RESEARCH ARTICLE

Effect of surfactant administration in respiratory distress syndrome in terms of radiological changes in preterm infants: A multi-centre study

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Abstract

Objective: To evaluate the immediate clinical and radiological outcomes of surfactant administration in preterm newborns with respiratory distress syndrome.

Method: The multicentre cohort study was conducted from January to August 2024 at the Pakistan Railway Hospital/Islamic International Medical College, and Khan Research Laboratories Hospital, Islamabad, Pakistan, and comprised preterm newborns diagnosed with respiratory distress syndrome who had been planned to receive surfactant therapy. Neonatal demographical and clinical characteristics were recorded along with the technique of surfactant administration. Post-surfactant management, the need for mechanical ventilation and chest X-ray findings were evaluated. Data was analysed using SPSS 26.

Results: Of the 84 newborns, 64(76.2%) were boys. The overall mean birthweight was 1.86±0.76kg. The most frequent post-treatment complications were pneumothorax 19(22.6%), hypotension 6(7.1%) and pulmonary haemorrhage 4(4.8%). Mechanical ventilation was required in 81(96.4%) cases. The median duration of intensive care was 9.24±6.41 days. Pulmonary haemorrhage (p=0.024), hypotension (p=0.005), post-treatment arterial blood gas potential of hydrogen (p=0.024), and duration of stay under intensive care (p=0.009) were significantly associated with mortality. Post-treatment chest X-ray staging showed significant improvement in infants receiving surfactant therapy (p<0.001). Binary logistic regression identified low birthweight (p=0.005) and cyanosis (p=0.006) at the time of presentation as independent predictors of mortality.

Conclusion: There were significant clinical and radiological benefits of surfactant therapy in preterm newborns with respiratory distress syndrome.

Keywords: Low birthweight, Mechanical ventilation, Pneumothorax, Pulmonary haemorrhage, Respiratory distress syndrome, Surfactant. (JPMA 76: 541; 2026) **DOI: https://doi.org/10.47391/JPMA.22923**

Introduction

Respiratory distress syndrome (RDS) primarily affects preterm infants, with its incidence inversely related to gestational age and birthweight.[1,2] RDS affects approximately 60-80% of infants born before 28 weeks of gestation, and about 10-15% of those born between 32 and 36 weeks.[3] The current recommended approach for managing RDS involves the early use of nasal continuous positive airway pressure (NCPAP) and selective surfactant administration for infants with escalating oxygen needs.[4] Surfactant therapy can help reduce the need for prolonged oxygen therapy, mechanical ventilation (MV), the risk of air-leak syndrome, and mortality.[5]

Surfactant delivery is typically performed using one of two methods. The most common method is Intubation, Surfactant administration and Extubation (INSURE), where the infant is first intubated to administer the surfactant, and then extubated afterward.[6] However, tracheal intubation may sometimes fail, leading to complications such as hypoxia, bradycardia, increased intracranial pressure, and injury to the respiratory system.[7] MV associated with intubation can cause barotrauma and lung injuries, increasing the risk of chronic lung disease in these vulnerable infants.[8]

RDS is a common and serious condition in preterm infants, primarily due to the immaturity of their lungs and the insufficient production of surfactant.[9] The administration of exogenous surfactant is an established therapeutic intervention in preterm infants with RDS, but local data, to our knowledge, is scarce. The current study was planned to fill the gap in literature by evaluating the immediate clinical and radiological outcomes of surfactant administration in preterm newborns with RDS.

