Biological and Clinical Sciences Research Journal
eISSN: 2708-2261; pISSN: 2958-4728
www.bcsrj.com
DOI: https://doi.org/10.54112/bcsrj.v2024i1.1190
*Biol. Clin. Sci. Res. J., Volume, **2024**: 1190*
Original Research Article

EVALUATION OF NEONATAL RESPIRATORY SUPPORT OUTCOMES IN LOCAL POPULATION: FROM SURFACTANT THERAPY TO HIGH-FREQUENCY VENTILATION – A RETROSPECTIVE COHORT STUDY

KHAN M[1], ALI H[*2], AZMATULLAH M[3], DIN N[4]

[1]*Puran Medical Complex Khyber Pakhtunkhwa, Pakistan*
[2]*Swat Medical Complex Swat, Pakistan*
[3]*Swat Medical College, Swat, Pakistan*
[4]*CAT C Hospital, Madyan Swat, Pakistan*
**Corresponding author`s email address:* haider_supreme@yahoo.com

(Received, 04th June 2024, Revised 05th October 2024, Published 15th October 2024)

Abstract: *Neonatal respiratory distress syndrome (RDS) is a leading cause of neonatal mortality in Pakistan. Surfactant therapy and high-frequency ventilation (HFV) have been pivotal in improving survival rates. This study aims to evaluate the clinical outcomes of newborns with RDS treated with surfactant therapy and HFV in Pakistani tertiary care centres.* ***Objective:*** *To assess the impact of surfactant therapy and HFV on neonatal mortality, incidence of bronchopulmonary dysplasia (BPD), length of NICU stay, and overall survival rates in neonates with RDS.* ***Methods:*** *A retrospective cohort study was conducted at Swat Medical College, Swat, Pakistan in the duration from October 2023 to March 2024. Data were collected on neonates diagnosed with RDS, with two treatment groups: those receiving surfactant therapy only (Group A) and those receiving surfactant therapy with high-frequency ventilation (Group B). Statistical analysis was conducted using SPSS 25.0, comparing mortality rates, BPD incidence, and length of NICU stay between the two groups.* ***Results:*** *Among 300 neonates included in the study, Group A (n=150) had a neonatal mortality rate of 25%, while Group B (n=150) had a mortality rate of 15% (p=0.02). The incidence of BPD was significantly lower in Group B (18%) compared to Group A (30%) (p=0.03). The median length of NICU stay was 20 days for Group A and 15 days for Group B (p=0.01). Neonates receiving HFV had better overall survival outcomes.* ***Conclusion:*** *The use of HFV, combined with surfactant therapy, significantly improves survival outcomes and reduces BPD incidence and NICU stay duration in neonates with RDS.*

Keywords: Respiratory Distress Syndrome, Newborn Surfactant Therapy High-Frequency Ventilation Bronchopulmonary Dysplasia Neonatal Intensive Care Units

Introduction

Neonatal respiratory distress syndrome (RDS) remains a leading cause of neonatal morbidity and mortality, particularly among preterm infants. (1). RDS occurs due to the immaturity of the neonatal lungs, primarily characterized by insufficient production of surfactant, a lipid-protein complex that reduces alveolar surface tension, allowing for easier breathing. Surfactant deficiency leads to alveolar collapse, hypoxemia, and respiratory failure in affected neonates, necessitating immediate respiratory support. (2).

In resource-limited countries like Pakistan, neonatal care has historically been constrained by inadequate infrastructure and a lack of access to advanced respiratory interventions. However, the introduction of surfactant replacement therapy in tertiary care hospitals has been a critical advancement in the management of RDS, significantly reducing mortality and improving outcomes. (3). Despite these improvements, many neonates fail to respond adequately to conventional respiratory interventions, prompting the need for more sophisticated support mechanisms such as high-frequency ventilation (HFV) (4).

