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Original Article

Deliveries with Meconium-Stained Amniotic Fluid and Outcomes: A Prospective Cohort Study

Mekonyumlu Gebeliklerde Doğum Eyleminin ve Sonuçlarının Değerlendirilmesi: Prospektif Kohort Çalışması

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Abstract

Background: The aim of this study was to determine the risk factors for meconium-stained amniotic fluid in a low-risk pregnancy and to evaluate birth complications and neonatal outcomes in deliveries with meconium-stained amniotic fluid (MSAF).

Material and Methods: This prospective study was conducted between April 2015 and September 2015 at Ankara Zekai Tahir Burak Women's Health Education and Research Hospital. 351 women with singleton pregnancies and cephalic position who had reached 37 weeks of gestation were included in the study. Women with known chronic systemic diseases, pregnancy complications, and previous uterine surgery were excluded. 151 cases with MSAF and 200 randomly selected control cases with clear amniotic fluid were included in this study. We compared the two groups in terms of maternal age, gravidity, parity, gestational age, intrapartum maternal fever, body mass index (BMI), duration of labor, cardiotocographic values (CTG), mode of delivery, neonatal outcomes, and admission to the neonatal intensive care unit.

Results: In our study, meconium aspiration syndrome (MAS) developed in 2.6% (4/151) of neonates with meconium staining at birth. Gestational age, intrapartum maternal fever and BMI were significantly increased in the MSAF group (p=0.003). The duration of the active phase of labor (cervical dilation from 6 cm to 10 cm) was similar in both groups, and the duration of the second phase of labor was longer in the MSAF group (p=0.002). MSAF was associated with an increased number of abnormal results in cardiotocographic examinations, birth complications, and neonatal outcome ($p < 0.001$).

Conclusion: Deliveries with meconium-stained amniotic fluid are associated with increased morbidity; therefore, intrapartum examinations should be performed more frequently and carefully, and precautions should be taken during labor in collaboration with pediatricians to reduce potential adverse neonatal outcomes.

Keywords: Meconium stained amniotic fluid; meconium aspiration syndrome; risc factors; neonatal outcome

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Öz

Amaç: Bu çalışmanın amacı, düşük riskli bir gebelikte mekonyum boyalı amniyotik sıvı için risk faktörlerini belirlemek ve mekonyum boyalı amniyotik sıvı (MBAS) varlığındaki doğumlarda doğum komplikasyonlarını ve yenidoğan sonuçlarını değerlendirmektir.

Gereç ve Yöntemler: Bu prospektif çalışma Nisan 2015-Eylül 2015 tarihleri arasında Ankara Zekai Tahir Burak Kadın Sağlığı Eğitim ve Araştırma Hastanesi'nde yapıldı. Çalışmaya 37. gebelik haftasına ulaşmış tekil gebelik ve baş pozisyonu olan 351 kadın dahil edildi. Bilinen kronik sistemik hastalıkları, gebelik komplikasyonları ve geçirilmiş uterin cerrahisi olan kadınlar çalışma dışı bırakıldı. Bu çalışmaya MBAS'lı 151 olgu ve berrak amniyotik sıvısı olan rastgele seçilmiş 200 kontrol olgusu dahil edildi. İki grubu anne yaşı, gravidite, parite, gebelik yaşı, intrapartum maternal ateş, vücut kitle indeksi (VKİ), doğum süresi, kardiyotokografik değerler, doğum şekli, neonatal sonuç ve yenidoğan yoğun bakım ünitesine yatış oranları açısından karşılaştırdık.

Bulgular: Çalışmamızda doğumda mekonyum boyanması olan yenidoğanların %2,6'sında (4/151) mekonyum aspirasyon sendromu (MAS) gelişti. MBAS grubunda gebelik yaşı, intrapartum maternal ateş ve VKİ anlamlı olarak yüksekti (p=0,003). Doğumun aktif fazının süresi (6 cm'den 10 cm'ye servikal dilatasyon) her iki grupta benzerdi ve MBAS grubunda doğumun ikinci fazının süresi daha uzundu (p=0,002). MBAS, kardiyotokografik incelemelerde, doğum komplikasyonlarında ve yenidoğan sonuçlarında artan sayıda anormal sonuçla ilişkili bulundu (p < 0,001).

