14 (20.6) vs 8 (8.8)	0.349	16 (23.5) vs 6 (9.7)	0.237	18 (17.3) vs 4 (3.8)	1.000	20 (17.5) vs 2 (12.5)	0.882
Preeclampsia	0 (0.0) vs 6 (5.4)	0.595	3 (7.7) vs 3 (3.3)	0.523	5 (12.8) vs 1 (1.1)	0.255	5 (7.4) vs 1 (1.6)	0.488	5 (4.8) vs 1 (3.8)	1.000	6 (5.3) vs 0 (0.0)	1.000
Cord or placental abnormalities	0 (0.0) vs 2 (1.8)	1.000	0 (0.0) vs 2 (2.2)	1.000	1 (1.5) vs 1 (1.2)	1.000	1 (1.5) vs 1 (2.0)	1.000	1 (1.0) vs 1 (3.8)	0.361	1 (0.9) vs 1 (6.3)	0.232
PROM	6 (33.3) vs 14 (12.5)	0.055	9 (23.1) vs 11 (12.1)	0.112	11 (16.2) vs 9 (14.5)	0.793	14 (20.6) vs 6 (9.7)	0.398	17 (16.3) vs 3 (11.5)	0.761	19 (16.7) vs 1 (6.3)	0.477
Maternal outcomes												
Observation time (min), median (IQR)	9.0 (0.0–23.3) vs 105.0 (69.5–173.8)	0.000	34.0 (9.0–48.0) vs 128.0 (84.0–195.0)	0.000	53.5 (30.8–74.8) vs 166.0 (126.8–240.0)	0.000	63.5 (34.3–84.0) vs 186.0 (148.0–288.0)	0.000	75.0 (40.0–120.0) vs 287.0 (206.8–428.0)	0.000	82 (45.0–133.5) vs 347 (288.0–475.0)	0.000
Thin / Thick amniotic fluid, n (%)	15 (83.3) vs 89 (79.5) / 3 (16.7) vs 23 (20.5)	0.949	31 (79.5) vs 73 (80.2) / 8 (20.5) vs 18 (19.8)	0.924	50 (73.5) vs 54 (87.1) / 18 (26.5) vs 8 (12.9)	0.053	61 (76.2) vs 43 (86.0) / 19 (23.8) vs 7 (14.0)	0.176	82 (78.8) vs 22 (84.6) / 22 (21.2) vs 4 (15.4)	0.511	89 (78.1) vs 15 (93.8) / 25 (21.9) vs 1 (6.2)	0.257