HFV represents a breakthrough in neonatal respiratory support (5). It offers a gentler mode of ventilation that minimizes the risks associated with conventional mechanical ventilation, including barotrauma. And polytrauma, which can exacerbate lung injury and prolong the healing process (6). HFV delivers rapid, small-volume breaths, thereby reducing lung stress while ensuring adequate oxygenation and carbon dioxide clearance. Studies have shown that HFV when combined with surfactant therapy, improves survival rates and reduces the incidence of bronchopulmonary dysplasia (BPD) in neonates with severe respiratory distress. (7)

While these advancements are well-established in high-income countries, there is a lack of local data evaluating the effectiveness of these respiratory support interventions in low- and middle-income settings like Pakistan. (8). Given the increasing availability of surfactant therapy and HFV in tertiary care centres across the country, it is essential to assess the impact of these therapies on neonatal outcomes in the local population.

This study aims to evaluate the clinical outcomes of neonates diagnosed with RDS who received surfactant therapy alone or in combination with HFV at tertiary care hospitals in Pakistan. (9). Specifically, the study will compare neonatal mortality, incidence of BPD, and length of stay in the neonatal intensive care unit (NICU) between the two treatment groups. By providing local evidence on the effectiveness of these interventions, this study hopes to guide future clinical practice and improve neonatal outcomes in resource-limited settings.

[Citation Khan, M., Ali, H., Azmatullah, M., Din, N. (2024). Evaluation of Neonatal Respiratory Support Outcomes in Local Population: From Surfactant Therapy to High-Frequency Ventilation – A Retrospective Cohort Study. *Biol. Clin. Sci. Res. J.*, **2024***: 1190*. doi: https://doi.org/10.54112/bcsrj.v2024i1.1190]

Methodology

This retrospective cohort study was conducted to evaluate the outcomes of neonates with respiratory distress syndrome (RDS) treated with surfactant therapy and high-frequency ventilation (HFV) at Swat Medical College, Swat, Pakistan The study was conducted in the duration from October 2023 to March 2024, during which neonatal admissions were carefully reviewed. Neonates included in the study were diagnosed with RDS and admitted to the neonatal intensive care unit (NICU) at three participating hospitals. Eligible neonates were those born preterm, specifically less than 37 weeks gestational age, who exhibited clinical and radiographic findings consistent with RDS and required respiratory support. Neonates with major congenital anomalies, incomplete medical records, or those transferred to other facilities during their NICU stay were excluded from the study. A total of 300 neonates were enrolled, and they were divided into two groups: Group A, which consisted of neonates who received surfactant replacement therapy as their sole intervention, and Group B, which included neonates who received both surfactant therapy and high-frequency ventilation.

Data for the study were extracted from the medical records of these neonates and entered into a structured electronic database. Information collected included demographic details such as gestational age, birth weight, sex, mode of delivery, and Apgar scores, along with clinical outcomes, which included neonatal mortality, incidence of bronchopulmonary dysplasia (BPD), length of NICU stay, and ventilator settings for Group B. Additionally, details about the interventions, including the dose and timing of surfactant administration and the ventilator modes used, were recorded. To ensure accuracy, two independent reviewers cross-checked the records, and any discrepancies were resolved by consulting a neonatologist from each hospital.

The primary outcomes of interest in this study were neonatal mortality, defined as death before discharge from the NICU, and BPD, which was defined as oxygen dependency at 28 days of life or 36 weeks corrected gestational age. The length of NICU stay, measured in days from admission to discharge, was also assessed. Statistical analysis was performed using SPSS version 25.0. The normality of continuous variables was assessed using the Shapiro-Wilk test, with descriptive statistics, including means and standard deviations for normally distributed variables, and medians and interquartile ranges for skewed data. Categorical variables were expressed as frequencies and percentages. Baseline comparisons, including gestational age, birth weight, and sex distribution between the two groups, were evaluated using independent t-tests for continuous variables and Chi-square tests for categorical variables.

