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OUTCOMES OF TERM NEONATES WITH MECONIUM-STAINED AMNIOTIC FLUID

Original Research

Anum Pervaiz[1]*, Talal Waqar[1], Muhammad Tariq Nadeem[1], Iqra Irfan[1], Muhammad Ali Zia[1], Adeel Mehmood[1]
[1]Department of Paediatrics, Combined Military Hospital, Kharian, Pakistan.
Corresponding Author: Anum Pervaiz, Department of Paediatrics, Combined Military Hospital, Kharian, Pakistan. anumpervaizch@gmail.com

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Abstract

Background: Meconium-stained amniotic fluid (MSAF) is a common complication in term pregnancies, occurring in approximately 5-20% of deliveries and often indicating fetal distress. While MSAF can lead to serious neonatal complications, including respiratory distress syndrome (RDS), hypoxic ischemic encephalopathy (HIE), and sepsis, not all cases of MSAF result in adverse outcomes. Identifying factors associated with MSAF is essential to enhance clinical management and improve neonatal outcomes.

Objectives: The primary objective was to determine the frequency of complications associated with MSAF in term neonates. The second objective was to assess the risk of maternal, neonatal, and gestational factors associated with the occurrence of MSAF in term neonates.

Methods: This case-control study was conducted in the Department of Pediatrics, Combined Military Hospital, Kharian, from October 2022 to September 2023. A total of 100 term neonates (50 with MSAF and 50 without) were enrolled. Neonates born between 37 and 42 weeks who experienced a trial of labor were included, while those delivered by elective cesarean section, with major congenital anomalies, or hemorrhagic amniotic fluid were excluded. Data on maternal, neonatal, and gestational characteristics were collected. All neonates were monitored for one month post-birth for any adverse outcomes in both inpatient and outpatient settings.

Results: Complications among neonates with MSAF included HIE in 3 (6.0%), RDS in 6 (12.0%), pneumothorax in 1 (2.0%), persistent pulmonary hypertension in 2 (4.0%), and sepsis in 12 (24.0%). Significant risk factors for MSAF included prolonged active labor over 6 hours (adjusted odds ratio [aOR]: 2.84, 95% confidence interval [CI]: 1.08–7.45, p=0.034), induction of labor (aOR: 4.65, 95% CI: 1.55–13.95, p=0.006), and gestational age at birth greater than 39 weeks (aOR: 4.01, 95% CI: 1.47–10.97, p=0.007).

Conclusion: MSAF is associated with significant neonatal complications, highlighting the need for careful management of risk factors such as prolonged labor, labor induction, and advanced gestational age to reduce the incidence and impact of MSAF.

Keywords: Aspiration Syndrome, Meconium, Gestational Age, Hypoxia-Ischemia, Brain, Labor, Induced, Meconium-Stained Amniotic Fluid, Neonatal Sepsis, Respiratory Distress Syndrome, Newborn.

INTRODUCTION

Meconium, a yellow-green or brown material produced in the gastrointestinal tract of a developing fetus, is typically excreted by neonates within the first 24 to 48 hours post-birth. Its presence during the peripartum period often signals acute in-utero hypoxia and potential fetal distress (1). Meconium-stained amniotic fluid (MSAF) occurs in approximately 5% to 20% of all deliveries, even in pregnancies previously classified as normal-risk for complications (2). Although only about 5% of neonates with MSAF develop meconium aspiration syndrome, the condition can lead to severe outcomes including respiratory distress, respiratory failure, persistent pulmonary hypertension (PPH), air-leak syndromes, acute respiratory distress syndrome (ARDS), and in the most severe cases, hypoxic ischemic encephalopathy (HIE) or death (3-5). The likelihood of MSAF increases as the fetus approaches and surpasses term due to increased gastrointestinal motility and relaxation of anal sphincters, often exacerbated by factors such as fetal hypoxia due to umbilical cord compression (6-8).