Amniotic fluid volume (mL), median (IQR)	500 (400~500) vs 500 (300~500)	0.152	500 (400~500) vs 500 (300~500)	0.302	500 (300~500) vs 500 (400~500)	0.241	500 (325~500) vs 500 (400~500)	0.696	500 (325~500) vs 500 (400~500)	0.970	500 (300~500) vs 500 (400~500)	0.919
Artificial rupture of membrane, n (%)	6 (33.3) vs 52 (46.4)	0.300	17 (43.6) vs 41 (45.1)	0.878	30 (44.1) vs 28 (45.2)	0.905	34 (42.5) vs 24 (48.0)	0.589	46 (44.2) vs 12 (46.2)	0.860	49 (43.0) vs 9 (56.3)	0.317
The mode of labor, n (%)												
Spontaneous	10 (55.6) vs 60 (53.6)	0.756	21 (53.8) vs 49 (53.8)	0.996	31 (44.1) vs 39 (62.9)	0.281	38 (42.5) vs 32 (64.0)	0.444	50 (48.1) vs 20 (76.9)	0.111	58 (50.9) vs 12 (75.0)	0.343
Rupture of membrane	3 (16.7) vs 15 (13.4)		5 (12.8) vs 13 (14.3)		10 (14.7) vs 8 (12.9)		12 (15.0) vs 6 (12.0)		17 (16.4) vs 1 (3.8)		18 (15.8) vs 0 (0.0)	
Balloon catheter	5 (27.8) vs 23 (20.5)		9 (23.1) vs 19 (20.9)		17 (25.0) vs 11 (17.7)		20 (25.0) vs 8 (16.0)		25 (24.0) vs 3 (11.5)		25 (21.9) vs 3 (18.8)	
Oxytocin	0 (0.0) vs 5 (4.5)		1 (2.6) vs 4 (4.4)		3 (4.4) vs 2 (3.2)		3 (3.8) vs 2 (4.0)		4 (3.8) vs 1 (3.8)		5 (4.4) vs 0 (0.0)	
Balloon catheter+ Oxytocin	0 (0.0) vs 9 (8.0)		3 (7.7) vs 6 (6.6)		7 (10.3) vs 2 (3.2)		7 (8.8) vs 2 (4.0)		8 (7.7) vs 1 (3.8)		8 (7.1) vs 1 (6.3)	
With intrapartum regional analgesia, n (%)	9 (50.0) vs 78 (69.6)	0.100	23 (59.0) vs 64 (70.3)	0.207	41 (60.3) vs 46 (74.2)	0.092	48 (60.0) vs 39 (78.0)	0.034	67 (64.4) vs 20 (76.9)	0.226	73 (64.0) vs 14 (87.5)	0.062
With Positive GBS, n (%)	0 (0.0) vs 6 (5.4)	0.595	2 (5.1) vs 4 (4.4)	1.000	2 (2.9) vs 4 (6.5)	0.593	2 (2.5) vs 4 (8.0)	0.306	3 (2.9) vs 3 (11.5)	0.174	4 (3.5) vs 2 (12.5)	0.159
Intrapartum fever, n (%)	5 (27.8) vs 36 (32.1)	0.711	11 (28.2) vs 30 (33.0)	0.592	26 (38.2) vs 15 (24.2)	0.085	28 (2.5) vs 13 (26.0)	0.283	37 (35.6) vs 4 (15.4)	0.047	39 (34.2) vs 2 (12.5)	0.080
With abnormal FHR, n (%)	9 (50.0) vs 47 (32.1)	0.523	16 (41.0) vs 40 (44.0)	0.757	34 (50.0) vs 22 (17.8)	0.095	38 (47.5) vs 18 (36.0)	0.198	48 (46.2) vs 8 (30.8)	0.157	51 (44.7) vs 5 (6.3)	0.308
Mode of delivery, n (%)												
Vaginal	5 (27.8) vs 28 (25.0)	0.899	13 (33.3) vs 20 (22.0)	0.111	16 (17.6) vs 17 (27.4)	0.688	21 (26.3) vs 12 (24.0)	0.838	27 (26.0) vs 6 (23.1)	0.527	30 (26.3) vs 3 (18.8)	0.344
Operative vaginal	5 (27.8) vs 38 (33.9)		8 (20.5) vs 35 (38.5)		13 (19.1) vs 30 (45.2)	0.000	19 (23.7) vs 24 (48.0)	0.010	32 (30.8) vs 11 (42.3)		35 (30.7) vs 8 (50.0)	
Cesarean	8 (44.4) vs 46 (41.1)		18 (46.2) vs 36 (39.5)		39 (57.4) vs 15 (24.2)	0.000	40 (50.0) vs 14 (28.0)	0.010	45 (43.3) vs 9 (34.6)		49 (43.0) vs 5 (31.3)	

(Continued)

Table 3 (Continued).

