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Assessing the Shifts: A 5-Year Analysis of Surfactant and Assisted Ventilation Trends in Neonatal Care in the United States (2016-2020)

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"Respiratory distress syndrome is the most common cause of respiratory problems in preterm infants."

Abstract:

Background: Respiratory distress syndrome is the most common cause of respiratory problems in preterm infants. Early nasal CPAP, combined with the INSURE method (INtubation-SURfactant-Extubation) as the primary respiratory support approach for preterm infants, has gained popularity over prophylactic surfactant with mechanical ventilation in recent years. Limited evidence exists to understand racial differences in resource usage among preterm infants.

Objective: To investigate the trends, gender, and racial differences in the use of surfactant and assisted ventilation for > 6 hours among newborns in the United States.

Methods: Using 2016-2020 population-based cohort data for all births from the Centers for Disease Control and Prevention's WONDER natality database, we calculated rates, examined trends, and investigated gender and racial differences for surfactant use and assisted ventilation. Contingency tables analyses and Chi-square calculations were performed to detect differences between the groups with statistical significance set at p<.05.

Results: Among >18 million newborn births, overall rates of surfactant use and assisted ventilation for the study period were 4.8 and 15.6 per 1000 live births, respectively. While surfactant use remained similar (p=.99), assisted ventilation rates increased from 13.6 to 17.8 per 1000 live births (p <.0001) during the study period. Subgroup analysis among term infants (37-42 weeks) showed statistically significant increases in surfactant use (4.3 to 5.1 per 1000 live births; p<.0001) and assisted ventilation (26.2 to 38.3 per 1000 live births; p< .0001). Late preterm infants (34-36 weeks GA) had increasing assisted ventilation rates (44 to 59 per 1000 live births; OR: 1.35; p<.0001) and trend toward lower surfactant use (11 to 10/1000 live births; OR: 0.95; p=.010) during the study period. Male and Black infants had the highest utilization rates of surfactant and assisted ventilation.

Conclusion: Assisted ventilation rates steadily increased across all gestational ages, while surfactant use remained stable during the study period. Racial and gender differences exist for surfactant use and assisted ventilation needs. Contemporary trends toward "gentle" approaches in early respiratory management and guidelines for surfactant administration might have contributed to the changes in utilization rates. Clinicians and stakeholders should consider such information when allocating assets to hospitals and planning regional perinatal programs.

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Introduction:

Over the past two decades, significant advancements in neonatal care have led to a transformative shift in the management of premature infants, particularly in surfactant use and mechanical ventilation (1,2). The prevalence of respiratory distress syndrome (RDS) among preterm infants necessitates critical interventions, where antenatal corticosteroids, surfactant administration, and assisted ventilation play pivotal roles. Fortunately, recent years have witnessed remarkable strides in surfactant therapy, with the development of new formulations and delivery techniques. Among these innovations, less invasive administration methods, such as minimally invasive surfactant therapy (MIST), have revolutionized the management of RDS (3,4). Notably, these developments not only enhance short-term respiratory outcomes but also reduce long-term complications associated with mechanical ventilation.

In parallel to the progress in surfactant therapy, the last decade has brought substantial improvements in the field of mechanical

ventilation for premature infants. Implementing novel strategies, such as lung protective ventilation, has significantly enhanced outcomes and mitigated the risk of long-term respiratory sequelae. Moreover, the integration of noninvasive ventilation modalities into the care of preterm infants has gained considerable traction in recent years (5). Both nasal continuous positive airway pressure (nCPAP) and nasal intermittent positive pressure ventilation (NIPPV) (6,7) have emerged as effective alternatives to invasive mechanical ventilation. By providing respiratory support while reducing the likelihood of lung injury, these noninvasive ventilation techniques have become indispensable components of contemporary care for premature infants.

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Methods:

In this cross-sectional study, we utilized data from the US National Vital Statistics System Expanded Natality (8) to examine trends in the use of surfactant and mechanical ventilation among all live births from 2016 to 2020. The data were obtained from 57 vital statistic jurisdictions of the Vital Statistics Cooperative Program (VSCP), which were collected by the National Center for Health Statistics (NCHS) and available for researchers through the Centers for Disease Control and Prevention (CDC)-WONDER platform. Since these data were publicly available, the Institutional Review Board at Cayuga Medical Center deemed this study exempt from review.