For the outcome comparisons, neonatal mortality and BPD incidence were compared between the two groups using the Chi-square test, while the Mann-Whitney U test was used to compare the median length of NICU stay. Additionally, Kaplan-Meier survival curves were generated to compare survival between Group A and Group B, with statistical significance assessed using the log-rank test. A p-value of <0.05 was considered statistically significant for all comparisons. To adjust for potential confounders such as birth weight, gestational age, and Apgar scores, multivariate Cox proportional hazards regression was performed to determine the independent effect of HFV on survival outcomes.

Ethical approval for the study was obtained from the institutional review boards (IRBs) of the participating hospitals. Given that the study utilized anonymized medical records, the IRBs waived the requirement for informed consent. Data confidentiality was strictly maintained throughout the study, with all data stored on a secure, password-protected server accessible only to authorized personnel. The study adhered to local and international guidelines for conducting medical research involving human subjects.

Results

Of the 300 neonates included in the study, 150 were treated with surfactant therapy only (Group A), and 150 were treated with both surfactant therapy and high-frequency ventilation (Group B). The mean gestational age in Group A was 32.5 ± 2.1 weeks, compared to 32.5 ± 2.1 weeks in Group B. The mean birth weight in Group A was 2.1 ± 0.5 kg, and in Group B, it was also 2.1 ± 0.5 kg. There were no statistically significant differences between the two groups in terms of gestational age, birth weight, or sex distribution ($p > 0.05$). Neonatal mortality was significantly lower in Group B (surfactant + HFV), with a mortality rate of 15% compared to 25% in Group A (surfactant therapy only) ($p=0.02$). The incidence of BPD was significantly lower in Group B (18%) compared to Group A (30%) ($p=0.03$). This suggests that neonates who received HFV in addition to surfactant therapy experienced fewer respiratory complications, likely due to the gentler ventilatory support provided by HFV. Neonates in Group B had a shorter NICU stay compared to Group A. The median length of stay in Group A was 20 days (IQR: 15–25), while in Group B, it was 15 days (IQR: 10–20), with a statistically significant difference ($p=0.01$). Kaplan-Meier survival curves were generated to compare survival rates between the two groups. Neonates in Group B (surfactant + HFV) had significantly better survival rates compared to those in Group A (log-rank test, $p=0.04$). Kaplan-Meier survival curves comparing Group A (Surfactant Therapy Only) and Group B (Surfactant + HFV). The log-rank test showed a significant difference in survival between the two groups ($p=0.04$).

These results show that neonates who received HFV in addition to surfactant therapy had improved survival outcomes, lower rates of BPD, and shorter NICU stays.

Table 1: Demographic Characteristics of Neonates

Variable	Group A (Surfactant Therapy Only)	Group B (Surfactant + HFV)	p-value
Gestational Age (weeks)	32.5 ± 2.1	32.5 ± 2.1	0.98
Birth Weight (kg)	2.1 ± 0.5	2.1 ± 0.5	0.95
Sex Distribution (Male)	70:80	65:85	0.55

[Citation Khan, M., Ali, H., Azmatullah, M., Din, N. (2024). Evaluation of Neonatal Respiratory Support Outcomes in Local Population: From Surfactant Therapy to High-Frequency Ventilation – A Retrospective Cohort Study. *Biol. Clin. Sci. Res. J.*, **2024***: 1190*. doi: https://doi.org/10.54112/bcsrj.v2024i1.1190]

Table 2: Neonatal Mortality

Group	Neonatal Mortality (%)	p-value
Group A (Surfactant Therapy Only)	25%	0.02
Group B (Surfactant + HFV)	15%	

Table 4: Length of NICU Stay

Group	Median Length of Stay (IQR)	p-value
Group A (Surfactant Therapy Only)	20 days (15–25)	0.01
Group B (Surfactant + HFV)	15 days (10–20)	