	30 Min (18 vs 112)		60 Min (39 vs 91)		90 Min (68 vs 62)		120 Min (80 vs 50)		180 Min (104 vs 26)		240 Min (114 vs 16)	
		P-value		P-value		P-value		P-value		P-value		P-value
24-hour vaginal bleeding volume (mL), median (IQR)	345 (300~400) vs 413 (310~520)	0.148	350 (300~410) vs 435 (315~540)	0.017	390 (300~473) vs 440 (320~543)	0.071	400 (300~498) vs 438 (320~525)	0.165	400 (300~500) vs 483 (355~520)	0.119	400 (300~515) vs 441 (330~515)	0.568
Routine blood test 24 hours after delivery												
WBC count (10⁹/l), median (IQR)	8.4 (6.5~9.6) vs 11.1 (8.7~14.4)	0.000	9.1 (7.6~10.4) vs 11.3 (8.8~14.7)	0.002	10.0 (8.0~13.8) vs 11.1 (8.1~14.1)	0.320	10.3 (8.1~13.5) vs 10.9 (7.9~14.9)	0.437	10.3 (8.1~14.1) vs 10.8 (7.7~14.0)	0.977	10.3 (8.0~14.1) vs 10.8 (8.4~13.6)	0.868
CRP (mg/l), median (IQR)	1.0 (0.0~7.5) vs 3.1 (0.6~43.3)	0.121	1.0 (0.0~7.0) vs 4.6 (1.0~54.0)	0.002	3.8 (0.0~61.4) vs 2.2 (0.9~12.1)	0.226	2.9 (0.1~57.6) vs 2.6 (0.5~13.6)	0.443	2.9 (0.6~50.0) vs 1.3 (0.0~16.8)	0.320	3.4 (0.5~46.0) vs 1.0 (0.0~6.0)	0.075
N (%), median (IQR)	73.8 (65.8~78.6) vs 76.6 (70.0~81.9)	0.197	74.5 (5.3~8.6) vs 76.7 (6.0~11.8)	0.103	76.5 (70.3~81.3) vs 74.9 (67.6~82.6)	0.484	76.8 (70.3~81.5) vs 74.4 (66.6~83.2)	0.267	76.5 (70.0~81.3) vs 72.4 (66.4~84.0)	0.391	76.1 (70.0~81.6) vs 72.1 (65.3~82.6)	0.361
N count (10⁹/l), median (IQR)	5.8 (4.2~7.7) vs 8.6 (5.9~11.5)	0.002	6.6 (68.6~78.3) vs 9.0 (70.0~83.0)	0.001	7.8 (5.8~11.1) vs 8.4 (5.8~11.6)	0.610	7.8 (5.8~11.0) vs 8.4 (5.6~11.8)	0.761	7.9 (5.8~11.2) vs 8.1 (5.3~11.5)	0.912	8.0 (5.8~11.2) vs 8.1 (5.8~12.3)	0.777
Neonatal outcome												
Male/Female, n (%)	8 (44.4) vs 59 (52.7) / 10 (0.0) vs 53 (47.3)	0.516	22 (56.4) vs 45 (49.5) / 17 (43.6) vs 46 (50.5)	0.467	36 (52.9) vs 31 (50.0) / 32 (47.1) vs 31 (50.0)	0.738	41 (51.3) vs 26 (52.0) / 39 (48.7) vs 24 (48.0)	0.934	56 (53.8) vs 11 (42.3) / 48 (46.2) vs 15 (57.7)	0.292	63 (55.3) vs 4 (25.0) / 51 (44.7) vs 12 (75.0)	0.023
Birth weight (g), median (IQR) or mean ± SD	3525 (3350~3700) vs 3450 (3200~3788)	0.861	3450 (3150~3650) vs 3500 (3250~3850)	0.135	3450 (3200~3738) vs 3500 (3300~3763)	0.365	3481 ± 510.1 vs 3485 ± 377.1	0.199	3450 (3200~3750) vs 3500 (3200~3763)	0.590	3450 (3200~3750) vs 3500 (3250~3875)	0.699
Abnormal fetal development, n (%)	0 (0.0) vs 1 (0.9)	1.000	0 (0.0) vs 1 (1.1)	1.000	0 (0.0) vs 1 (1.6)	0.477	0 (0.0) vs 1 (2.0)	0.385	0 (0.0) vs 1 (3.8)	0.200	0 (0.0) vs 1 (6.3)	0.123
Apgar I min (4~7), n (%)	1 (5.6) vs 4 (3.6)	0.531	2 (5.1) vs 3 (3.3)	1.000	4 (5.9) vs 1 (1.6)	0.419	5 (6.3) vs 0 (0.0)	0.182	5 (4.8) vs 0 (0.0)	0.569	5 (4.4) vs 0 (0.0)	1.000
Apgar 5 min (4~7), n (%)	1 (5.6) vs 0 (0.0)	0.138	1 (2.6) vs 0 (0.0)	0.300	1 (1.5) vs 0 (0.0)	1.000	1 (1.3) vs 0 (0.0)	1.000	1 (1.0) vs 0 (0.0)	1.000	1 (0.9) vs 0 (0.0)	1.000
NICU admission, n (%)	3 (16.7) vs 17 (2.5)	1.000	6 (15.4) vs 14 (15.4)	1.000	10 (14.7) vs 10 (16.1)	0.822	11 (13.8) vs 9 (18.0)	0.513	18 (17.3) vs 2 (7.7)	0.362	19 (16.7) vs 1 (6.3)	0.477

Abbreviation: N, neutrophil.

