ORIGINAL ARTICLE e-ISSN: 2349-0659 p-ISSN; 2350-0964

From Meconium Staining to Respiratory Support: Clinical Spectrum and Early Neonatal Outcomes across Two Referral Centers

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Abstract

Background: Meconium-stained amniotic fluid (MSAF) is associated with neonatal respiratory morbidity, including meconium aspiration syndrome (MAS). **Objective:** The objective of this study was to evaluate the clinical characteristics, spectrum of respiratory support required, and short-term outcomes among neonates born through MSAF in two referral centers. **Materials and Methods:** This prospective two-center cohort study included 72 neonates born through MSAF. Maternal, obstetric, and neonatal characteristics were recorded. Neonates were assessed for respiratory distress, MAS, need for oxygen, continuous positive airway pressure (CPAP), mechanical ventilation, complications, and in-hospital outcome. **Results:** MAS developed in 19/72 neonates (26.4%), while respiratory distress occurred in 26/72 (36.1%). Neonates with MAS had significantly lower Appearance, Pulse, Grimace, Activity, and Respiration (APGAR) scores at 1 min (5.40 vs. 7.40) and 5 min (7.50 vs. 8.50; both $P = 0.001$). Among neonates with respiratory distress, 26.9% settled within 2 h, 30.8% received oxygen by hood, 26.9% required CPAP, and 15.4% required mechanical ventilation. Pneumothorax occurred in 4.2%, while persistent pulmonary hypertension, septicemia, hypoxic-ischemic encephalopathy, and shock each occurred in 2.8%. Two of 19 neonates with MAS died. **Conclusion:** MAS was common among MSAF-exposed neonates and was associated with lower APGAR scores and substantial respiratory morbidity.

Keywords: Appearance, pulse, grimace, activity, and respiration score, Meconium aspiration syndrome, Meconium-stained amniotic fluid, Neonatal outcome, Respiratory distress

Asian Pac. J. Health Sci., (2026); DOI: 10.21276/apjhs.2026.13.3.07

Introduction

Meconium-stained amniotic fluid (MSAF) occurs in about 5–20% of women in labor and is more likely to occur as the gestation period progresses. Most babies who are exposed to meconium are fine after birth, but some have respiratory distress and other complications. The most significant of these is meconium aspiration syndrome (MAS) which remains a major cause of neonatal morbidity, especially in term and post-term infants.[1,2]

The diagnosis of MSAF is typically made when a neonate born through MSAF develops respiratory distress, has compatible chest-radiographic findings, and has no other clear cardiopulmonary cause. It has a multifactorial pathogenesis. Meconium can block the airways, cause chemical pneumonitis, affect surfactant function, cause ventilation-perfusion mismatch, cause pulmonary vasoconstriction, cause air leak, and cause persistent pulmonary hypertension. The clinical course is highly variable, from a short period of supplemental oxygen to a severe respiratory failure necessitating continuous positive airway pressure (CPAP), mechanical ventilation, and hemodynamic support.[2,3]

The management of neonates exposed to meconium in the delivery room has evolved significantly over the years. Intubation and tracheal suctioning of vigorous neonates were no longer recommended as a routine practice as it did not decrease the incidence of MAS or other respiratory complications.[4] Nevertheless, a seemingly stable transition at birth does not exclude subsequent deterioration of respiration. Singh *et al*. demonstrated that respiratory distress, such as MAS, can occur after birth in vigorous neonates born through MSAF, highlighting the importance of close monitoring during the early neonatal period.[5]

A number of maternal, intrapartum, and neonatal factors have been linked to MAS. These include thick meconium, fetal distress, prolonged labor, abnormal cardiotocography, cesarean delivery, low appearance, pulse, grimace, activity, and respiration (APGAR) scores and need for resuscitation at birth.[5-7] Some of these characteristics also seem to be linked to more severe disease and a higher risk of needing respiratory assistance. Their predictive value is not consistent, however, and the clinical course is still hard to predict in individual neonates.