Adverse outcomes in neonates with MSAF are linked to various neonatal and maternal factors. Neonatally, lower gestational age, low APGAR scores, sepsis, respiratory failure, and the necessity for mechanical ventilation have been associated with poor prognosis (9,10). Maternally, less studied factors like diabetes mellitus, hypertension, oligohydramnios, and tobacco use might contribute to the risk, alongside fetal/placental issues such as growth restriction and umbilical cord prolapse (6,9,10). This study aims to identify and analyze the frequency of different outcomes in neonates with MSAF, with a specific focus on mortality, and to assess the association of various maternal, fetal, and gestational characteristics with the occurrence of MSAF. Understanding these associations will enhance clinical vigilance and response strategies when managing cases with identified risk factors, thereby potentially mitigating the development of severe complications.

METHODS

This case-control study was conducted from October 2022 to September 2023 at the Department of Pediatrics, Combined Military Hospital, Kharian. A total of 100 full-term neonates were enrolled; half had been born with meconium-stained amniotic fluid (MSAF) and the other half with clear amniotic fluid, serving as controls. Enrollment was based on informed consent from parents or guardians in accordance with the Declaration of Helsinki and institutional ethical guidelines. Participants were selected using consecutive, non-probability sampling. The sample size was calculated using the Open-Epi calculator, aiming for a 95% confidence level and 95% power, with a case to control ratio of 1:1. Based on a 3.0% exposure rate in controls (6) and an odds ratio of 69.60 (6) from previous studies, the initial sample size was set at 28 per group, which was subsequently increased to 50 per group to enhance the study's robustness.

Neonates born between 37 and 42 weeks of gestation who had undergone a trial of labor were included. Those delivered by elective cesarean section, born with major congenital anomalies, intra-uterine growth restriction, or hemorrhagic amniotic fluid were excluded. The mothers underwent an initial session to document demographic and pregnancy-related characteristics. All cases were attended by a neonatologist to manage any arising complications, with subsequent care decisions based on clinical judgment. Amniotic fluid was classified into three grades: grade 1 for transparent yet slightly yellow-green fluid; grade 2 for opalescent fluid; and grade 3 for opaque fluid (6). Chorioamnionitis was clinically defined by maternal fever, leucocytosis above 15,000/µL, fetal tachycardia, uterine tenderness, and foul-smelling amniotic fluid (11). The presence of meconium aspiration syndrome (MAS) was confirmed through laryngoscopy and a chest x-ray showing bilateral patchy infiltrates, coupled with respiratory failure (12).

All neonates were monitored for complications such as hypoxic ischemic encephalopathy (HIE), acute respiratory distress syndrome (ARDS), pneumothorax, persistent pulmonary hypertension (PPH), sepsis, and prolonged neonatal intensive care unit (NICU) stay over seven days. Diagnostic criteria for HIE were adhered to as per established guidelines (13). Follow-ups were conducted for one month post-discharge to track any adverse outcomes, including mortality. Data were analyzed using SPSS version 27.0. Quantitative variables, such as maternal age, parity, duration of labor, gestational age at birth, and birth weight, were summarized using means and standard deviations or medians and interquartile ranges. Qualitative variables were described in terms of frequencies and percentages and analyzed using Chi-square or Fisher's exact tests as appropriate. Variables that showed significance in univariate analyses were further

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explored through binary logistic regression in a multivariate framework. A p-value of less than 0.05 was considered statistically significant.

RESULTS

This study involved 100 full-term neonates and their mothers, who presented for delivery. The median age of mothers at enrollment was 27 years (IQR: 9 years). Among them, 19% had hypertension, 11% had diabetes mellitus, and only 1% was a smoker. The median parity was 2 (IQR: 1), and oligohydramnios was observed in 7% of the pregnancies. The median duration of active labor was 6 hours (IQR: 4 hours), with 25% of the deliveries performed via cesarean section. Epidural analgesia was administered in 48% of cases, while labor was induced in 27%. The median gestational age at birth was 39 weeks (IQR: 2 weeks), and male neonates constituted 57% of the births. The median birth weight was 3202.5 grams (IQR: 598 grams). APGAR scores demonstrated improvement, with a median of 8 at one minute (IQR: 2) and 9 at five minutes post-delivery (IQR: 2).