Table 4 The Differences Between Grade III MSAF with and without Abnormal FHR

	The First Stage of Labor			The Second Stage of Labor		
	Without Abnormal FHR (n=74)	With Abnormal FHR (n=56)	P-value	Without Abnormal FHR (n=168)	With Abnormal FHR (n=47)	P-value
Baseline characteristics						
Age (year), median (IQR)	29 (28~33)	30 (28~33)	0.970	29 (27~31)	29 (27~31)	0.793
BMI (Kg/m ²), median (IQR)	26.8 ± 3.4	27.4 ± 3.3	0.247	26.9 (24.9~28.9)	26.9 (25.3~28.7)	0.825
Pregnant gestation (weeks), median (IQR)	40.1 (39.3~40.6)	40.3 (39.5~41.0)	0.281	40.2 (39.5~40.6)	40.2 (39.5~41.0)	0.905
Primipara, n (%)	17 (23.0)	12 (21.4)	0.834	36 (21.4)	9 (19.1)	0.734
ART, n (%)						
IVF-ET	2 (2.7)	7 (12.5)	0.067	7 (4.2)	2 (4.3)	0.621
IUI	0 (0.0)	0 (0.0)		3 (1.8)	1 (2.1)	
Ovulation induction	0 (0.0)	0 (0.0)		1 (0.6)	1 (2.1)	
Complications, n (%)						
DM	11 (14.9)	11 (19.6)	0.472	27 (16.1)	8 (17.0)	0.876
Preeclampsia	3 (4.1)	3 (5.4)	1.000	9 (5.4)	2 (4.3)	1.000
Cord or placental abnormalities	1 (1.4)	1 (1.8)	1.000	14 (8.3)	2 (4.3)	0.530
PROM	10 (13.5)	10 (17.9)	0.664	25 (14.9)	5 (10.6)	0.634
Maternal outcome						
Observation time (min), median (IQR)	101.5 (129)	84.0 (100)	0.535	6.5 (51)	0.0 (41)	0.058
Thin/Thick amniotic fluid, n (%)	63 (85.1) / 11 (14.9)	41 (73.2) / 15 (26.8)	0.092	163 (97.0) / 5 (3.0)	37 (78.7) / 10 (21.3)	0.000
Amniotic fluid volume (mL), median (IQR)	500 (375~500)	500 (400~500)	0.354	500 (500~500)	500 (400~500)	0.728
Early/Active labor, n (%)	35 (47.3) / 39 (52.7)	31 (55.4) / 25 (44.6)	0.363	/	/	/
Artificial rupture of membrane, n (%)	27 (36.5)	31 (55.4)	0.032	59 (35.1)	22 (46.8)	0.144
The mode of labor, n (%)						
Spontaneous	43 (58.1)	27 (48.2)	0.596	88 (52.4)	27 (46.8)	0.692
Rupture of membrane	10 (13.5)	8 (14.3)		10 (6.0)	3 (6.4)	
Balloon catheter	15 (20.3)	13 (23.2)		40 (23.8)	8 (17.0)	
Oxytocin	3 (4.1)	2 (3.6)		3 (1.8)	2 (4.3)	
Balloon catheter+ Oxytocin	3 (4.1)	6 (10.7)		27 (16.1)	7 (14.9)	
With intrapartum regional analgesia, n (%)	49 (66.2)	38 (67.9)	0.844	124 (73.8)	35 (74.4)	0.928
With Positive GBS, n (%)	5 (6.8)	1 (1.8)	0.360	11 (6.5)	5 (74.5)	0.529
Intrapartum fever, n (%)	16 (21.6)	25 (44.7)	0.005	35 (20.8)	19 (40.4)	0.006

(Continued)

Table 4 (Continued).

