ISSN: 2581 – 3633

International Journal of Medical Science and Advanced Clinical Research (IJMACR)

Available Online at: https://www.ijmacr.com

Volume – 9, Issue – 4, August – 2026, Page No.: 198 – 205

To evaluate the effect of surfactant administration in the treatment of term and late preterm neonates with me conium aspiration syndrome (MAS) in relation to outcome (Death/Discharge)

[1]Dr. Kirti Bardia, Department of Paeditrics, P.B.M. Hospital, S. P. Medical College, Bikaner.

[2]Dr. Mukesh Kumar Beniwal, Department of Paeditrics, P.B.M. Hospital, S. P. Medical College, Bikaner.

Corresponding Author: Dr. Kirti Bardia, Department of Paeditrics, P.B.M. Hospital, S. P. Medical College, Bikaner.

How to citation this article: Dr. Kirti Bardia, Dr. Mukesh Kumar Beniwal, "To evaluate the effect of surfactant administration in the treatment of term and late preterm neonates with me conium aspiration syndrome (MAS) in relation to outcome (Death/Discharge)", IJMACR– August – 2026, Volume – 9, Issue –4, P. No. 198 – 205.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Background: The transition from intrauterine to extra uterine life is a critical period for neonates accompanied by significant physiological adjustments. However, complications arising during this transition can lead to significant morbidity and mortality (5% to 12%). To evaluate the effect of surfactant administration in the treatment of term and late preterm neonates with me conium aspiration syndrome (MAS) in relation to outcome (Death/Discharge)

Methods: This study evaluated and compared the clinical outcomes of surfactant administration in term and late preterm neonates with Me conium Aspiration Syndrome (MAS) at P.B.M. Hospital, Bikaner.

Results- Infants who got surfactant early needed oxygen for about 43 hours, compared to about 51 hours for the late group. Ventilation time was also slightly shorter for early treatment (about 8.5 hours vs. 10.4 hours). Hospital stays were almost the same—7.1 days for early and 7.5 days for late. The p-values for all outcomes are above 0.05, suggesting these differences are not statistically significant. In other words, the timing of surfactant made less of a difference in full-term infants than in late preterm newborns. The small differences seen here might not be meaningful in practice.

So, while early surfactant is still a good idea, the biggest benefit is seen in preterm babies rather than those born at full term.

Conclusion: The results highlight that late preterm neonates with MAS experience significantly poorer clinical outcomes compared to term counterparts, including higher mortality, more severe respiratory distress, and prolonged need for respiratory support and hospitalization. Late preterm infants showed greater systemic involvement — evidenced by elevated in flammatory markers, more severe radiographic findings, and lower APGAR scores — reflecting their increased physiological vulnerability. Importantly, early

administration of surfactant was associated with improved clinical outcomes across both groups, notably reducing the duration of mechanical ventilation, oxygen therapy, and hospital stay. These benefits were more pronounced in the late preterm group, suggesting that timely intervention is particularly crucial in this population. While the difference in mortality rates between early and late surfactant administration was not statistically significant, trends indicated a potential survival benefit with early intervention, especially among late preterm neonates. The study emphasizes that early surfactant therapy, guided by clinical severity, can significantly enhance morbidity outcomes even if mortality impacts are variable.

Keywords: Neonates, Surfactant, MAS.

Introduction

The transition from intrauterine to extra uterine life is a critical period for neonates accompanied by significant physiological adjustments. However, complications arising during this transition can lead to significant morbidity and mortality (5% to 12%) 1. Among these, Me conium Aspiration Syndrome (MAS) presents a formidable challenge in term and late preterm neonates, particularly in developing nations where perinatal care infrastructure may be limited. Me conium Aspiration Syndrome (MAS) is a serious respiratory condition that occurs when a newborn inhales a mixture of me conium (the thick, greenish-black substance that forms in the intestines during fetal development) and amniotic fluid into the lungs during or shortly after delivery. Normally me conium is expelled after birth but fetal distress, often caused by hypoxia or intrauterine stress, leads to the passage of me conium into the amniotic fluid, inhalation of which causes severe respiratory issues, lung damage and other complications that need immediate medical care. Me conium is composed of water (72% to 80%), exfoliated skin cells, lanugos, vernixcaseosa, and gastrointestinal secretions2. Three randomized controlled trials confirm some benefits of the administration of several boluses of a natural surfactant in the treatment of MAS. Although overall mortality was no difference between the treatment group and the placebo group in each of these trials, the administration of several doses of a natural preparation was found to improve oxygenation in all three, to reduce the need for ECMO in two, and to reduce the risk of pneumothorax in one. 3 Surfactant therapy is one of the newer promising modes of therapeutic interventions in babies with severe MAS4-7. Current evidence would support the use of bolus surfactant therapy on a case by case basis in nurseries with a relatively high mortality associated with MAS, or the lack of availability of other forms of respiratory support such as HFV or NO[8].