There are also differences in the burden of MAS between hospitals and populations. In a prospective study in India, 11.3% of neonates born by MSAF developed MAS, with a significant number needing mechanical ventilation. Other complications reported included air leak, persistent pulmonary hypertension, sepsis, severe birth asphyxia, and death.[8] The variation between

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How to cite this article: Dar TMUD, Khan OA, Mir NY, Charoo BA. From Meconium Staining to Respiratory Support: Clinical Spectrum and Early Neonatal Outcomes across Two Referral Centers. Asian Pac. J. Health Sci., 2026;13(3):25-29.

Source of support: Nil.

Conflicts of interest: None.

Received: 15/06/2026 **Revised:** 02/08/2026 **Accepted:** 08/08/2026

studies may be due to differences in referral patterns, obstetric risk, meconium consistency, diagnostic criteria, and access to neonatal intensive care.

Thus, there remains a need for setting specific data on presentation and early course of neonates born through MSAF. The present two-center prospective cohort study was conducted to describe maternal and neonatal characteristics, to determine the proportion of neonates who developed MAS, to compare selected perinatal features between the MAS and non-MAS groups, and to document the requirement for respiratory support, complications, and short-term in-hospital outcomes.

Materials and Methods

Study Design and Setting

This prospective, hospital-based observational cohort study was conducted in the Department of Pediatrics and Neonatology, Sher-i-Kashmir Institute of Medical Sciences (SKIMS), Soura, and the Department of Pediatrics, SKIMS Medical College, Bemina. Neonates born through MSAF were consecutively enrolled during the study period.

Study Participants

Neonates born through MSAF were eligible for inclusion. Neonates were excluded when parental consent was declined or when congenital heart disease, congenital diaphragmatic hernia, congenital pulmonary airway malformation, or another major congenital pulmonary anomaly was present.

Data Collection and Clinical Assessment

Maternal, obstetric, and neonatal information was recorded using a structured pro forma. Maternal variables included parity, mode of delivery, and underlying maternal conditions. Neonatal variables included sex, gestational age, APGAR scores at 1 and 5 min, clinical signs of respiratory distress, respiratory-support requirements, complications, and in-hospital outcome.

Clinical signs assessed included tachypnoea, nasal flaring, subcostal retraction, grunting, and cyanosis. Respiratory distress was identified on the basis of documented clinical findings during neonatal assessment.

Definition of MAS

MAS was diagnosed in neonates born through MSAF who developed respiratory distress with compatible chest-radiographic findings and no alternative congenital cardiopulmonary explanation.

Respiratory Support and Complications

The respiratory course was documented for all affected neonates. Maximum respiratory support was categorized as spontaneous resolution within 2 h without assisted respiratory support, oxygen by hood, CPAP, or mechanical ventilation.

Recorded complications included pneumothorax, persistent pulmonary hypertension of the newborn, septicemia, hypoxic-ischemic encephalopathy, and shock. Complications were not mutually exclusive. Short-term outcome was categorized as discharge alive or in-hospital death.

Outcome Measures

The primary outcome was the development of MAS among neonates born through MSAF.

Secondary outcomes included:

- Occurrence of respiratory distress;
- Respiratory-support requirement;
- Neonatal complications;
- APGAR scores at 1 and 5 min; and
- In-hospital survival.

Statistical Analysis

Categorical variables were summarized as frequencies and percentages, and continuous variables as mean ± standard deviation. Neonates were categorized into MAS and non-MAS groups for comparative analysis.

Sex distribution was compared using Fisher's exact test. Continuous variables, including gestational age and APGAR scores, were compared using Welch's independent-samples *t*-test. Mean differences and odds ratios were reported with corresponding 95% confidence intervals where appropriate. Major proportions were presented with 95% confidence intervals.

All tests were two-tailed, and $P < 0.05$ was considered statistically significant. Data were entered into Microsoft Excel and analyzed using IBM Statistical Package for the Social Sciences Statistics.

Ethical Considerations

The study was conducted after approval from the Institutional Ethics Committee. Written informed consent was obtained from the parent or legal guardian of each neonate before enrolment. Participant confidentiality was maintained throughout the study.