	The First Stage of Labor			The Second Stage of Labor		
	Without Abnormal FHR (n=74)	With Abnormal FHR (n=56)	P-value	Without Abnormal FHR (n=168)	With Abnormal FHR (n=47)	P-value
Mode of delivery, n (%)						
Vaginal	24 (32.4)	9 (16.1)	0.014	118 (70.2)	26 (55.3)	0.117
Operative vaginal	27 (36.5)	16 (28.5)	0.355	39 (23.2)	18 (38.3)	
Cesarean	23 (31.1)	31 (55.4)	0.014	11 (6.5)	3 (6.4)	
24-hour vaginal bleeding volume (mL)	388 (300~483)	413 (325~548)	0.047	370 (310~470)	380 (305~555)	0.628
Routine blood test 24 hours after delivery						
WBC count ($10^9/l$), median (IQR)	9.8 (7.8~13.2)	11.5 (9.2~14.7)	0.015	9.9 (7.9~12.9)	10.7 (8.6~16.8)	0.037
CRP (mg/l), median (IQR)	1.6 (0.0~16.8)	6.2 (0.5~55.8)	0.088	1.0 (0.0~4.6)	3.0 (0.5~9.0)	0.088
N (%), median (IQR)	74.3 (69.4~79.7)	79.1 (71.9~83.5)	0.054	74.3 (67.7~79.0)	78.0 (74.1~83.3)	0.001
N count ($10^9/l$), median (IQR)	7.8 (5.5~10.9)	9.2 (6.4~11.8)	0.058	7.3 (5.3~9.8)	8.4 (6.5~11.4)	0.011
Neonatal outcome						
Male/ Female, n (%)	33 (44.6) / 41 (55.4)	34 (60.7) / 22 (39.3)	0.069	87 (51.8) / 81 (48.2)	27 (57.4) / 20 (42.6)	0.492
Birth weight (g), median (IQR) or mean \pm SD	3450 (3200~3750)	3500 (3213~3838)	0.447	3496 \pm 396.4	3520 \pm 361.9	0.712
Abnormal fetal development, n (%)	1 (1.4)	0 (0.0)	0.383	2 (1.2)	2 (4.3)	0.209
Apgar I min (4~7), n (%)	2 (2.7)	3 (5.4)	0.750	4 (2.4)	5 (10.6)	0.037
Apgar 5 min (4~7), n (%)	0 (0.0)	1 (1.9)	0.431	3 (1.8)	2 (4.3)	0.656
NICU admission, n (%)	5 (6.8)	15 (26.8)	0.002	30 (17.9)	18 (38.3)	0.003

Abbreviation: N, neutrophil.

Discussion

The etiology of MSAF is unknown, although studies of the difference between women with clear AF and MSAF have reported that some risks associated with the occurrence of MSAF include advanced maternal age, prolonged labor, postterm pregnancy, maternal complications (such as DM, hypertensive disorders of pregnancy, and intrahepatic cholestasis of pregnancy), and oligohydramnios.^{3,14} In our study, only women with grade III MSAF were selected, but in women with thick grade III MSAF, a longer gestational week, a lower AF volume, and a higher incidence of intrapartum fever were observed compared with women with thin AF. In another study on the difference in the degree of MSAF (yellow, green and thick groups), more women with intrapartum fever were in the thick AF group, and the authors explained that the occurrence of MSAF, especially thick MSAF, might be a potential alert of maternal infection.¹⁵ However, it cannot explain why not all women with MSAF have an intrapartum fever, or why this acute response is not shown by a change in routine blood tests, for WBC, CRP and neutrophil percentage. The causal association between intrapartum fever and MSAF or more severe MSAF (thick AF) remains unknown. Maternal intrapartum fever might result in the occurrence of thick MSAF, and in turn, MSAF might be a risk factor for uterine infection or a stress-induced maternal response via of intrapartum fever.