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Patients and Methods

The multicentre cohort study was conducted from January to August 2024 at the Pakistan Railway Hospital/Islamic International Medical College (IIMC), and Khan Research Laboratories Hospital, Islamabad, Pakistan. After approval from respective institutional ethics review committees, the sample size was calculated using online OpenEpi sample size calculator with 95% confidence level and 7% margin of error considering good short-term outcome (survival and discharge) following surfactant administration in preterm infants to be 87.8%.[10] The sample was raised using convenience sampling technique. Those included were preterm newborns admitted to the neonatal intensive care unit (NICU) on the first day of life after being diagnosed to have RDS, and who had been planned to receive surfactant therapy. Those with congenital anomalies were excluded, and so were those whose parents or caregivers did not consent to be part of the study. RDS was diagnosed based on prematurity, characterised by a respiratory rate >60 breaths per minute, along with symptoms such as subcostal or intercostal chest retractions, grunting, nasal flaring and cyanosis.[11] Radiological indicators included a bilateral diffuse reticulogranular (ground glass) pattern, the presence of air bronchograms, and reduced lung expansion.

After taking written informed consent from parents/guardians, neonatal data was recorded, including demographic and clinical details, such as birthweight, Appearance-Pulse-Grimace-Activity-Respiration (APGAR) score, respiratory rate, and the presence of complications. Maternal variables included maternal age, gravidity, antenatal care (ANC) history, and pregnancy complications. The administration of surfactant adhered strictly to established NICU protocols.[12] The technique of surfactant administration was noted, and so was the need for MV post-surfactant administration. Chest X-ray (CXR) findings were evaluated before and after surfactant treatment according to plain radiography staging of RDS.[13] The data was collected on a specially designed proforma. The study followed the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines (Figure 1).[14]

Data was analysed using SPSS 26. Descriptive statistics were used to summarise the data, including mean±standard deviation and median with interquartile range (IQR) for continuous variables, and frequencies and percentages for categorical variables. Comparative analyses were used to evaluate the association between outcome and demographical, clinical and treatment-related variables. Chi-square or Fisher's exact test was used for categorical variables, while t-test or Mann-Whitney U test was applied for continuous variables. Multivariate logistic regression analysis was performed to identify independent predictors of outcomes, considering variables with $p<0.020$, and adjusting for potential confounding factors. For all inferential statistics, $p<0.05$ was taken as statistically significant.

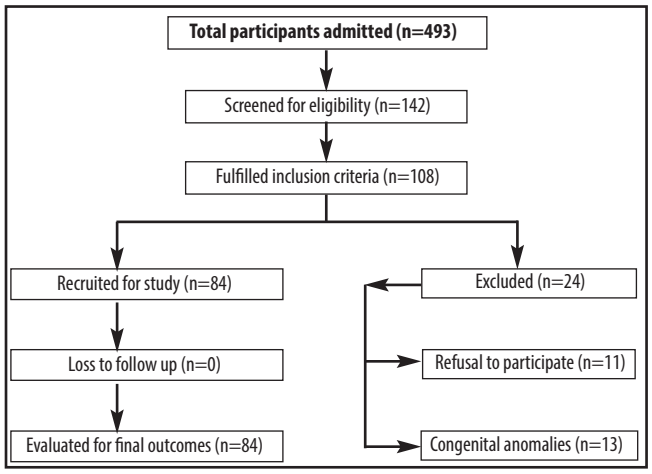

Figure-1: Strengthening the Reporting of Observational studies in Epidemiology (STROBE) flow diagram.

Results

Of the 84 newborns, 64(76.2%) were boys. The mean

Table-1: Comparison of baseline characteristics with outcome (n=84).

Characteristics	Discharged (n=46) [n (%)]	Mortality (n=38) [n (%)]	*p*-value
Gender			
Male	38 (82.6)	23 (60.5)	0.024
Female	8 (17.4)	15 (39.5)	
Mean Birth weight (kg)	2.07±0.63	1.61±0.83	0.006
Mean APGAR score (1 minute)	6.68±1.73	6.36±1.69	0.419
Mean APGAR score (5 minutes)	8.50±0.65	7.73±1.59	0.007
Nasal flaring	31 (67.4)	18 (47.4)	0.064
Expiratory grunting	29 (63.0)	12 (31.6)	0.004
Cyanosis	14 (30.4)	22 (57.9)	0.011
Intercostal recession	25 (54.3)	12 (31.6)	0.036
Irregular respirations	19 (41.3)	5 (13.2)	0.004
Apnoea	3 (6.5)	4 (10.5)	0.509
Sepsis	-	4 (10.3)	0.028
Chest X-ray			
Stage-1	3 (6.5)	-0.303	
Stage-2	12 (26.1)	14 (36.8)	0.303
Stage-3	17 (37.0)	15 (39.5)	
Stage-4	14 (30.4)	9 (23.7)	
Mean Arterial blood gas analysis			
pH	7.26±0.49	7.22±0.45	0.763
PCO_2	34.49±9.93	31.00±10.25	0.567
HCO_3	14.17±2.38	14.08±2.37	0.949
PO_2	200.86±53.12	83.40±12.56	0.001
Surfactant administration technique			
Invasive	40 (87.0)	36 (94.7)	0.227
Non-invasive	6 (13.0)	2 (5.3)	