Results

Clinical Profile of the Study Population

A total of 72 neonates born through MSAF were included in the study. There were 35 (48.6%) male and 37 (51.4%) female neonates. Cesarean section was the predominant mode of delivery, accounting for 62 (86.1%) deliveries, while 10 (13.9%) neonates were delivered vaginally. Forty-two mothers (58.3%) were primiparous and 30 (41.7%) were multiparous. Most mothers had no underlying medical condition (70.8%). Pregnancy-induced hypertension was the commonest maternal comorbidity (13.9%), followed by gestational diabetes mellitus (5.6%), anemia (4.2%), oligohydramnios (2.8%), and antepartum hemorrhage (2.8%).

MAS developed in 19 of the 72 neonates (26.4%), whereas 53 (73.6%) did not develop MAS. Gestational age and sex distribution were comparable between the MAS and non-MAS groups ($P = 0.382$ and $P = 0.281$, respectively). However, neonates who developed MAS had significantly lower APGAR scores at both 1 min (5.4 ± 1.62 vs. 7.4 ± 1.4; $P = 0.001$) and 5 min (7.5 ± 0.3 vs. 8.5 ± 0.2; $P = 0.001$) [Table 1].

Clinical Presentation

Respiratory distress was observed in 26 neonates (36.1%). Tachypnoea was the most frequent presenting feature, followed

Table 1: Clinical profile of neonates born through meconium-stained amniotic fluid

Characteristic	*Overall (n=72) (%)*	*MAS (n=19) (%)*	*Non-MAS (n=53) (%)*	*P-value*
Sex				
Male	35 (48.6)	8 (42.1)	27 (50.9)	
Female	37 (51.4)	11 (57.9)	26 (49.1)	**0.281**
Mode of delivery				
Vaginal delivery	10 (13.9)	–	–	–
Cesarean section	62 (86.1)	–	–	–
Parity				
Primiparous	42 (58.3)	–	–	–
Multiparous	30 (41.7)	–	–	–
Maternal underlying conditions				
Pregnancy-induced hypertension	10 (13.9)	–	–	–
Gestational diabetes mellitus	4 (5.6)	–	–	–
Anemia	3 (4.2)	–	–	–
Oligohydramnios	2 (2.8)	–	–	–
Antepartum hemorrhage	2 (2.8)	–	–	–
No underlying condition	51 (70.8)	–	–	–
Gestational age (weeks)	–	39.04±2.4	38.01±2.8	**0.382**
APGAR score				
At 1 min	–	5.4±1.62	7.4±1.4	**0.001**
At 5 min	–	7.5±0.3	8.5±0.2	**0.001**

"Bold values indicate statistically significant differences (P < 0.05).

by nasal flaring, subcostal retractions, grunting, and cyanosis [Figure 1].

Treatment Received

Among the 26 neonates who developed respiratory distress, 7 (26.9%) improved within 2 h without assisted respiratory support. Oxygen by hood was administered to 8 (30.8%) neonates, 7 (26.9%) required CPAP, and 4 (15.4%) required mechanical ventilation [Table 2 and Figure 2].

Clinical Outcomes

Pneumothorax was the most common complication, occurring in 3 neonates (4.2%). Persistent pulmonary hypertension of the newborn, septicemia, hypoxic-ischemic encephalopathy, and shock were each observed in 2 neonates (2.8%). Among the 19 neonates diagnosed with MAS, 17 (89.5%) were discharged following clinical improvement, while 2 (10.5%) died during hospitalization [Table 3].

Discussion

In this two-center cohort of 72 neonates born through MSAF, 19 (26.4%) developed MAS, while respiratory distress occurred in 26 (36.1%). The APGAR scores at 1 and 5 min were significantly lower in neonates with MAS, while there was no difference between groups in terms of gestational age or sex. Of the neonates with respiratory distress, 26.9% improved within 2 h, 30.8% were given oxygen by hood, 26.9% needed CPAP, and 15.4% needed mechanical ventilation. The most common complication was pneumothorax, and two of the 19 neonates who developed MAS died in the hospital.