Table 1 Maternal/Delivery/Neonatal characteristics at Delivery (n=100)

Variable	Cases (n=50)	Controls (n=50)	p-value
Maternal Age (years)	29.50 (IQR: 10.0)	25.50 (IQR: 7.00)	0.052
Maternal Hypertension	11 (22.0%)	8 (16.0%)	0.444
Maternal Diabetes Mellitus	7 (14.0%)	4 (8.0%)	0.525
Maternal Smoking	1 (2.0%)	-	1.000
Parity	2.00 (IQR: 2.00)	2.50 (IQR: 1.00)	0.027*
Oligohydramnios	3 (6.0%)	4 (8.0%)	1.000
Duration of Active Labor (hours)	6.50 (IQR: 3.00)	5.00 (IQR: 3.00)	0.007*
Mode of Delivery			
Vaginal Delivery	36 (72.0%)	39 (78.0%)	0.488
Caesarean Section	14 (28.0%)	11 (22.0%)	
Epidural Analgesia	28 (56.0%)	20 (40.0%)	0.109
Induction of Labor	20 (40.0%)	7 (14.0%)	0.003*
Gestational Age at Birth (weeks)	39.50 (IQR: 2.00)	38.00 (IQR: 1.00)	0.005*
Gender			
Male	31 (62.0%)	26 (52.0%)	0.313
Female	19 (38.0%)	24 (48.0%)	
Birth-Weight (g)	3180.00 (621.00)	3211.00 (644.00)	0.674
APGAR Score at One Minute Post-Birth	7.00 (IQR: 2.00)	8.00 (IQR: 2.00)	0.015*
APGAR Score at Five Minute Post-Birth	8.00 (IQR: 1.00)	9.00 (IQR: 2.00)	0.023*

Maternal, delivery, and neonatal characteristics were assessed between cases and controls. The maternal age of cases was slightly higher than controls (29.5 vs. 25.5 years), with a near-significant difference (p=0.052). Significant differences were noted in parity (p=0.027),

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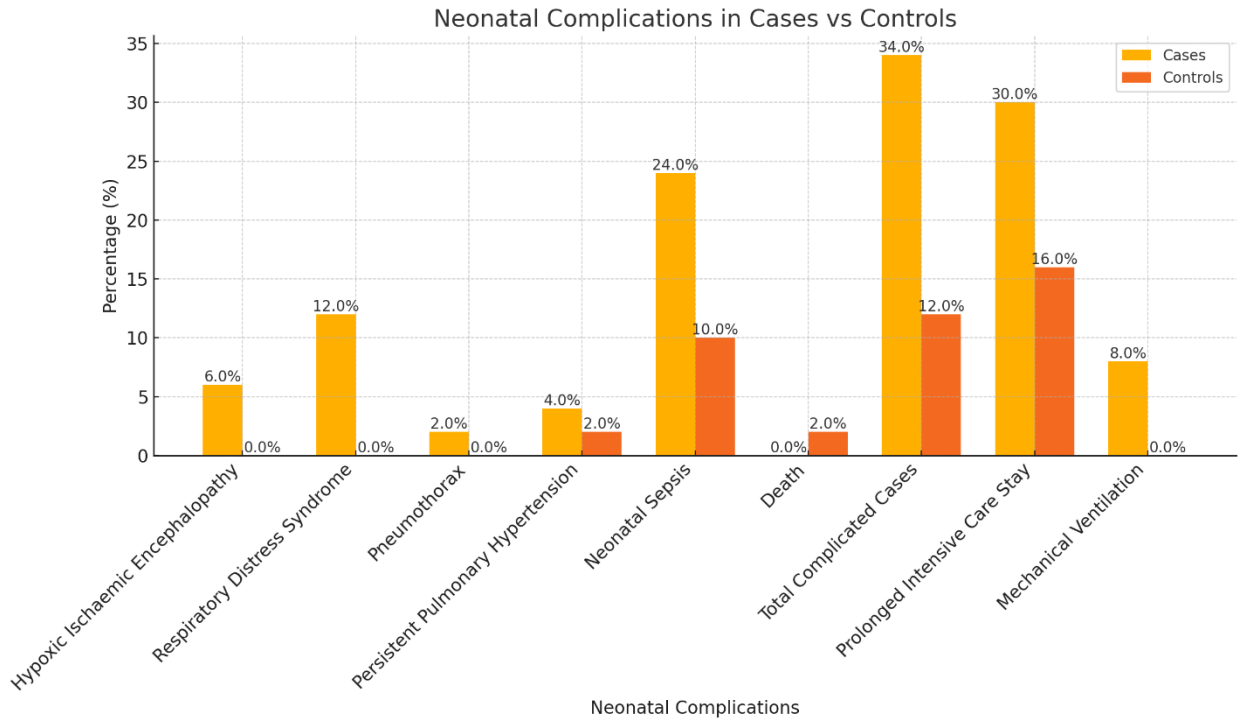
the duration of active labor (p=0.007), induction of labor (p=0.003), gestational age at birth (p=0.005), and APGAR scores at both one and five minutes (p=0.015 and p=0.023, respectively). Other maternal characteristics, including hypertension, diabetes, and smoking, did not show significant associations.