Table 5 The Differences Between Thin and Thick MSAF

	The First Stage of Labor			The Second Stage of Labor		
	Thin AF (n=104)	Thick AF (n=26)	P-value	Thin AF (n=200)	Thick AF (n=15)	P-value
Baseline characteristics						
Age (year), median (IQR)	30 (28–33)	29 (28–33)	0.615	29 (27–31)	29 (27–30)	0.604
BMI (Kg/m²), median (IQR) or mean ± SD	26.9 ± 3.4	27.8 ± 2.9	0.185	27.0 (25.1–28.9)	26.3 (25.4–27.9)	0.296
Pregnant gestation (weeks), median (IQR)	40.1 (39.3–40.6)	40.5 (40.1–41.0)	0.023	40.2 (39.5–40.6)	40.2 (40.0–40.5)	0.745
Primipara, n (%)	21 (20.2)	8 (30.8)	0.247	43 (21.5)	2 (13.3)	0.674
ART, n (%)						
IVF-ET	7 (6.7)	2 (7.7)	1.000	9 (4.5)	0 (0.0)	0.439
IUI	/	/		3 (1.5)	1 (6.7)	
Ovulation induction	/	/		2 (1.0)	0 (0.0)	
Complications, n (%)						
DM	17 (16.3)	5 (19.2)	0.953	31 (15.5)	4 (26.7)	0.443
Preeclampsia	3 (2.9)	3 (11.5)	0.174	11 (5.5)	0 (0.0)	1.000
Cord or placental abnormalities	2 (1.9)	0 (0.0)	1.000	15 (7.5)	1 (6.7)	1.000
PROM	16 (15.4)	4 (15.4)	1.000	30 (15.0)	0 (0.0)	0.218
Maternal outcome						
Observation time, median (IQR)	100 (52.8–169.8)	77.5 (43.5–124.5)	0.193	0.0 (49)	18.0 (40)	0.569
Amniotic fluid volume (mL), median (IQR)	500 (400–500)	300 (200–500)	0.000	500 (450–500)	500 (500–500)	0.946
Early/Active labor, n (%)	48 (46.2) / 56 (53.8)	18 (69.2) / 8 (30.8)	0.035	/	/	/
Artificial rupture of membrane, n (%)	45 (43.3)	13 (50.0)	0.537	78 (39.0)	3 (20.0)	0.143
The mode of labor, n (%)						
Spontaneous	61 (58.7)	9 (34.6)	0.045	106 (53.0)	9 (60.0)	0.191
Rupture of membrane	12 (11.5)	6 (23.1)	0.199	10 (5.0)	3 (20.0)	
Balloon catheter	22 (21.2)	6 (23.1)	0.795	46 (23.0)	2 (13.3)	
Oxytocin	2 (1.9)	3 (11.5)	0.045	5 (2.5)	0 (0.0)	
Balloon catheter+ Oxytocin	7 (6.7)	2 (7.7)	1.000	33 (16.5)	1 (6.7)	
With intrapartum regional analgesia, n (%)	72 (69.2)	15 (57.7)	0.263	147 (73.5)	12 (80.0)	0.804
With Positive GBS, n (%)	4 (3.8)	2 (7.7)	0.754	15 (7.5)	1 (6.7)	1.000
With abnormal FHR, n (%)	41 (39.4)	15 (57.7)	0.092	37 (18.5)	10 (66.7)	0.000
Intrapartum fever, n (%)	28 (26.9)	13 (50.0)	0.024	45 (22.5)	9 (60.0)	0.003
Mode of delivery, n (%)						
Vaginal	28 (26.9)	5 (19.2)	0.615	135 (67.5)	9 (60.0)	0.738
Operative vaginal	41 (39.4)	2 (7.7)	0.001	52 (26.0)	5 (26.7)	
Cesarean	35 (33.7)	19 (73.1)	0.001	13 (6.5)	1 (6.7)	
24-hour vaginal bleeding volume (mL), median (IQR)	398 (300–498)	470 (363–580)	0.034	378 (306–480)	380 (175.0)	0.950

(Continued)

Table 5 (Continued).