The proportion of observed MAS was greater than that reported in many larger delivery cohorts. Liu and Harrington conducted a prospective study of 708 meconium-exposed births and reported that 6.8% had respiratory symptoms, with only 24 infants having symptoms consistent with MAS, and 45.8% of these infants requiring ventilatory support. Important predictors were thick meconium, fetal distress, APGAR scores <7 at 1 and 5 min, and resuscitation. The estimated probability of respiratory

Table 2: Treatment received among neonates with respiratory distress (*n*=26)

Treatment	*Frequency*	*Percentage*
Settled within 2 h	7	26.9
Oxygen by hood	8	30.8
Continuous positive airway pressure	7	26.9
Mechanical ventilation	4	15.4
Total	26	100

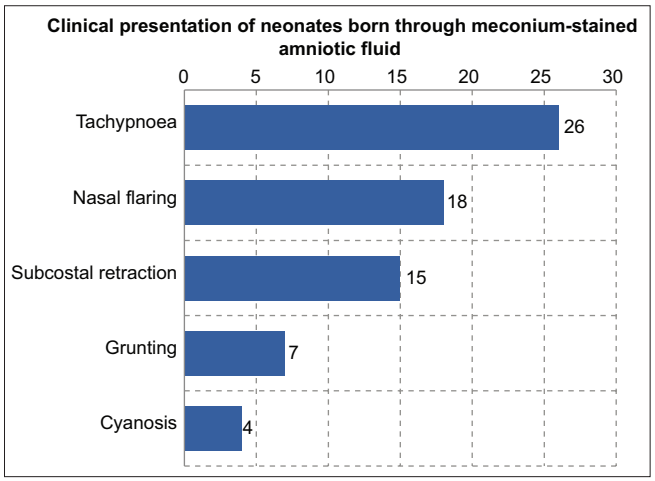

Figure 1: Distribution of clinical signs among neonates born through meconium-stained amniotic fluid

symptoms was 79.8% when all three factors were present, and 0.8% when they were not.[9] This may be due to referral to tertiary neonatal units, selection of cases or a higher underlying obstetric risk in our cohort.

The correlation between low APGAR scores and MAS in our study is similar to that reported in previous studies. In a secondary analysis of a multicenter trial of thick MSAF, Xu *et al.* identified marked fetal heart-rate abnormalities as a predictor of moderate-to-severe MAS, and meconium below the vocal cords and immediate resuscitation as predictors of early MAS and late-onset respiratory distress. They also demonstrated that non-respiratory

Table 3: Clinical outcomes among neonates born through meconium-stained amniotic fluid

Outcome	*Frequency*	*Percentage*
Complications		
Pneumothorax	3	4.2
Persistent pulmonary hypertension of the newborn	2	2.8
Septicemia	2	2.8
Hypoxic-ischemic encephalopathy	2	2.8
Shock	2	2.8
Final outcome among MAS cases (*n*=19)		
Discharged alive	17	89.5
In-hospital death	2	10.5

MAS: Meconium aspiration syndrome

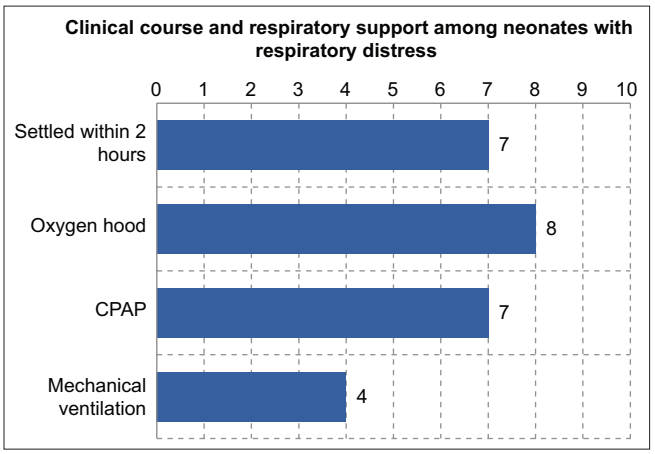

Figure 2: Maximum respiratory support required among neonates with respiratory distress

morbidity was associated with the severity of respiratory disease.[10] These results indicate that close monitoring is warranted even if respiratory failure is not evident at birth.