Material and method

Study Setting: The study was conducted in the Department of Paediatrics, PBM Hospital, S. P. Medical College, Bikaner.

Study Design: Prospective observational study

Sample Size: The sample size was calculated based on a previous study that reported prevalence of Me conium Aspiration Syndrome in me conium stained amniotic fluid was taken as 7.7 %, 95 % level of confidence and Error rates et at 0.05 levels. Total 110 cases were required to conduct the study.

$$N = \frac{Z^2 P (1-P)}{d^2}$$

$$N = \frac{(1.96)^2 (7.7) (92.3) (5)^2}{}$$

- N = sample size

- Z^2 = Standard normal deviate (taken as 1.96 for 95 % confidence level)
- P = Expected prevalence of me conium aspiration syndrome in me conium-stained amniotic fluid (taken as 7.7) [39]
- D = Absolute allowable error (taken as 5%)

Based on the formula, we took sample size as 110 cases.

Sampling Technique:

All neonates with me conium aspiration syndrome in me conium-stained amniotic fluid considering inclusion and exclusion criteria were included in the study till the desired sample size was required.

Study Population Inclusion Criteria

Gestation age >=34 weeks, presence of MSAF or me conium staining of skin, umbilicalcordor nails, non-vigorous babies, presence of respiratory distress (Downes score>=6), chest radiograph suggestive of me conium aspiration and age<48hr.

Exclusion Criteria

- This study excluded congenital abnormalities antenatally diagnosed congenital heart disease, hydrops fetalis, pneumothorax, pulmonary hemorrhage.
- It also excluded babies with septicemia and respiratory distress syndrome.

Results and observations

Table1**:** Demographic and Baseline Characteristics of the patients in each group.

Parameter	Term group (n=49)	Late Pre-term Group (n=61)	P-value
Male*	35 (71.4%)	44 (72.1%)	0.551
Female*	14 (28.6%)	17 (27.9%)	
Gestational Age**	39.04 ± 1.54	35.00 ± 0.8	
Birth wt.**	2692.86 ± 414.65	2114.29 ± 83.82	
Age at Surfactant Administration(hours)**	2.67 ± 1.29	2.91 ± 1.45	0.376

The demographic and baseline characteristics showed no significant difference between the Term and Late Pre - term groups in terms of gender distribution (male: 71.4% vs. 72.1%, p=.551; female: 28.6% vs. 27.9%). The mean gestational age of term group and late pre –term group were found to be 39.04 ± 1.54 and 35.00 ± 0.8 weeks, respectively. Birth weight was found to be 2692.86 ± 414.65 g in Term group while 2114.29±83.82 in Late Pre-term group. The age at surfactant administration did not differ significantly between the groups (2.67±1.29 vs 2.91±1.45 hours, p=0.376).

Table 2: Number of patients with type of surfactant in each group.

Table 2 compares the types of surfactants administered to two groups, namely, term and late pre-term infants. In Table 3, which compares the number of patients receiving different types of surfactant in the Term Group (49 patients) and the Late Pre-term Group (61 patients), the distribution shows that Curo surf was administered to 30 out of 49 term patients (61.2%) and 32 out of 61 late pre- term patients (52.5%). On the other hand, Neo surf was given to19out of49 term patients (38.8%) and 29 out of 61 late pre-term patients (47.5%). These figures indicate a slightly higher percentage of Curo surf use in the term group compared to the late pre-term group, with a higher proportion of Neo surf being used in the late pre-term group. This may reflect availability of brand of surfactant at the time of use.