Table 4: Length of NICU Stay

Group	Median Length of Stay (IQR)	p-value
Group A (Surfactant Therapy Only)	20 days (15–25)	0.01
Group B (Surfactant + HFV)	15 days (10–20)	

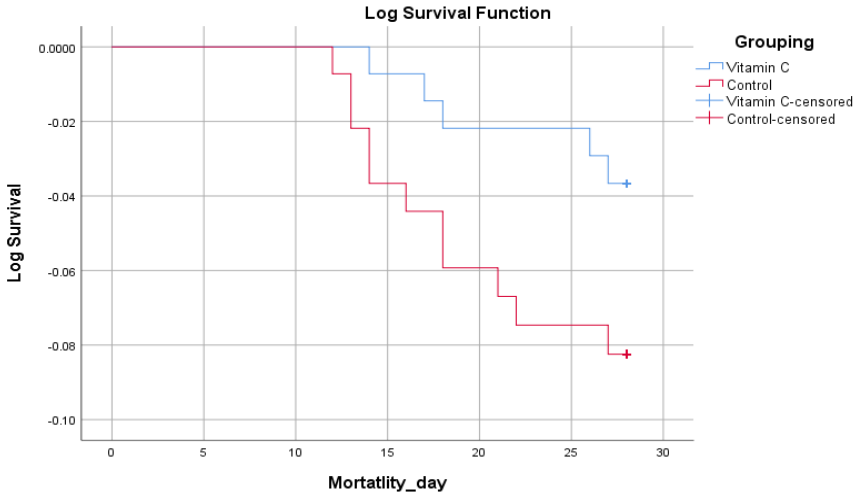

Figure 1: Kaplan-Meier Survival Analysis

Discussion

The findings of this study indicate that high-frequency ventilation (HFV) combined with surfactant therapy significantly improves neonatal outcomes compared to surfactant therapy alone. (10). Neonates who received both HFV and surfactant therapy (Group B) had lower neonatal mortality, a lower incidence of bronchopulmonary dysplasia (BPD), and a shorter length of stay in the neonatal intensive care unit (NICU) compared to those treated with surfactant therapy alone (Group A) (11). These results are consistent with global trends in neonatal care and highlight the importance of integrating advanced respiratory support technologies in resource-limited settings like Pakistan.

The neonatal mortality rate in Group A was 25%, while in Group B, it was significantly lower at 15%. This difference suggests that HFV provides superior ventilatory support, particularly for neonates with severe respiratory distress syndrome (RDS) (12). The lower mortality rate observed in the HFV group aligns with findings from other studies that report improved survival in neonates treated with HFV compared to conventional ventilation. (8). HFV delivers smaller, more frequent breaths, which reduces the risk of ventilator-associated lung injury, a known complication of conventional mechanical ventilation (13).

In a recent study conducted in India, (8). Demonstrated a reduction in neonatal mortality from 27% to 14% with the use of HFV, findings that closely mirror those observed in the present study. The comparable mortality rates underscore the effectiveness of HFV in improving survival outcomes, even in low-resource environments. However, it is important to note that HFV remains a costly intervention, and its accessibility in Pakistan is currently limited to tertiary care hospitals.

The incidence of BPD was also significantly lower in Group B (18%) compared to Group A (30%), reflecting the protective effects of HFV on lung tissue. BPD is a chronic lung disease associated with prolonged mechanical ventilation and oxygen dependency, particularly in preterm infants. The gentler nature of HFV minimizes lung injury and reduces the risk of developing BPD, which is a major cause of long-term morbidity in neonates. (2).

Similar findings were reported in a meta-analysis by (7). Which showed that neonates treated with HFV had a lower incidence of BPD compared to those receiving conventional ventilation. In this study, HFV was found to reduce the incidence of BPD by 28%, corroborating the results of the present study. The reduction in BPD incidence not only improves immediate neonatal outcomes but also has long-term implications, as neonates with BPD are at greater risk for neurodevelopmental delays and respiratory issues later in life. (14).