APGAR: Appearance-Pulse-Grimace-Activity-Respiration score, pH: Potential of hydrogen, PCO_2: Partial pressure of carbon dioxide, HCO_3: Bicarbonate, PO_2: Partial pressure of oxygen.

birthweight was 1.86±0.76kg. At the time of presentation, nasal flaring, expiratory grunting, cyanosis, intercostal recession, irregular respirations and apnoea were present in 49(58.3%), 41(48.8%), 36(42.9%), 37(44%), 24(28.6%) and 7(8.3%) newborns, respectively. Maternal medical history revealed that pregnancy-induced hypertension (PIH), gestational diabetes mellitus (GDM) and placental abnormalities were present in 18(21.4%), 23(27.4%) and 5(6%) mothers, respectively. Primigravidity was noted in 24(28.6%) cases. Premature rupture of membranes (PROM) was reported in 15(17.9%) cases. Mortality was noted among 38(45.2%) infants. Female gender (p=0.024), low birthweight (LBW) (p=0.006), lower APGAR score at 5 minutes (p=0.007), cyanosis (p=0.011), sepsis (p=0.028) and arterial blood gas component bicarbonate (HCO_3) (p=0.001) were significantly associated with mortality (Table 1).

Table-2: Association of post-treatment variables with outcome.

Post-Treatment Variables	Discharged (n=46) [n (%)]	Mortality (n=38) [n (%)]	*p*-value
Complications			
Pulmonary haemorrhage	-	4 (10.5)	0.024
Hypotension	-	6 (15.8)	0.005
Pneumothorax	11 (23.9)	8 (21.1)	0.755
Mechanical ventilation required	43 (93.5)	38 (100)	0.109
Chest X-ray			
Stage-1	9 (19.6)	4 (10.5)	0.115
Stage-2	28 (60.9)	22 (57.9)	
Stage-3	3 (6.5)	9 (23.7)	
Stage-4	6 (13.0)	3 (7.9)	
Mean Arterial blood gas analysis			
pH	7.34±0.05	7.28±0.027	0.024
PCO_2	40.55±9.60	33.40±8.11	0.166
HCO_3	41.58±11.36	42.40±13.52	0.481
PO_2	113.05±46.57	114.88±35.95	0.939
Duration of ventilation post-surfactant (days)	3 (1-5)	4 (1-6)	0.243
Duration of NICU stay (days)	10.89 (5.00-14.00)	(3.00-9.50)	0.009

pH: Potential of hydrogen, PCO_2: Partial pressure of carbon dioxide, HCO_3: Bicarbonate, PO_2: Partial pressure of oxygen, NICU: Neonatal intensive care unit.

Table-3: Binary logistic regression analysis analysing predictors of mortality.

	Log Odds	Standard Error	Wald	*p*-value	Odds Ratio	95% CI (Lower-Upper)
Gender (male)	-0.24	0.85	0.08	0.78	0.79	0.15-4.19
Birth weight (kg)	-1.36	0.49	7.83	0.005	0.26	0.10-0.67
APGAR score(5 minutes)	-0.58	0.34	3.02	0.082	0.56	0.29-1.08
Nasal flaring	-0.66	0.81	0.67	0.414	0.52	0.11-2.52
Expiratory grunting	-0.73	0.94	0.61	0.436	0.48	0.08-3.04
Cyanosis	2.84	1.04	7.48	0.006	17.12	2.24-131.09
Intercostal recession	-0.31	0.77	0.46	0.693	0.74	0.16-3.35
Irregular respirations	-3.69	1.23	8.95	0.003	0.03	0.01-0.28

APGAR: Appearance-Pulse-Grimace-Activity-Respiration score, CI: Confidence interval.