Table 2 Maternal/Neonatal Complications during study period (n=100)

Variable	Cases (n=50)	Controls (n=50)	p-value
Grade of Meconium Staining			
None	-	50 (100%)	-
Grade 1	23 (46.0%)	-	
Grade 2	22 (44.0%)	-	
Grade 3	5 (10.0%)	-	
Maternal Complications			
Placental Abruption	10 (20.0%)	3 (6.0%)	0.071*
Umbilical Cord Prolapse	3 (6.0%)	-	0.242
Uterine Rupture	2 (4.0%)	1 (2.0%)	1.000
Clinical Chorioamnionitis	7 (14.0%)	2 (4.0%)	0.160
Neonatal Complications			
Hypoxic Ischaemic Encephalopathy	3 (6.0%)	-	0.242
Respiratory Distress Syndrome	6 (12.0%)	-	0.027*
Pneumothorax	1 (2.0%)	-	1.000
Persistent Pulmonary Hypertension	2 (4.0%)	1 (2.0%)	1.000
Neonatal Sepsis	12 (24.0%)	5 (10.0%)	0.062*
Death	-	1 (2.0%)	1.000
Total Complicated Cases	17 (34.0%)	6 (12.0%)	0.009*
Prolonged Intensive Care Stay	15 (30.0%)	8(16.0%)	0.096
Mechanical ventilation	4 (8.0%)	-	0.117

Complications during the study period were observed in both maternal and neonatal groups. Placental abruption occurred in 13% of cases, umbilical cord prolapse in 3%, uterine rupture in 3%, and clinical chorioamnionitis in 9%. Among neonatal complications, hypoxic ischemic encephalopathy (HIE) was noted in 3%, respiratory distress syndrome (RDS) in 6%, pneumothorax in 1%, persistent pulmonary hypertension (PPH) in 3%, and sepsis in 17%. Mortality was recorded for one neonate during the study period. The overall complication rate in neonates was significantly higher in the cases group (34%) compared to the controls (12%), with statistical significance (p=0.009).



Further analysis revealed that neonates with meconium-stained amniotic fluid were classified according to the degree of staining: grade 1 (46%), grade 2 (44%), and grade 3 (10%). Maternal complications, such as placental abruption, tended to occur more frequently in cases than controls (20% vs. 6%), though this difference did not reach statistical significance (p=0.071). The occurrence of respiratory distress syndrome (p=0.027) and prolonged NICU stays (>7 days) also showed higher trends among cases, while the need for mechanical ventilation was observed exclusively in cases (8%).

Table 3 Adjusted odds ratios for factors significant on univariate analysis with presence of meconium-stained amniotic fluid

Variable	Adjusted Odds Ratio	p-value
Parity <3	2.20 (CI 95% 0.85 – 5.73)	0.105
Duration of Active Labor >6 hours	2.84 (CI 95% 1.08 – 7.45)	0.034*
Induction of Labor	4.65 (CI 95% 1.55 – 13.95)	0.006*
Gestational Age at Birth >39 weeks	4.01 (CI 95% 1.47 – 10.97)	0.007*
Male Gender	2.16 (CI 95% 0.78 – 5.99)	0.138
APGAR Score at One Minute Post-Birth <7	3.47 (CI 95% 0.82 – 14.69)	0.091
APGAR Score at Five Minutes Post-Birth <7	0.98 (CI 95% 0.06 – 15.59)	0.988

Binary logistic regression identified significant associations for factors linked to meconium-stained amniotic fluid. These included duration of active labor exceeding six hours (p=0.034), induction of labor (p=0.006), and gestational age at birth beyond 39 weeks (p=0.007). Parity less than three, male gender, and lower APGAR scores at one minute also showed potential associations with MSAF but did not reach statistical significance in multivariate analysis.