Sonuç: Mekonyum boyalı amniyotik sıvı ile yapılan doğumlar artmış morbidite ile ilişkilidir; bu nedenle intrapartum muayeneler daha sık ve dikkatli yapılmalı ve olası olumsuz yenidoğan sonuçlarını azaltmak için doğum sırasında çocuk doktorları ile işbirliği içinde önlemler alınmalıdır.

Anahtar Kelimeler: Mekonyum boyalı amniyon sıvı; mekonyum aspirasyon sendromu; risk faktörleri; neonatal sonuç

1. Introduction

Meconium consists of debris, including cells from the intestine and skin, gastrointestinal mucus, lanugo, hair, oily material from the vernix caseosa, amniotic fluid, and intestinal secretions (1). The gastrointestinal tract of a newborn contains 60-200 g of meconium (2). The amount, appearance, and viscosity of meconium in amniotic fluid vary. Cases with fine meconium in the amniotic fluid are yellow-green, dark green, particulate cases are called dark meconium (2). Infants with dark meconium in the amniotic fluid have more severe respiratory distress and higher morbidity and mortality (3). A yellow or yellow-brown color of the amniotic fluid indicates that old meconium was removed long before birth; a green color of the amniotic fluid indicates that meconium has leaked recently (4). Meconium has been found to superficially stain the umbilical cord and placenta within one hour, and pigment-containing macrophages were found in the amnion and chorion after three hours (5). While the ability of meconium to stain tissue is directly related to the duration of meconium exposure, a relationship with meconium density has not been demonstrated (6). Meconium is sterile, however, when aspirated into the lungs, it stimulates the release of cytokines and vasoactive substances that cause cardiovascular and inflammatory responses in the fetus and infant (7,8). Aspirated meconium can disrupt the normal respiratory mechanism by causing airway obstruction, chemical irritation, inflammation, infection, and surfactant inactivation (9).

Meconium aspiration syndrome (MAS) is a respiratory distress syndrome that occurs in neonates with meconium-contaminated amniotic fluid and whose clinical manifestations range from mild to life-threatening respiratory failure (10). Amniotic fluid is contaminated with meconium in approximately 12.5% (8-22%) of all pregnancies (11). MAS is caused by aspiration of meconium by the infant before, during, or shortly after birth (12). MAS is observed in approximately 2-10% of newborns with MSAF (13). Advanced gestational age, black and South Asian races, and vaginal breech delivery are independent risk factors for MSAF (14). The highest incidence of MAS and MSAF is observed in postpartum pregnancies and in pregnancies with small for gestational age (SGA) newborns (15). The pathophysiology of MAS has a very complex structure that includes many and overlapping elements (16). The fact that there is not always a correlation between the rate of meconium staining and the development of respiratory distress, can be explained by the presence of other factors involved in the development of MAS. The pathophysiology of MAS includes intrauterine meconium

passage, aspiration, pulmonary diseases causing hypoxemia and acidosis (17). Depression at birth is found in 20-33% of infants with MSAF (18). The reason for this situation is primarily pathological intrauterine events with chronic asphyxia and infections, and this intrauterine stress causes meconium passage and aspiration of the fetus (19).

In this study, we investigated the clinical significance of MSAF. We also aimed to determine possible associations between meconium concentration and neonatal outcome.

2. Materials and Methods

The study protocol was approved by the Ethics Committee of Zekai Tahir Burak Women Health Education and Research Hospital (April 2015 #24/2015), and the principles of the Declaration of Helsinki were followed. All patients signed an informed consent form to participate in the study.

This prospective cohort study was enrolled by healthy pregnant women at term (37 weeks or more). Singleton pregnancies with vertex presentation and active labor (with regular uterine contractions and cervical dilation of 6 cm or more) were eligible for the study (20). Patients with diabetes, hypothyroidism, hyperthyroidism, and hypertension; pregnant women with systemic diseases; fetal anomalies; preeclampsia, eclampsia, and other obstetric problems; previous cesarean sections; major uterine surgery; and patients in breech presentation were excluded from the study. Of the patients included in the study, 151 patients in whom meconium was detected in the amniotic fluid after rupture of the membranes were designated as the study group, and 200 patients with clear amniotic fluid were designated as the control group. For the control group, the first 200 patients who were followed up in the delivery room and met the criteria were randomly selected. The power analysis to calculate the sample size was based on the previous study by Shaikh et al (6). Using the independent-samples t test with a power of 0.9604514 and an α-value of 0.05, the power (1-β) was calculated to be 0.95 with 26 participants. To ensure the safety of the study, 151 patients were included. Because this number is higher than was achieved, we assume that power did not decrease.