	The First Stage of Labor			The Second Stage of Labor		
	Thin AF (n=104)	Thick AF (n=26)	P-value	Thin AF (n=200)	Thick AF (n=15)	P-value
Routine blood test 24 hours after delivery						
WBC count (10⁹/l), median (IQR)	10.2 (7.9–13.5)	12.5 (9.2–14.8)	0.060	10.2 (8.1–13.2)	10.4 (7.3–18.5)	0.719
CRP (mg/l), median (IQR)	2.5 (0.5–25.8)	9.0 (0.0–58.9)	0.385	1.1 (0.0–5.0)	3.4 (0.5–7.5)	0.217
N (%), median (IQR)	75.2 (68.7–81.3)	77.9 (71.0–82.6)	0.410	74.8 (68.6–80.0)	80.6 (74.2–89.3)	0.007
N count (10⁹/l), median (IQR)	7.8 (5.8–11.1)	9.6 (6.3–11.8)	0.138	7.7 (5.7–10.2)	8.4 (5.9–16.5)	0.386
Neonatal outcome						
Male/ Female, n (%)	51 (49.0) / 53 (51.0)	16 (61.5) / 10 (38.5)	0.254	104 (52.0) / 96 (48.0)	10 (66.7) / 5 (33.3)	0.407
Birth weight (g), median (IQR) or mean ± SD	3500 (3213–3750)	3325 (3188–3725)	0.382	3504 ± 382.8	3463 ± 471.4	0.690
Abnormal fetal development, n (%)	0 (0.0)	1 (3.8)	0.200	3 (1.5)	1 (6.7)	0.253
Apgar 1 min (4–7), n (%)	3 (2.9)	2 (7.7)	0.569	4 (2.0)	5 (33.3)	0.000
Apgar 5 min (4–7)	1 (1.0)	0 (0.0)	1.000	3 (1.5)	2 (13.3)	0.040
NICU admission, n (%)	13 (12.5)	7 (26.9)	0.129	39 (19.5)	9 (60.0)	0.001

Abbreviation: N, neutrophil.

Unignorablely, some maternal and perinatal outcomes might increase as the staining and consistency of amniotic fluid increases,¹² which might affect a doctor's decision regarding intervention in cases of MSAF. Some studies reported the difference between MSAF and clear AF, and their results showed increasing rates of cesarean section, puerperal infection, postpartum hemorrhage (PPH) and even mortality (such as labor dystocia) among women with MSAF.^{16,17} It is easy to understand the increasing rates of cesarean section or operative vaginal delivery with the occurrence of MSAF; these shorten the delivery time, especially when accompanied by thick AF or abnormal FHR in the first stage of labor, in cases of poor neonatal outcome. In addition, our results showed that in women with thick MSAF in the first stage of labor, the 24-hour vaginal bleeding volume was greater than that in women with thin MSAF, but the rate of PPH was not significantly different (data not shown). Previously published literature revealed that MSAF is significantly associated with a higher risk of moderate (1000–2000 mL) and severe (>2000 mL) PPH than clear AF,¹⁸ but another study reported the risk is higher for minor (500–1000 mL) and moderate but not for severe PPH,¹⁹ a finding which may need further studies. Regarding puerperal infections, our results showed only a slight change in WBC count, CRP and neutrophil percentage or count, and no cases of puerperal infection or death existed in our data, which may be due to the use of antibiotics.

To neonates, MAS, a neonatal complication of MSAF, can develop into a serious condition and even cause mortality.²⁰ MAS is mainly characterized by the early onset of respiratory distress with poor lung compliance and hypoxemia and is diagnosed by a chest X-ray. Treatment for MAS may even require mechanical ventilation and intubation.²⁰ Most importantly, the incidence of MAS increased with gestational age, from 1.3% at 38 weeks to 4.8% at 42 weeks.¹⁰ Prolonged gestation might be an independent risk factor for the occurrence of neonatal MAS in nulliparous women.²¹ Other associated neonatal short-term adverse effects of MSAF include acidosis, NICU admission, respiratory distress, hypoglycemia, and seizures.²² Our results showed a higher NICU admission rate in pregnancies with grade III MSAF and an abnormal FHR either in the first or second stage of labor. FHR reflects the fetal condition in the uterus, and abnormal FHR indicates intrauterine fetal hypoxia. Normal FHR is between 110–160 bpm, as defined by