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DISCUSSION

The findings of this study offer valuable insights into the factors influencing the development of meconium-stained amniotic fluid (MSAF) in term neonates and the associated neonatal outcomes. The study showed that 46% of neonates had Grade 1 MSAF, with 44% and 10% exhibiting Grades 2 and 3 staining, respectively, indicating a varied severity in staining among cases.

Maternal complications such as placental abruption, umbilical cord prolapse, uterine rupture, and clinical chorioamnionitis did not demonstrate a statistically significant association with MSAF, aligning with findings from previous research by Dani et al. and Tolu et al., which reported no marked differences in the occurrence of these complications between MSAF and non-MSAF pregnancies (6,14). Similarly, Kim et al., through histological placental examination, concluded that chorioamnionitis was not significantly correlated with MSAF or meconium aspiration syndrome (MAS) (15). This consistency across studies suggests that MSAF may not directly arise from these maternal complications, underscoring the importance of other contributory factors that influence MSAF independently.

In examining neonatal outcomes, this study found no significant increase in the incidence of hypoxic ischemic encephalopathy (HIE), pneumothorax, persistent pulmonary hypertension (PPH), neonatal sepsis, or mortality among neonates with MSAF, although respiratory distress syndrome (RDS) was observed at a higher frequency ($p=0.027$). This aligns with findings by Dani et al., who also reported an elevated incidence of RDS in MSAF cases ($p=0.013$) and indicated a trend of increased risk with higher grades of MSAF (6). Furthermore, the overall complication rate was higher in neonates with MSAF than in those without, which is consistent with previous findings, reinforcing the association of MSAF with an increased likelihood of adverse neonatal outcomes.

A prolonged active phase of labor (>6 hours) emerged as a significant factor associated with MSAF (OR: 2.84; CI 95% 1.08–7.45, $p=0.034$), corroborating previous research by Addisu et al., who reported an association between total labor duration exceeding 24 hours and elevated MSAF risk (16). In contrast, Tantu et al. observed no significant correlation between prolonged labor and MSAF; however, their study assessed gestations across all phases of labor, potentially accounting for this discrepancy (17). The focus on term gestations in active labor in this study offers a more precise understanding of the impact of labor duration on MSAF development, suggesting that labor dynamics at term may play a critical role in meconium passage.

The induction of labor was also significantly associated with MSAF in this study (OR: 4.65; CI 95% 1.55–13.95, $p=0.006$). Consistent with findings from Addisu et al. and Abate et al., labor induction or augmentation was linked with an increased risk of MSAF (16,18). This observation suggests that induced labor might contribute to meconium passage, possibly due to increased uterine activity and stress responses during artificial labor progression, warranting careful monitoring in induced cases.

Gestational age exceeding 39 weeks was identified as another significant risk factor for MSAF (OR: 4.01; CI 95% 1.47–10.97, $p=0.007$). This finding aligns with studies by Dereje et al., who reported a notably higher MSAF risk in gestations extending beyond 42 weeks, and Shekari et al., who observed a progressive increase in MSAF frequency as gestation advanced through term (19,20). The increased risk at later gestational ages may reflect maturational changes in fetal gastrointestinal motility and stress responses, emphasizing the importance of gestational timing in monitoring for MSAF risk.

This study benefits from a carefully defined case-control design and a focus on term gestations, enhancing its applicability to clinical settings where term deliveries predominate. However, limitations include the single-center setting and the reliance on clinical documentation for certain diagnoses, which may introduce bias. Despite these limitations, the study adds valuable knowledge regarding factors influencing MSAF and associated neonatal outcomes, particularly the roles of prolonged labor, labor induction, and gestational age, which may inform targeted management strategies to mitigate complications associated with MSAF.

CONCLUSION

Meconium-stained amniotic fluid is a frequently encountered complication in obstetric practice, often linked with serious neonatal outcomes. This study highlights that factors such as labor induction, prolonged active labor, and advanced gestational age at delivery significantly increase the risk of MSAF development. Addressing these risk factors with careful monitoring and management may help reduce associated complications, improving outcomes for vulnerable neonates. Future research should continue exploring strategies to mitigate these influences, with the ultimate goal of enhancing neonatal health and safety.

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