The gestational age of the patients was determined on the basis of the last menstrual period and the ultrasound findings of the first week. Based on the history, physical examination, and routine laboratory tests, it was determined that no other diseases were present. The patients' ages, gravidity, parities, and BMI (body mass index), which was calculated from height and body weight values measured during hospitalization, were recorded. Follow-up examinations of patients during pregnancy were obtained from hospital records. The duration of active labor (time between 6 cm and 10 cm cervical opening), duration of the second stage of labor, results of electronic fetal monitoring, intrapartum maternal fever scores, complications of labor, and mode of delivery were recorded. Neonatal sex and weight, Apgar scores at the 1st and 5th minutes, admission to the neonatal intensive care unit, and length of stay were evaluated for neonatal outcomes.

Statistical analysis

Statistical Package for the Social Sciences - SPSS 22 (SPSS Inc, Chicago, IL) was used for statistical analysis. The distribution of parameters was tested with the Shapira-Wilk normality test. Data were expressed as mean ± standard deviation and median (min-max). For normally distributed data, the independent samples t test was used, and for non-normally distributed variables, the Mann Whitney U test was used. For analysis of categorical variables, the Chi-square test or Fisher's extract test was used. A type I error level of 5% overall was used to derive statistical significance.

3. Results

The mean age of pregnant women in the study was 26.44±5.80 years, and the mean gestational age was 39.53±1.29 weeks. The mean body mass index was 29.09±4.28 kg/m^2. In 86.3% (n=303) of the studied pregnant women, 3 or more prenatal follow-up examinations took place, and aneuploidy screening results were available in 85.2% (n=299). Ultrasound screening for fetal anomalies in the second trimester was performed in 86.9% (n=305) of these pregnant women, and a 50-gram glucose screening test was performed in 72.6% (n=255) of them. During the physical examinations of the pregnant women, the mean intrapartum maternal fever was 36.59±0.30 °C. While 80.6% (n=283) of the examined pregnant women delivered vaginally, 19.4% (n=68) delivered by cesarean section. The mean birth weight of the babies born was 3289.02 ± 447.00 grams. While the mean Apgar score of the babies in the first minute was 7.86±0.72, the mean score in the fifth minute was 9.80±0.55, and 3.4% (n=12) of them required neonatal intensive care. While amniotic fluid was clear in 57% (n=200) of the examined pregnant women, meconium was detected in 43% (n=151). The distribution of descriptive characteristics in the study is shown in table 1.

Table 1. Baseline and clinical characteristics of the study population

	Control Group (n=200)	MSAF (n=151)	p
Maternal Age (years)	26.41 ± 5.66	26.48 ± 5.98	0.956
Gravidy	2.07 ± 1.47	2.12 ± 1.39	0.548
Parity	0.80 ± 1.14	0.84 ± 1.15	0.667
Gestational Age (Weeks)	39.39 ± 1.35	39.71 ± 1.18	**0.030**
Fewer (°C)	36.53 ± 0.28	36.67 ± 0.31	**<0.001**
Body Mass Index BMI (kg/m²)	28.55 ± 4.15	29.79 ±4.36	**0.016**

Table 2. Comparison of the characteristics of labor between 2 groups

	Control Group	Study Group	p
Active Phase Time (minute)/Hourly Progress Amount (cm)	135.98±76.23/ 2.60±2.10	121.23±76.13/ 2.86±2.02	0.055
Second Phase Time (Minute)	10.36±11.63	11.85±9.58	**0.002**

Table 3. Comparison of neonatal and perinatal outcomes

	Control Group (n=200)	Study Group (n=151)	p
Cardiotocography Result			
Normal	195 (97.5)	120 (79.5)	**<0.001**
Abnormal	5 (2.5)	31 (20.5)	
Delivery Method			
Vaginal delivery	183 (91.5)	100 (66.2)	**<0.001**
Ceserean section	17 (8.5)	51 (33.8)	
Birth weights			
≤2500 gram	8 (4.0)	5 (3.3)	0.127
2501-3999 gram	184 (92.0)	132 (87.4)	
≥4000 gram	8 (4.0)	14 (9.3)	
Complication			
No	180 (90.0)	103 (68.2)	**< 0.001**
Yes	20 (10.0)	48 (31.8)	
Neonatal Intensive Care Unit Needs			
No	199 (99.5)	140 (92.7)	**0.001**
Yes	1 (0.5)	11 (7.3)	

The duration of active labor and hourly values of cervical dilation of pregnant women included in the study are shown in table 2. While there was a significant difference in the duration of the second stage between the two groups (p=0.002), no significant difference was found in the duration of active labor (p=0.055). The duration of the second phase was significantly longer in the study group than in the control group (11.85±9.58 min/10.36±11.63 min).