Table 3: Duration of ventilation (hours), oxygenation (hours) and Hospital Stay (days) in late preterm in relation to the time of surfactant administration

Time of Surfactant Administration	Duration of oxygenation (hours)	P- value	Duration of ventilation (hours)	P-value	Hospital Stay (days)	P- value
≤2Hours	65.22±37.57	<0.001	12.39±12.3	<0.001	7.0±1.46	<0.001
>2Hours	107.79±30.46		30.58±16.70		9.1± 1.41	

Table 3 examines only late pre-term newborns, comparing those who received surfactant within 2 hours to those who received it later. This table compares outcomes based on when they received surfactant. Infants who got surfactant within 2 hours spent much less time needing extra oxygen (about 65 hours) compared to those treated later (about 107hours). The need for ventilation was also shorter if surfactant was given early—just over 12 hours versus more than 30 hours for the late group. Hospital stays were slightly shorter for the early group (7 days vs. nearly 9 days). The p-values for oxygenation, ventilation time and hospital stay are below 0.001, showing that these differences are statistically significant. This means the results are unlikely to be due to chance. Overall, early surfactant clearly helps late preterm infants recover faster, spend less time in intensive care, and get discharged sooner. Delaying surfactant more than doubles the time these babies need oxygen and ventilation. Early inter ventionis especially important in this group to reduce complications and hospital time.

Table 4: Duration of ventilation (hours), oxygenation (hours), Hospital Stay (days) in term group in relation to the time of surfactant administration

Time of Surfactant Administration	Duration of oxygenation (hours)	P-value	Duration of ventilation (hours)	P-value	Hospital Stay (days)	P-value
≤2Hours	43.06±29.35		8.53±8.59		7.12±1.36	
>2Hours	51.06±30.26	0.378	10.44±12.63	0.580	7.50±1.27	0.333

This table focuses on term newborns and compares the same outcomes. Here, the difference between early (≤2 hours) and late (>2 hours) surfactant administration is smaller than in late preterm babies. Infants who got surfactant early needed oxygen for about 43 hours, compared to about 51 hours for the late group. Ventilation time was also slightly shorter for early treatment (about 8.5 hours vs. 10.4 hours). Hospital stays were almost the same—7.1 days for early and 7.5 days for late. The p-values for all outcomes are above 0.05, suggesting these differences are not statistically significant. In other words, the timing of surfactant made less of a difference in full-term infants than in late preterm newborns. The small differences seen here might not be meaningful in practice. So, while early surfactant is still a good idea, the biggest benefit is seen in preterm babies rather than those born at full term.

Table 5: Outcome in terms of death and discharge in various group.

Group	Outcome	Age of Surfactant Administration		Total	P-Value
		≤2Hours	>2Hours		

Late Pre Term	Death	6(26%)	14(36.8%)	20(32.7%)	0.386
	Discharge	17(74%)	24 (63.1%)	41(67.2%)	
Term	Death	2(11.7%)	2 (6.25%)	4(8.16%)	0.502
	Discharge	15(88.2%)	30(93.75%)	45(91.8%)	
Overall	Death	8(20%)	16(22.8%)	24(21.8%)	0.727
	Discharge	32(80%)	54(77.1%)	86(78.2%)	

Table 5 compares the outcome (death or discharge) between babies who received surfactant within 2 hours and those who received it later, across all groups. More deaths occurred among new born s given surfactant after 2 hours (16 vs. 8 overall). In the late pre-term group, the difference is even more notable (14 deaths after late surfactant vs. 6 deaths with early). For term babies, the number of deaths is equal (2 in each group), suggesting less impact of timing in this sub group. More new born s survived and were discharged when they received early surfactant (32 vs 54overall; 17 vs 24 in late pre-term; 15 vs 30 in term) but none of the data was statistically significant. Chi – square analysis was used, and p-value was calculated. Still, the trend strongly suggests that earlier surfactant saves more lives and improves discharge rates, especially in late pre-term infants. This highlights the importance of fast surfactant delivery to improve survival in this population.

Discussion

Me conium Aspiration Syndrome especially in developing countries contributes in significant cause of respiratory diseases in term and late preterm neonates. However, the severity may be controlled due to improved management practices, still there are significant MAS cases.

Table 6: Summary of our findings with that of previous studies.

