Biological and Clinical Sciences Research Journal
eISSN: 2708-2261; pISSN: 2958-4728
www.bcsrj.com
DOI: https://doi.org/10.54112/bcsrj.v6i12.2196
*Biol. Clin. Sci. Res. J., Volume 6(12), **2025**: 2196*
Original Research Article

Complications of Surfactant Treatment in Late Preterm Infants with Respiratory Distress Syndrome

Tarifa Ilyas*, Urwa Khalil, Tahir Masood

Department of Paediatrics, Arif Memorial Teaching Hospital, Lahore, Pakistan
**Corresponding author`s email address:* teff6496@gmail.com

(Received, 14th November 2025, Accepted 18th December 2025, Published 31st December 2025)

Abstract: *Respiratory distress syndrome remains a common cause of morbidity in late preterm infants due to surfactant deficiency and immature lung function. Surfactant therapy administered via minimally invasive techniques has improved respiratory outcomes; however, early complications may still occur.* ***Objective:*** *To determine the frequency of early complications following surfactant therapy in late preterm infants with respiratory distress syndrome.* ***Methods:*** *A prospective observational study was conducted at the Department of Paediatrics, Arif Memorial Teaching Hospital, Lahore, from 3rd June 2025 to 3rd November 2025. A total of 111 late preterm infants with gestational age between 32 and 36 weeks diagnosed with respiratory distress syndrome and requiring surfactant therapy were enrolled through non-probability consecutive sampling. Surfactant was administered using the minimally invasive surfactant therapy technique while maintaining continuous positive airway pressure support. Early complications occurring within 24 hours after surfactant administration were recorded, including pulmonary haemorrhage, bradycardia, tachycardia, need for mechanical ventilation, requirement of a second dose of surfactant, and mortality. Data were entered and analyzed using SPSS version 25. Stratification was performed to control potential effect modifiers such as gestational age and birth weight. Associations were assessed using the Chi-square test, with a p-value ≤0.05 considered statistically significant.* ***Results:*** *The mean gestational age of the neonates was 34.1 ± 1.2 weeks, and the mean birth weight was 2145 ± 320 grams. Mechanical ventilation was required in 23.4% of infants. Early complications included pulmonary hemorrhage in 16.2% of neonates, bradycardia in 8.1%, and tachycardia in 4.5%. A second dose of surfactant was required in 33.3% of cases. Overall mortality was observed in 15.3% of neonates. Early complications were significantly more frequent among infants with gestational age 32–33 weeks compared with those aged 34–36+6 weeks (p < 0.001).* ***Conclusion:*** *Late preterm infants remain at risk of respiratory complications despite receiving surfactant therapy. Infants with lower gestational age within the late preterm range tend to experience a higher frequency of early complications. Standardized treatment protocols and larger multicenter studies may help improve the safety and effectiveness of surfactant therapy in this population.*

Keywords: Infant, Premature; Pulmonary Surfactants; Respiratory Distress Syndrome, Newborn; Respiratory Insufficiency; Treatment Outcome.

[***How to Cite:*** Ilyas T, Khalil U, Masood T. Complications of surfactant treatment in late preterm infants with respiratory distress syndrome. *Biol. Clin. Sci. Res. J.*, **2025;** 6(12): 46-49. doi: https://doi.org/10.54112/bcsrj.v6i12.2196

Introduction

Respiratory distress syndrome (RDS) is a common cause of respiratory failure in premature infants and results primarily from insufficient synthesis and secretion of pulmonary surfactant within the alveoli. The occurrence of RDS decreases as gestational age increases, indicating that lower gestational maturity is the primary risk factor for its development(1, 2). Respiratory distress (RD) occurs in up to 20% of infants born at 32–34 weeks of gestation and approximately 8% of those born between 34–36 weeks. Furthermore, RDS affects nearly 80% of infants born at 28 weeks' gestation, with the incidence increasing to approximately 90% at 24 weeks(3, 4). The pathophysiology involves surfactant deficiency leading to alveolar collapse, impaired gas exchange, and disruption of the alveolar–capillary barrier due to inflammatory and oxidative injury. Clinically, RDS presents with acute respiratory distress, characteristic bilateral alveolar opacities on chest radiography, reduced lung compliance, increased intrapulmonary shunting, and histological evidence of diffuse alveolar damage(5).