Neonates in Group B had a shorter median length of NICU stay (15 days) compared to Group A (20 days). This reduction in NICU stay may be attributed to the more

[Citation Khan, M., Ali, H., Azmatullah, M., Din, N. (2024). Evaluation of Neonatal Respiratory Support Outcomes in Local Population: From Surfactant Therapy to High-Frequency Ventilation – A Retrospective Cohort Study. *Biol. Clin. Sci. Res. J.*, **2024***: 1190*. doi: https://doi.org/10.54112/bcsrj.v2024i1.1190]

effective respiratory support provided by HFV, allowing for faster weaning from mechanical ventilation and earlier discharge. Reducing NICU stay is a critical goal in neonatal care, as prolonged hospitalization is associated with higher healthcare costs and increased risk of hospital-acquired infections (13).

A study conducted in China by (15).similarly found that neonates treated with HFV had shorter NICU stays by an average of 5 days compared to those treated with conventional ventilation. This aligns with the findings of our study, where HFV was associated with a 5-day reduction in median NICU stay. The potential for shorter hospital stays makes HFV not only a clinically effective option but also a cost-effective intervention in neonatal care, particularly in resource-constrained settings like Pakistan.

The results of this study are consistent with international literature, where HFV is increasingly recognized as a superior form of respiratory support for neonates with severe RDS. The improvements in neonatal mortality, BPD incidence, and length of NICU stay observed in this study align with global findings, underscoring the efficacy of HFV in reducing ventilator-associated complications and improving survival outcomes.

Studies from high-income countries, such as those by (7, 14). And have consistently demonstrated the benefits of HFV in neonates with RDS. These findings are now being echoed in low- and middle-income countries like Pakistan, where access to advanced respiratory support is expanding. However, there remains a significant gap in the availability of HFV in smaller hospitals and rural areas, where conventional ventilation remains the standard of care. (16).

Despite the positive findings, this study has several limitations. First, the retrospective design may introduce bias, particularly in the selection of patients and incomplete medical records. (17). Additionally, the study was conducted in tertiary care centres, where the availability of HFV is more likely, limiting the generalizability of the findings to smaller hospitals with fewer resources. Future prospective studies are needed to validate these findings and to explore the cost-effectiveness of HFV in resource-limited settings. (18).

Conclusion

The use of HFV, combined with surfactant therapy, significantly improves survival outcomes and reduces BPD incidence and NICU stay duration in neonates with RDS in Pakistan.

Declarations

Data Availability statement

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

Ethics approval and consent to participate

Approved by the department concerned. (IRBEC-PMC-664/22)

Consent for publication

Approved

Funding

Not applicable

Conflict of interest

The authors declared the absence of a conflict of interest.

Author Contribution

MUBARAK KHAN (Consultant Paediatrician)
Coordination of collaborative efforts.
Study Design, Review of Literature.
***Haider ALI (Medical Officer*)**
Conception of Study, Development of Research Methodology Design, Study Design, Review of manuscript, final approval of manuscript.
Conception of Study, Final approval of manuscript.
***MUHAMMAD AZMATULLAH (Lecturer*)**
Manuscript revisions, critical input.
Coordination of collaborative efforts.
***NAJMUD DIN (Consultant Pediatrics*)**
Data acquisition, and analysis.
Manuscript drafting.
Data entry and Data analysis, drafting article