Our respiratory-support findings also highlight the wide clinical spectrum of MAS. Hernández *et al*. studied 82 neonates with clinical and radiographic MAS, 39 of which (48%) needed mechanical ventilation. Ventilation was predicted by fetal tachycardia, longer time from meconium detection to delivery, low 5-min APGAR score, delivery room intubation, and cesarean delivery. They found that their model had a sensitivity of 72% and a specificity of 64%, but misclassified 32% of cases, indicating that clinical variables alone are not precise.[11] Four neonates with respiratory distress in our study required mechanical ventilation, whereas only four neonates with respiratory distress were treated with mechanical ventilation in the other studies. The denominators and severity profiles are different, so direct comparisons are not possible.

The high rate of cesarean delivery in our cohort (86.1%) may be due to the obstetric risk of MSAF and the referral profile of the centers participating in the study. Levin *et al*. identified that adverse neonatal outcomes of MSAF-affected deliveries could be estimated by maternal and intrapartum variables and created a simple prediction model for this purpose.[12] Dani *et al*. also showed a graded relationship between the severity of the meconium and the neonatal outcome: the adjusted odds ratio for a composite adverse outcome was 16.82 for grade 2 MSAF and 33.79 for grade 3 MSAF. They were included in their composite resuscitation, cord pH < 7.10, MAS, persistent pulmonary hypertension, respiratory disease, hypoxic-ischemic encephalopathy, and sepsis.[13] Unfortunately, in our study, we were unable to record meconium thickness, and we were unable to determine if the high operative-delivery and MAS rates were limited to neonates exposed to thick meconium.

Complications in the current cohort were pneumothorax, persistent pulmonary hypertension, septicemia, hypoxic-ischemic encephalopathy, and shock. Even after controlling for fetal heart-rate abnormalities and maternal disease, Berkus *et al*. found that moderate or thick meconium was independently associated with adverse neonatal outcome, with a relative risk of 3.2.[14] This is a plausible explanation for the clustering of pulmonary and neurological complications seen in more severe MAS, but cannot be confirmed in our data set because meconium grading was not included.

The mortality rate for MAS cases (10.5%) should be viewed with caution as it is based on only two deaths and has a large confidence interval. However, it suggests that MAS continued to be clinically significant in this group. Mazouri *et al*. reported that higher lactate levels in the umbilical cord were correlated with pulmonary hemorrhage, persistent pulmonary hypertension, intraventricular hemorrhage, and respiratory failure requiring ventilatory support in neonates with MAS. A lactate level >4.1 mmol/L also discriminated between thick and thin meconium in neonates.[15] Biochemical predictors were not explored in this second manuscript, but these observations indicate that future clinical models could benefit from incorporating obstetric data, APGAR scores, meconium grade, and cord-blood markers.

The prospective design, consecutive enrolment, inclusion of two centers, and systematic documentation of respiratory support and complications are strengths of this study. The main limitations are the small sample (19 MAS events), the lack of meconium grading and fetal heart-rate data, and the lack of multivariable analysis. The high cesarean rate could also restrict the generalizability to lower-risk delivery populations. Furthermore, complications were reported for the entire cohort and not separately by MAS status, and outcomes were limited to hospitalization without longer-term respiratory or neurodevelopmental follow-up.

Conclusion

More than one-quarter of neonates born through MSAF developed MAS, and over one-third experienced respiratory distress. Lower 1- and 5-min APGAR scores were strongly associated with MAS, while a clinically important minority required CPAP or mechanical ventilation. Pneumothorax, persistent pulmonary hypertension, neurological injury, sepsis, shock, and in-hospital death further demonstrate the potential severity of the condition. Careful early assessment and continued observation of MSAF-exposed

neonates are therefore warranted, particularly when low APGAR scores or other signs of perinatal compromise are present.

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