Surfactant replacement therapy remains the cornerstone in the management of RDS and has significantly reduced neonatal mortality and major morbidities associated with prematurity(6). Administration of exogenous surfactant improves lung compliance, enhances oxygenation, decreases the requirement for mechanical ventilation, and reduces overall hospitalization duration(7). Evidence suggests that surfactant therapy has contributed to up to a 40% reduction in mortality among very preterm infants(8). Historically, prophylactic surfactant administration in the delivery room was recommended for infants at high risk of RDS. However, this approach requires endotracheal intubation, making it invasive and associated with potential complications such as bradycardia, hypoxia, hypotension, and pulmonary hemorrhage(9, 10). Consequently, there is growing interest in evaluating the safety profile and respiratory outcomes associated with surfactant administration, particularly in late preterm infants, where evidence remains limited.

A recent study by Zulqarnain et al. (2024) reported that 18.8% of neonates required ventilator support following surfactant administration, with a mean ventilator duration of 41.12±8.88 hours and CPAP duration of 43.59±22.70 hours. A second surfactant dose was required in 53.1% of cases. Reported complications included pulmonary hemorrhage (25%) and bradycardia (7.8%), with an overall mortality rate of 25%(11). These findings highlight the need for further evaluation of treatment-related respiratory complications and outcomes in different gestational age groups.

Despite the established benefits of surfactant therapy, limited data are available from Pakistan regarding the frequency and spectrum of complications following surfactant administration in late preterm infants with RDS. Local evidence is essential for optimizing treatment protocols and improving neonatal outcomes in resource-limited settings.

Therefore, the objective of this study is to determine the effects of surfactant treatment and to assess the frequency and types of respiratory complications in late preterm infants (LPT) diagnosed with respiratory distress syndrome.

Methodology

This prospective observational study was conducted at the Department of Pediatrics, Arif Memorial Teaching Hospital, Lahore, from 3rd June 2025

to 3rd November 2025. Following approval by the hospital's Ethical Review Committee, the study was initiated. A total of 111 preterm neonates were enrolled using non-probability consecutive sampling. The sample size was calculated at 95% confidence and a 5% margin of error, assuming an expected bradycardia frequency of 7.8% in neonates receiving surfactant therapy. Preterm infants of either gender with a gestational age of 32–36 +6 weeks diagnosed with respiratory distress syndrome (as per operational definition) requiring CPAP and surfactant administration were included after written informed parental consent. Neonates with major congenital anomalies, Apgar score <5 at 5 minutes, or those requiring positive pressure ventilation with or without intubation in the delivery room were excluded.

Baseline demographic data were recorded. All neonates received surfactant via Minimally Invasive Surfactant Therapy (MIST) while maintaining CPAP support. Complications within 24 hours were documented, including duration of mechanical ventilation and CPAP, need for a second surfactant dose, pulmonary hemorrhage, bradycardia, tachycardia, discharge status, and mortality. Standardized departmental protocols were followed to minimize bias. Statistical analysis was performed using SPSS version 25. Continuous variables were summarized as means with standard deviations, whereas categorical variables were described using frequencies and percentages. Stratification was done for effect modifiers, and a post-stratification Chi-square test was applied, with $p \leq 0.05$ considered significant.

Results

A total of 111 late preterm infants diagnosed with respiratory distress syndrome were included in the study. The mean gestational age was 34.1 ± 1.2 weeks, and the mean birth weight was 2145 ± 320 grams. Among the neonates, 64 (57.7%) were male, and 47 (42.3%) were female. Cesarean section was the most common mode of delivery, observed in 72 (64.9%) cases (Table 1).

Following surfactant administration via MIST, 26 (23.4%) neonates required mechanical ventilation, while 85 (76.6%) were managed successfully on CPAP alone. The mean duration of surfactant administration was 8.6 ± 2.1 minutes. The mean duration of mechanical ventilation was 38.4 ± 10.2 hours, and the mean duration of CPAP support was 41.7 ± 15.6 hours (Table 2).

Early complications observed within 24 hours of surfactant therapy included pulmonary hemorrhage in 18 (16.2%) neonates, bradycardia in 9 (8.1%), and tachycardia in 5 (4.5%). A second dose of surfactant was required in 37 (33.3%) infants. At the time of discharge, 94 (84.7%) neonates were discharged in stable condition, while mortality was observed in 17 (15.3%) cases (Table 3).

Stratification analysis showed a statistically significant association between lower gestational age (32–33 weeks) and increased frequency of complications ($p < 0.001$). No significant association was observed with gender or mode of delivery ($p > 0.05$) (Table 4).