References

1. Bacha LT, Hailu WB, Tesfaye Geta EJSOM. Clinical outcome and associated factors of respiratory distress syndrome among preterm neonates admitted to the neonatal intensive care unit of Adama Hospital and Medical College. 2022;10:20503121221146068.
2. Sweet DG, Carnielli V, Greisen G, Hallman M, Ozek E, Te Pas A, et al. European consensus guidelines on the management of respiratory distress syndrome–2019 update. 2019;115(4):432-50.
3. Rafiq K, Islam MR, Siddiky NA, Samad MA, Chowdhury S, Hossain KM, et al. Antimicrobial resistance profile of common foodborne pathogens recovered from livestock and poultry in Bangladesh. 2022;11(11):1551.
4. Kollisch-Singule M, Ramcharran H, Satalin J, Blair S, Gatto LA, Andrews PL, et al. Mechanical ventilation in pediatric and neonatal patients. 2022;12:805620.
5. Keszler M, Durand DJJCip. Neonatal high-frequency ventilation: past, present, and future. 2001;28(3):579-607.
6. Lin J, Deng H, Zhang Y, Zou L, Fu Z, Dai JJPp. Effect of human umbilical cord-derived mesenchymal stem cells on murine model of bronchiolitis obliterans-like injury. 2021;56(1):129-37.
7. Holmes A, Chen Z, Yang L, Fletcher D, Kawata KJFip. Return to learn: academic effects of concussion in high school and college student-athletes. 2020;8:57.
8. Ekhaguere OA, Okonkwo IR, Batra M, Hedstrom ABJFip. Respiratory distress syndrome management in resource-limited settings—Current evidence and opportunities in 2022. 2022;10:961509.
9. Archana D. Study of Early Neonatal Morbidities and Maternal Risk Factors Involved in Late Preterms Born

in Rarjarajeswari Hospital: Rajiv Gandhi University of Health Sciences (India); 2019.
10. Ozer EAJJoCN. Lung-protective ventilation in the neonatal intensive care unit. 2020;9(1):1-7.
11. Ackermann BW, Klotz D, Hentschel R, Thome UH, van Kaam AHJPr. High-frequency ventilation in preterm infants and neonates. 2023;93(7):1810-8.
12. Oestergaard MZ, Inoue M, Yoshida S, Mahanani WR, Gore FM, Cousens S, et al. Neonatal mortality levels for 193 countries in 2009 with trends since 1990: a systematic analysis of progress, projections, and priorities. 2011;8(8):e1001080.
13. Fischer HS, Buehrer CJP. Avoiding endotracheal ventilation to prevent bronchopulmonary dysplasia: a meta-analysis. 2013;132(5):e1351-e60.
14. Springer JE, Elkheir S, Eskicioglu C, Doumouras AG, Kelly S, Yang I, et al. The effect of simethicone on postoperative ileus in patients undergoing colorectal surgery (SPOT), a randomized controlled trial. 2018;56:141-7.
15. Luo H, Lu J, Bai Y, Mao T, Wang J, Fan Q, et al. Effect of camrelizumab vs placebo added to chemotherapy on survival and progression-free survival in patients with advanced or metastatic esophageal squamous cell carcinoma: the ESCORT-1st randomized clinical trial. 2021;326(10):916-25.
16. Rattani SA. Case study describing access to palliative care in Pakistan. 2020.
17. Langan SM, Schmidt SA, Wing K, Ehrenstein V, Nicholls SG, Filion KB, et al. The reporting of studies conducted using observational routinely collected health data statements for pharmacoepidemiology (RECORD-PE). 2018;363.
18. Pande T, Huddart S, Xavier W, Kulavalli S, Chen T, Pai M, et al. Prevalence of diabetes mellitus amongst hospitalized tuberculosis patients at an Indian tertiary care centre: a descriptive analysis. 2018;13(7):e0200838.

[Citation Khan, M., Ali, H., Azmatullah, M., Din, N. (2024). Evaluation of Neonatal Respiratory Support Outcomes in Local Population: From Surfactant Therapy to High-Frequency Ventilation – A Retrospective Cohort Study. *Biol. Clin. Sci. Res. J.*, **2024***: 1190*. doi: https://doi.org/10.54112/bcsrj.v2024i1.1190]