Parameter	Present Study Findings	Findings in Published Literature	References
Gestational Age (weeks)	Term:39.04±1.54; Late Preterm: 35.00± 0.80	MAS rare before 34 weeks	[9]
Birth Weight (g)	Term:2692.85 ±414.64; Late Preterm:2114.29±83.82	matches INTER GROWTH – 21 st data	[10]
Gender (%male)	Term: 71.4%;LatePreterm:72.1%	Slight male preponderance or near-Equal sex ratio	[11]
Preeclampsia/ Eclampsia (%)	Higher in late preterm (39.3%) vs. term (2%)	Preeclampsia/PIH increases MAS risk; late preterm higher maternal Risk factors	[12]
Maternal Diabetes Mellitus (%)	Higher in late preterm (26.2%) vs Term (8.2%)	Maternal DM more in late preterm births	[13]
No. of Antenatal checkup	Latepreterm:4.77±0.97; Term:7.34±0.97	Reduced number of antenatal Checkup increases MAS risk	[14]

Shock (%)	Latepreterm:39.3%;Term:4%	Shock is more common in late preterm MAS;	[15]
Cyanosis (%)	Latepreterm:77%;Term:24.4%	Cyanosis, hypoxemia, and severe respiratory distress more common in Preterm MAS	[15]
Hypothermia (%)	Latepreterm: 26.2%; Term: 0%	Hypothermia more frequent with severe illness/ preterm status	[15]
Oxygen Saturation (SpO_2%)	Late preterm: 82.0 ± 6.38; Term:88.5± 6.02	Lower SpO_2 in severe/ late preterm MAS; matches literature	[16]
WBC(cells/mcL)	Late preterm: 12515; ?81.48;p=0.02(lower in late pre-term)	WBC often lower in preterm due to immature immune system	[16]
Platelet Count (cells/mcL)	Late preterm: 177023. 90; Term: 223985. 54; P < 0.001 (lower in late preterm)	Thrombocy to peniacan occur in late Preterm due to immature immune function	[17]
CRP Positive (%)	Late preterm: 82 %; Term: 40.8%	CRP of ten elevated in severe MAS; Higher in preterm/infection	[18]
APGARat1min APGARat5min	Term:5.39±0.74 Latepreterm:4.89±0.91 Term:6.66±1.00 Latepreterm:5.79±1.24	APGAR scores were significantly lower in late preterm newborn compared to term new born	[19]
Patchy Infiltrates (%)	Late preterm: 54.1 %; Term: 22.4 %; Overall: 40%	Patchy infiltrates =classic MAS finding; Late Preterm more common	[20]
Deaths (%)	Total mortality: 21.% Early surfac tantmortality:20 % Late surfactant mortality: 22.8%	Higher mortality in late age of surfactant than early surfactant administration	[21]
Ventilation duration (hrs)	Surfactan within 2 hours: 0.75±10.93 Surfactant after 2 hours: 21.37±17.98	Prolonged ventilation needed when Age of administration is more	[21]
Hospital stay(days)	Surfactant within 2 hours:7.13±1.44 Surfactant after 2 hours:8.34±1.57	Shorter length of hospital stay for those Who received early surfactant	[21]
Oxygenation duration (Hours)	Surfactant within 2 hours: 55.80 ± 35.68 Surfactant after2 hours: 81.69±41.52	Prolonged oxygenation needed when age of administration is more	[21]

Conclusion

This study evaluated and compared the clinical outcomes of surfactant administration in term and late preterm neonates with Me conium Aspiration Syndrome (MAS) at P.B.M. Hospital, Bikaner.

The results highlight that late preterm neonates with MAS experience significantly poorer clinical outcomes compared to term counterparts, including higher mortality, more severe respiratory distress, and

prolonged need for respiratory support and hospitali zation.

Late preterm infants showed greater systemic involvement—evidenced by elevated inflammatory markers, more severe radiographic findings, and lower APGAR scores—reflecting their increased physiological vulnerability. Importantly, early administration of surfactant was associated with improved clinical outcomes across both groups, notably reducing the duration of mechanical ventilation, oxygen therapy, and hospital stay. These benefits were more pronounced in the late preterm group, suggesting that timely intervention is particularly crucial in this population. While the difference in mortality rates between early and late surfactant administration was not statistically significant, trends indicated a potential survival benefit with early intervention, especially among late preterm neonates. The study emphasizes that early surfactant therapy, guided by clinical severity, can significantly enhance morbidity outcomes even if mortality impacts are variable.

In conclusion this study re in forces the importance of evidence - based, early respiratory interventions in reducing complications and improving clinical outcomes in neonates affected by MAS.

Future research should focus on multicenter, randomized trials with larger cohorts to validate these findings and explore the efficacy of different surfactant types and delivery methods. Long-term follow-up assessing neuro developmental outcomes in both term and late pre-term MAS patients is crucial. Evaluating non-invasive surfactant techniques may also offer safer alternatives, especially for vulnerable neonates.

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