Table 1: Baseline Characteristics of Study Participants (n=111)

Variable	Mean ± SD / Frequency (%)
Gestational age (weeks)	34.1 ± 1.2
Birth weight (grams)	2145 ± 320
Male	64 (57.7%)
Female	47 (42.3%)
Cesarean Section	72 (64.9%)
Vaginal Delivery	39 (35.1%)

Table 2: Respiratory support characteristics following surfactant administration (n = 111)

Variable	Frequency (%) / Mean ± SD
Mechanical ventilation required	26 (23.4%)
Managed on CPAP only	85 (76.6%)
Mean duration of surfactant administration (minutes)	8.6 ± 2.1
Mean duration on ventilator (hours)	38.4 ± 10.2
Mean duration on CPAP (hours)	41.7 ± 15.6
Second dose of surfactant	37 (33.3%)

Table 3: Early complications following surfactant therapy (n = 111)

Complication	Frequency (%)
Pulmonary hemorrhage	18 (16.2%)
Bradycardia	9 (8.1%)
Tachycardia	5 (4.5%)
Discharged	94 (84.7%)
Mortality	17 (15.3%)

Table 4: Stratification of complications by gestational age (n=111)

Gestational Age (Weeks)	Complication Present	Complication Absent	P-value
32-33	21	18	<0.001
34-36 +6	11	61	

Discussion

LPT infants account for a substantial proportion of preterm births and remain at increased risk of respiratory morbidity compared to term neonates. Although they are more mature than very preterm infants, physiological immaturity of the lungs, reduced endogenous surfactant production, and delayed alveolar fluid clearance predispose them to RDS and subsequent complications. Studies have consistently demonstrated that LPT infants have higher rates of respiratory failure, NICU admission, and mortality compared to term infants(7, 12)

In our study, 23.4% of late preterm infants required mechanical ventilation following surfactant therapy, while the majority were managed successfully on CPAP. These findings are comparable to previous observational reports indicating that although LPT infants often respond to non-invasive ventilation, a significant subset requires escalation to invasive respiratory support. Ramaswamy et al. reported variability in respiratory support requirements among LPT infants treated with surfactant, largely influenced by institutional practices and the severity of RDS (7).

The frequency of early complications in our cohort included pulmonary hemorrhage (16.2%), bradycardia (8.1%), and tachycardia (4.5%). Zulqarnain et al. reported bradycardia in 7.8% of neonates following surfactant administration, which closely aligns with our findings(11). Pulmonary hemorrhage remains a recognized but relatively uncommon complication of surfactant therapy and is more frequently reported in more premature neonates. The rates observed in our study are consistent with previously published data, suggesting that surfactant administration via minimally invasive techniques is generally safe in late preterm infants(13, 14)

A second dose of surfactant was required in 33.3% of infants in our study. Similar variability in repeat dosing has been described in the literature, particularly in moderate-to-severe RDS cases. The European Consensus Guidelines on the Management of RDS recommend repeat dosing when oxygen requirements persist despite initial therapy. However, clear thresholds for late preterm infants remain undefined(15). This lack of standardized criteria may explain the variability in repeat dosing across different settings.

One of the most important findings of our study was a significant association between lower gestational age (32–33 weeks) and a higher frequency of complications (53.8% vs 15.3%, $p < 0.001$). This highlights that even within the late preterm category, infants at the lower gestational boundary behave more similarly to very preterm neonates in terms of respiratory vulnerability. Previous epidemiological studies have shown a stepwise increase in respiratory morbidity with decreasing gestational age, even within the 32–36 week range(12). These findings emphasize the need for risk stratification within the late preterm population rather than treating it as a homogeneous group.

The mortality rate in our cohort was 15.3%. While mortality among LPT infants is substantially lower than in extremely preterm neonates, studies have demonstrated that LPT infants still have significantly higher mortality compared to term infants, primarily due to respiratory complications(7, 12). The relatively high discharge rate (84.7%) in our study suggests that timely surfactant administration contributed to clinical stabilization in most cases.

Surfactant therapy is well established for very preterm infants; however, its role in late preterm neonates remains less clearly defined. Current international guidelines primarily focus on infants born prior to 32 weeks of gestation, and no evidence-based FiO_2 threshold has been universally recommended for LPT infants(7, 15). This uncertainty likely contributes to practice variability and underscores the need for further research to develop standardized treatment algorithms for this subgroup.

Our study provides important local data regarding early complications of surfactant therapy in late preterm infants, a population that remains underrepresented in regional literature. However, there are certain limitations as well. The observational design precludes causal inference, and the single-center setting may limit generalizability. Additionally, long-term respiratory and neurodevelopmental outcomes were not assessed. Larger multicenter prospective studies are required better to define optimal surfactant use strategies in this gestational group.

Conclusion

Late preterm infants with respiratory distress syndrome remain vulnerable to early respiratory complications despite surfactant therapy. Infants born at 32–33 weeks demonstrated a significantly higher frequency of complications compared to those born at 34–36+6 weeks. Surfactant therapy administered via a minimally invasive technique was generally effective and safe; however, a substantial proportion required mechanical ventilation and repeat dosing. These findings highlight the need for careful monitoring of late preterm infants born at lower gestational age and the Development of standardized management guidelines to optimize outcomes in this population.