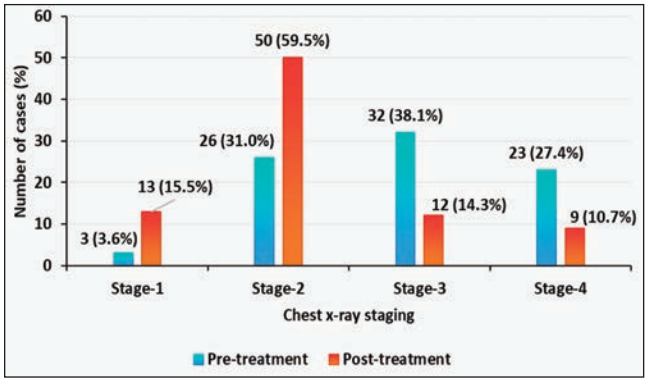

Figure-2: Comparison of baseline and post-surfactant treatment chest X-ray stagings.

The most frequent post-treatment complications were pneumothorax, hypotension and pulmonary haemorrhage, noted in 19(22.6%), 6(7.1%) and 4(4.8%) infants, respectively. MV was required in 81(96.4%) cases. The median duration of NICU stay was 8.00 (4.00-8.00) days. Pulmonary haemorrhage (p=0.024), hypotension (p=0.005), post-treatment acidosis (p=0.024) and duration of NICU stay (p=0.009) were significantly associated with mortality (Table 2).

Post-treatment CXR staging improved significantly among the infants (p<0.001) (Figure 2).

Birthweight, cyanosis and irregular respirations showed a significant association with mortality (Table 3).

Discussion

Surfactant therapy has been a cornerstone in the management of RDS, improving clinical outcomes and survival rates. However, variations in response to surfactant therapy based on gender and birthweight remain areas of active research. The gender distribution in the current study showed a predominance of male newborns (76.2%) among preterm infants, consistent with findings of Kumar et al. (77%), attributing this to the slower lung maturation in male foetuses compared to female.[15] Kansakar et al. reported the proportion of male newborns with RDS to be 70%.[16] This gender difference underscores the importance of early intervention in male preterms, who may be at a higher RDS risk. The mean birthweight in the current study was 1.86±0.76 kg, which is consistent with the findings of Dhale et al.[17] This consistency in birthweight data underscores the reliability of the current findings, and supports the generalisability of the reported outcomes. The most frequent post-treatment complications observed in the current study were pneumothorax, hypotension and pulmonary haemorrhage, with pneumothorax occurring in 22.6% cases. This incidence is comparable to the findings of Naidu et al.[18]

The observed mortality rate of 45.2% in this study is notably high, and reflects the severe nature of RDS in preterm infants, and underscores the challenges in managing this condition effectively. Kumar et al. reported a mortality rate of 34.4%, which, though significant, is lower than the current findings.[15] Phuljhele et al. noted a mortality rate of 65.2% with early surfactant therapy and 85.2% with late therapy,[19] highlighting that while the current study's mortality rate is considerable, it still falls within the range of reported outcomes, particularly for severely ill infants.

The presence of cyanosis at presentation was significantly associated with mortality (p=0.011) in the current study, highlighting the severity of hypoxaemia as a critical factor in RDS prognosis. This is in line with Kumar et al.[15] LBW was significantly associated with higher mortality in the current cohort, a finding corroborated by earlier studies.[16,19] These findings emphasise the need for tailored interventions, particularly for LBW infants.