cardiotocography monitoring. However, one recent study demonstrated that a baseline FHR between 150 and 160 bpm might be a signal of MSAF, which was approximately 2.6 times more likely to occur than in 110~149 bpm group.²³ A previously published report viewed MSAF as a predictor of delayed closure among neonates with gastroschisis.²⁴ In our data, only 5 abnormal fetal developments (3 cases of congenital heart disease, 1 case of anotia, and 1 case of agenesis of the corpus callosum), were likely not directly associated with the occurrence of MSAF. Among pregnancies with thick MSAF in the second stage of labor, a higher rate of NICU admission and more Apgar scores of 4~7 (indicating fetal distress) at 1 and 5 min occurred than in pregnancies with thin AF. Similar research was published in which thick MSAF was associated with a low APGAR score, a high rate of emergency cesarean section, and MAS.¹¹ A possible explanation is that an exposure under thick MSAF, where there is a lack of oxygen compared with “light”-stained MSAF, resulted in the intestinal ischemia. Then, the fetal anal sphincter relaxed and gastrointestinal peristalsis increased, leading to the passage of meconium when umbilical vein oxygen saturations was below 30%.²⁵ In addition to the abovementioned short-term neonatal outcomes, recent studies have followed up on the long-term outcome in newborns. Fetal exposure to MSAF during labor and delivery may result in lower rates of long-term infectious-related hospitalizations, lower incidence of long-term infectious morbidity in the offspring,⁴ lower rates of long-term respiratory-related hospitalizations,⁵ and an independent protective factor for dermatitis and skin rash-related hospitalizations throughout childhood and adolescence.^{22,26}

It seems that MSAF may affect newborns more than women, but newborns also benefit from the long-term effects of MSAF. Researchers have even put forward the view that “MSAF is more like a symptom rather than a syndrome”,²⁷ but no clinical practice guidelines have been developed by any international organization such as the world health organization or gynecological and obstetrical society. Although it is well-known that intensive delivery room and continuous fetal heart monitoring by the midwife regarding the intrapartum management,¹⁵ and non-necessary routine endotracheal suctioning at birth in vigorous term meconium-stained babies²⁸ and other routine postnatal care. However, the observation time once MSAF is found remains unknown. Our results showed non significantly different maternal or neonatal outcomes even after a wait of up to 4 hours, regardless of abnormal FHR or thick MSAF, but a watershed of significantly different rates of operative vaginal delivery time or cesarean section with a wait of 90–120 min, which was associated with our doctor’s decision. One study found a higher rate of composite adverse neonatal outcomes when secondary MSAF (a transition from clear AF to MSAF) was diagnosed >3 h before delivery.²⁹

In conclusion, it might be plausible that waiting for up to 4 hours after finding grade III MSAF in the first stage of labor if labor was progressed and without abnormal FHR. However, the limitations of our study should also be noted. The present study was a single-center retrospective study with a small population size sample. More cases, and more centers, even in different countries, would be needed to design a prospective study. The differences between early and active labor and the observation time in the two labor stages respectively must be investigated. It is unclear whether 4 hours is that the endpoint for observation in the first stage of labor, or whether it is 5 or more hours; more studies are needed. Due to a lack of objectivity in the definition and quantitative diagnostic criteria for MSAF, many scholars questioned the timing of intervention for MSAF, especially grade III MSAF, but have not investigated it. In the future, we hope there will be quantitative diagnostic methods and further investigation to dilute the subjective bias of MSAF diagnosis.

Abbreviations

MSAF, meconium stained amniotic fluid; AF, amniotic fluid; BMI, body mass index; ART, assisted reproductive technology; IVF-ET, in vitro fertilization-embryo implantation; IUI, intrauterine insemination; DM, diabetes mellitus; ICP, intrahepatic cholestasis; PROM, premature rupture of membrane; GBS, group B Streptococcus; FHR, fetal heart rate; WBC, white blood cell; CRP, C-reactive protein; NICU, neonatal intensive care unit; MAS, meconium aspiration syndrome; PPH, postpartum hemorrhage.

Acknowledgment

Xinxin Zhu, Shiyun Huang, Yuxuan Tang, Zhonglan Wu contributed equally to this work (co-first authors). Qing Zuo, Zhiping Ge, Ziyang Jiang contributed equally to this work (co-corresponding authors).

Disclosure

The authors report no conflicts of interest in this work.

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