Declarations

Data Availability statement

All data generated or analysed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department concerned. (IRBEC-AMTH-232-24)

Consent for publication

Approved

Funding

Not applicable

Conflict of interest

The authors declared no conflict of interest.

Author Contribution

TI (Postgraduate Trainee)

Manuscript drafting, Study Design,

UK (Postgraduate Trainee)

Review of Literature, Data entry, Data analysis, and drafting articles.

TM (Professor and HOD)

Conception of Study, Development of Research Methodology Design

All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the study's integrity.

References

1. Shapiro-Mendoza CK, Lackritz EM. Epidemiology of late and moderate preterm birth. Semin Fetal Neonatal Med. 2012;17(3):120-125. https://doi.org/10.1016/j.siny.2012.01.007
2. Ma YJ, Sun Y, Zhang CH. Adverse perinatal outcomes associated with respiratory distress syndrome in preterm infants: a retrospective analysis. Ital J Pediatr. 2025;51(1):235. https://doi.org/10.1186/s13052-025-02061-0
3. Fanaroff AA, Martin RJ. Neonatal-perinatal medicine: diseases of the fetus and infant. 6th ed. St. Louis: Mosby; 1997.
4. Bos LDJ, Ware LB. Acute respiratory distress syndrome: causes, pathophysiology, and phenotypes. Lancet. 2022;400(10358):1145-1156. https://doi.org/10.1016/S0140-6736(22)01485-4
5. Grotberg JC, Reynolds D, Kraft BD. Management of severe acute respiratory distress syndrome: a primer. Crit Care. 2023;27(1):289. https://doi.org/10.1186/s13054-023-04572-w
6. Abiramalatha T, Ramaswamy VV, Bandyopadhyay T, Somanath SH, Shaik NB, Pullattayil AK, et al. Interventions to prevent bronchopulmonary dysplasia in preterm neonates: an umbrella review of systematic reviews and meta-analyses. JAMA Pediatr. 2022;176(5):502-516. https://doi.org/10.1001/jamapediatrics.2021.6619
7. Ramaswamy VV, Abiramalatha T, Bandyopadhyay T, Boyle E, Roehr CC. Surfactant therapy in late preterm and term neonates with respiratory distress syndrome: a systematic review and meta-analysis. Arch Dis Child Fetal Neonatal Ed. 2022;107(4):393-397. https://doi.org/10.1136/archdischild-2021-322890
8. Rehman A, Ahmad M, Quddusi AI, Nadeem A, Iqbal I. The impact of surfactant administration techniques (LISA vs INSURE) on the

outcomes of respiratory distress syndrome in premature babies. Prof Med J. 2021;28(6):808-812. https://doi.org/10.29309/TPMJ/2021.28.06.5330
9. Gaertner VD, Thomann J, Bassler D, Rüegger CM. Surfactant nebulization to prevent intubation in preterm infants: a systematic review and meta-analysis. Pediatrics. 2021;148(5):e2021052504. https://doi.org/10.1542/peds.2021-052504
10. Wandita S. Newer technique in surfactant administration. Indones J Perinatol. 2023;4(2):44-49. https://doi.org/10.51559/inajperinatol.v4i2.41
11. Zulqarnain H, Nadeem MT, Hussain S, Mujtaba A, Zaman S, Ali W. Early complications of surfactant administration in neonates. Pak Armed Forces Med J. 2024;74(3):821-824. https://doi.org/10.51253/pafmj.v74i3.8675
12. Natile M, Ventura ML, Colombo M, Bernasconi D, Locatelli A, Plevani C, et al. Short-term respiratory outcomes in late preterm infants. Ital J Pediatr. 2014;40(1):52. https://doi.org/10.1186/1824-7288-40-52
13. Papile LA, Burstein J, Burstein R, Koffler H. Incidence and evolution of subependymal and intraventricular hemorrhage: a study of infants with birth weights less than 1,500 gm. J Pediatr. 1978;92(4):529-534. https://doi.org/10.1016/S0022-3476(78)80282-0
14. Jobe AH. The new BPD. NeoReviews. 2006;7(10):e531-e545. https://doi.org/10.1542/neo.7-10-e531
15. Sweet DG, Carnielli VP, Greisen G, Hallman M, Klebermass-Schrehof K, Ozek E, et al. European consensus guidelines on the management of respiratory distress syndrome: 2022 update. Neonatology. 2023;120(1):3-23. https://doi.org/10.1159/000528914