The administration of surfactant was a pivotal aspect of RDS management in the current study, with 96.4% infants requiring MV post-surfactant administration. The high rate of MV contrasts with findings reported by Halim et al. of a significantly reduced need for MV.[11] The divergence in outcomes may be attributed to differences in the severity of illness at presentation, the timing of surfactant administration, and the techniques used for surfactant delivery. The association of pulmonary haemorrhage and hypotension with mortality in the current study further highlights the delicate balance required in managing these critically ill infants. As noted by Halim et al., pulmonary haemorrhage remains a significant complication in neonates receiving surfactant therapy, often necessitating prompt and aggressive management to improve outcomes.[11] The current study demonstrated a significant improvement in CXR staging post-surfactant administration (p<0.001), indicating the effectiveness of surfactant in alleviating the clinical and radiological manifestations of RDS. This finding is consistent with the results reported by Kalan et al.[20] The improvement in radiological staging post-treatment underscores the importance of timely surfactant administration in improving lung function and overall outcomes in preterm infants. Sabzehei et al.[21] compared minimally invasive with invasive surfactant administrations, and found that the minimally invasive technique was associated with a shorter hospitalisation time and fewer complications. The current study compared invasive and non-invasive modes of surfactant administration, and did not yield any significant differences with respect to final outcomes. The high incidence of MV and complications in the cohort suggests that more minimally invasive approaches, like Minimally Invasive Surfactant Therapy (MIST), could potentially improve outcomes in similar populations. Ramaswamy et al,[22] concluded that Fraction of Inspired Oxygen (FiO2) requirement ≥40% could be a reasonable threshold for surfactant administration. The current findings support the importance of early and appropriate surfactant therapy, particularly in infants with significant oxygen requirements. The significant association between post-treatment arterial blood gas potential of hydrogen (pH) and mortality in the study further underscores the need for careful monitoring of acid-base status and timely intervention in these vulnerable infants. Dhale et al.[17] highlighted the benefits of early surfactant administration, particularly within the first two hours of life, in improving survival rates.

The association of clinical and treatment-related variables with mortality in the current study has important implications for RDS management in preterm infants. The findings suggest that timely and appropriate surfactant administration, coupled with vigilant monitoring and management of complications, can significantly improve outcomes in this high-risk population. The study's observation of a higher incidence of complications, such as pneumothorax and pulmonary haemorrhage, underscores the need for careful consideration of the risks and benefits of surfactant therapy. These complications, while not uncommon, highlight the delicate balance required in managing preterm infants with RDS, particularly those with severe disease. The association between hypotension and mortality observed in the study further emphasises the importance of maintaining haemodynamic stability in these infants, particularly following surfactant administration. The improvement in radiological outcomes post-surfactant administration observed in the study is a testament to the efficacy of surfactant therapy in resolving the clinical manifestations of RDS. However, the high rate of MV and the associated complications suggest that alternative approaches to surfactant administration may offer potential benefits in reducing the need for invasive ventilation and its associated risks.

The current study has limitations as it did not randomise patients to groups based on different surfactant administration techniques. This could have introduced selection bias and limited the ability to directly compare outcomes between treatment modalities. The study was conducted across multiple centres, leading to potential variability, which might have influenced the consistency of the treatment and outcomes. The study did not explore long-term outcomes beyond the immediate neonatal period, limiting the ability to assess the full impact of surfactant therapy on the overall health and development

of these preterm infants.

Conclusion

There were significant clinical and radiological benefits of surfactant therapy in preterm newborns with RDS. Despite these advantages, the high mortality rate and the vulnerability of preterm infants highlight the need for further research to optimise treatment protocols and improve outcomes for this fragile population.

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Conflict of Interest: None.

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Author Contribution:

IQ & AF: Concept, design, data acquisition, drafting, final approval and agreement to be accountable for all aspects of the work.
AA: Concept, data analysis, drafting, revision, final approval and agreement to be accountable for all aspects of the work.
AZ: Data interpretation, critical revision, final approval and agreement to be accountable for all aspects of the work.
KW & MH: Data acquisition, analysis, drafting, final approval and agreement to be accountable for all aspects of the work.