In the study groups, cardiotachography results were abnormal in 20.5% (n=31) of pregnant women with MSAF; in 2.5% (n=5) of pregnant women with clear amniotic fluid (p < 0.001), in 33.8% (n=51) of pregnant women with meconium amnion delivered by cesarean section; however, this rate was 8.5% (n=17) in the control group (p<0.001). A statistically significant difference was also found in neonatal outcome and neonatal intensive care needs (p<0.001 and p=0.001, respectively) (Table 3). The percentage of women with meconium in the amniotic fluid who had an abnormal neonatal outcome and required neonatal intensive care was significantly higher than in women with clear amniotic fluid. In 11 of 12 patients who required neonatal intensive care, the amniotic fluid was stained with meconium, and they were admitted to the neonatal intensive care unit for a mean of 8.27±11.05 (min-max:1-36) days. 40% (n=14) of the abnormal neonatal outcomes in the infants with meconium stained amnion were LGA, 28.6% (n=10) had respiratory distress, 17.1% (n=6) were SGA, 11.4% (n=4) had MAS, 8.6% (n=3) had neonatal jaundice, and 2.9% (n=1) had neonatal hypoglycemia.

The influence of some predictors identified as a result of the univariate comparisons and literature review on the prediction of MSAF development was assessed with multivariate logistic regression analysis (Table 4). This showed that intrapartum fever and BMI were effective predictors of MSAF development (p<0.001 and p=0.045, respectively), whereas gestational age was not (p > 0.05). A 1 °C increase in intrapartum fever increased the risk of MSAF development by 5.017-fold, while a 1 kg/m² increase in BMI increased the risk of MSAF development by 1.055-fold.

Table 4. Evaluation of MSAF development by predictive multivariate logistic regression analysis

	B	Standard deviation	Wald	df	OR	%95	p
Gestational Age	0.166	0.089	3.510	1	1.181	0.992-1.405	0.061
Fewer (°C)	1.613	0.415	15.090	1	5.017	2.224-11.321	**<0.001**
BMI (kg/m²)	0.054	0.027	4.018	1	1.055	1.001-1.112	**0.045**

4. Discussion

Meconium aspiration syndrome is one of the most common respiratory disorders in neonates (21). The incidence of MAS in deliveries with MSAF has been reported to be 3-8% (22). In a study conducted in our hospital between 2008 and 2009, 8450 of 39699 live births were admitted to the neonatal intensive care unit (NICU), and 218 infants were diagnosed with MSAF and/or MAS (23). These patients accounted for 2.6% of patients admitted to the NICU (23). Our study found that the incidence of MAS in deliveries with MSAF was 2.6%, which is consistent with previous studies and the literature.

There are studies in the literature showing that maternal age is an important risk factor for MSAF. However, in these studies, this rate was found to be higher in pregnancies older than 40 years (24). In contrast, some studies reported that, they did not demonstrate an association between maternal age and MSAF, as in our study. On the other hand, there are many studies that have found an increase in the incidence of MSAF with gestational age. In particular, studies have shown that there is a strong association with MSAF from 41 weeks of gestation, whereas this association is more pronounced below 40 weeks (25, 26). This increase, which correlates with the increase in gestational age, supports the view that fetal maturation and meconium passage are important factors. Staining of amniotic fluid with meconium is another mechanism associated with prenatal infections. In a study of 707 women undergoing amniocentesis, the positivity of amniotic fluid cultures was higher in pregnant women whose amniotic fluid stained with meconium than in pregnant women whose amniotic fluid was not stained, even when the amniotic membrane was not ruptured (27). In a study by Balchin et al, maternal fever was found to be an independent risk factor for predicting MSAF in term pregnancies (28). In this study, maternal fever had an odds ratio of 1.62. In our study, a 1 °C increase in maternal fever was found to increase the risk of developing meconium in the amniotic fluid by 5.017-fold. This highlights the possibility that meconium staining of the amniotic fluid is related to prenatal infections and shows the importance of monitoring maternal fever during labor. In studies examining the association between body mass index (BMI) and MSAF, the cut-off value was 30, and the risk was found to increase 1.37-fold at values above that. These results show that our study is consistent with the literature.

In studies examining the relationship between MSAF and duration of labor, it was concluded that all phases from the first stage of labor were longer in pregnant women with MSAF. Considering that the presence of meconium in the amniotic fluid may affect the duration of labor, it should be remembered that this is a risk factor for prolonged labor, and appropriate follow-up should be performed. In the study conducted by Odongo et al. in 2010, they concluded that the incidence of pathologic cardiotocography patterns (CTG) was increased in patients with MSAF (RR 1.096, 95%CI 0.65-1.84) (29). Similarly, the study by Wong et al. found that the frequency of abnormal KTG patterns in the MSAF group was 9.8%, whereas it was 6.4% in the unencumbered group and was considered statistically significant (30). Considering that the high rate of abnormal CTG in patients with MSAF may affect the Apgar score and neonatal outcomes, these patients should be monitored more closely during the intrapartum period. In addition, the literature found that the rate of cesarean sections performed after the onset of labor was 23.1% in the MSAF group and was statistically significantly higher than in the control group (26). They related these high cesarean section rates to the higher incidence of abnormal fetal heart rate patterns in patients with MSAF and the obstetrician's decision to perform cesarean section as part of labor management because heart rate patterns such as CTG category 2 pose a dilemma. The study by Wong et al. found a cesarean section rate of 13.2% in the MSAF group and 8.8% in the control group, and the cesarean section rates were quite low compared with other studies (30). They explained the low cesarean section rate in their study by the use of intrapartum fetal scalp pH measurement in combination with CTG. In our study, the cesarean section rate in the MSAF group was 33.8%, whereas it was 8.5% in the control group. The difference in the cesarean section rate between the two groups can be explained by the increase in medicolegal problems, which have become more common in our country in recent years and cause

anxiety among physicians. In this case, physicians avoid invasive methods and opt noninvasive methods. The simultaneous presence of CTG category 2 traces and MSAF lead to a liberal cesarean section.

In a retrospective study by Becker et al 1123 MSAF were detected at 11226 births, they concluded that an Apgar score of 6 and below was associated with MSAF at the fifth minute (31). Similarly, Khazardoost et al showed that low Apgar scores in the 5th minute were associated with MSAF and MAS (32). In our study, a strong correlation was found between low APGAR scores in the fifth minute and MSAF. In one study, the rate of poor neonatal outcomes was found to be 22.5% in patients with MSAF from 37 weeks, whereas the rate was 10.9% in unaffected patients (OR 2.39) (28). Ziadeh et al. concluded that MSAF is associated with poor neonatal outcomes (33). In our study, the presence of MSAF was found to be associated with the risk of birth complications and poor neonatal outcomes. It is known that the duration of active labor in infants with MSAF is long, and prolongation of labor leads to poor neonatal outcomes. Many studies have found that infants with MSAF require more neonatal intensive care during pregnancy than the clear amnion group (33,34). The presence of meconium in amnion can lead to disturbances in intrapartum fetal CTG and affect umbilical cord blood flow and cord blood pH. The high rate of birth complications and poor neonatal outcomes in patients with MSAF support this finding.

In conclusion, high intrapartum maternal fever, prolongation of the second stage of labor, frequency of abnormal cardiotocography (CTG), labor complications, increased cesarean section rate, low Apgar score at 5 minutes, poor neonatal outcome, and need of neonatal intensive care are more common in pregnancies with MSAF than in pregnancies with clear amniotic fluid requiring treatment. Prospective or retrospective studies with large case series including large numbers of patients and thus neonatal morbidity/mortality are needed to better assess the incidence of MSAF, associated predictive factors, and potential neonatal outcomes.

Author contribution

Study conception and design: FÖA, EGYE; data collection: CT; analysis and interpretation of results: NOC and MCI; draft manuscript preparation: MCI and EGYE. All authors reviewed the results and approved the final version of the manuscript.

Ethical approval

The study was approved by the Ethics Committee for Noninterventional Studies of Zekai Tahir Burak Women Health Education Research Hospital (Protocol no. 24/28.04.2015).

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Conflict of interest

The authors declare that there is no conflict of interest.

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Araştırma fikri ve tasarımı: FÖA, EGYE; veri toplama: CT; sonuçların analizi ve yorumlanması: NOC and MCI; araştırma metnini hazırlama: MCI and EGYE. Tüm yazarlar araştırma sonuçlarını gözden geçirdi ve araştırmanın son halini onayladı.

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