The inclusion criteria encompassed all live-born neonates categorized by their gestational age (GA) at birth, who required assisted ventilation for more than 6 hours and received surfactant replacement therapy. GA determination was based on the best obstetric estimate (OE) in completed weeks, following the guidelines provided by the American College of Obstetricians and Gynecologists (ACOG) (9). The study included cases of assisted ventilation for more than 6 hours, employing various methods of conventional or high-frequency mechanical ventilation (including CMV, IMV, HFV, IPPV, HFJV, INO, and NIPPV), as well as continuous positive airway pressure while excluding cases using only free-flow oxygen and nasal cannula supplementation. The surfactant therapy encompassed both natural and synthetic surfactant use.

The primary outcome was to assess the surfactant and mechanical ventilation usage trends over the study period for each GA category. To achieve this, we calculated the proportion of newborns who required these interventions by dividing the number of such newborns by the total number of live births for each specific GA. Additionally, we evaluated the utilization of mechanical ventilation and surfactant among different races.

For the presentation of descriptive statistics, we expressed the frequencies as percentages (%), and to compare rate differences among the groups, we utilized rate ratios along with their Poisson 95% confidence intervals (CI). Furthermore, we calculated odds ratios (ORs) with 95% CIs to measure associations, particularly for binary outcomes between groups. All p-values were obtained from two-sided tests, and results were considered statistically significant when $p < 0.05$.

Results:

In the CDC-WONDER database spanning from 2016 to 2020, out of 18,939,599 live births, 90,645 (0.48%) newborns received surfactant therapy, and 295,221 (1.56%) required mechanical ventilation during their birth hospitalization in the United States. The majority (93%) of surfactant use and assistant ventilation use occurred among infants born at <34 weeks GA (Figure 1).

Over the five-year period, overall surfactant use remained stable at 0.48% (Rate Ratio 0.99; [95% CI: 0.98, 1.01, p=0.91]), while assisted ventilation rates significantly increased from 1.4% to 1.8% (Rate Ratio 1.29 [95% CI: 1.28, 1.31, P<0.001]) among all live births.

Interestingly, among late preterm infants (34-36 weeks GA), surfactant use rates declined from 1.15% in 2016 to 1.09% in 2020 (Rate Ratio 0.94, [95% CI: 0.90, 0.99, p=.039]), while mechanical ventilation rates increased from 4.42% in 2016 to 5.90% in 2020 (Rate Ratio 1.33, 95% CI: 1.30, 1.36; p<.001]) (Figure 2). Subgroup analysis showed statistically significant increases in surfactant use (4.3 to 5.1 per 1000 live births ;p<.0001) and assisted ventilation (26.2 to 38.3 per 1000 live births; p< .0001) in term infants (Figure 3).

When comparing infants born to White individuals with those born to Black individuals, it was observed that infants of Black individuals had higher rates of both mechanical ventilation (OR 1.30, [95% CI: 1.28-1.31, p<.001]) and surfactant use (OR 1.49, [955 CI: 1.46, 1.50, p<.001]) (Table 1). Specifically, the surfactant use and mechanical ventilation rates among Black infants were 6.7 and 19.4 per 1000 live births, respectively, while among White infants, the rates were 4.5 and 15.1 per 1000 live births (Table 2)

Additionally, male infants displayed higher needs for both surfactant therapy and mechanical ventilation when compared to female infants (OR 1.23, [95% CI: 1.21, 1.24, p<.001].

Discussion:

In this cross-sectional study, we observed a consistent and noteworthy increase in the use of mechanical ventilation among newborns in the United States from 2016 to 2020. However, during the same period, rates of surfactant use remained stable. Additionally, we identified notable disparities, with significantly higher rates of surfactant use and need for mechanical ventilation among Black infants compared to White infants.

We speculate that the rise in mechanical ventilation rates was primarily attributed to the increased adoption of noninvasive assisted ventilation strategies aimed at avoiding intubation and invasive

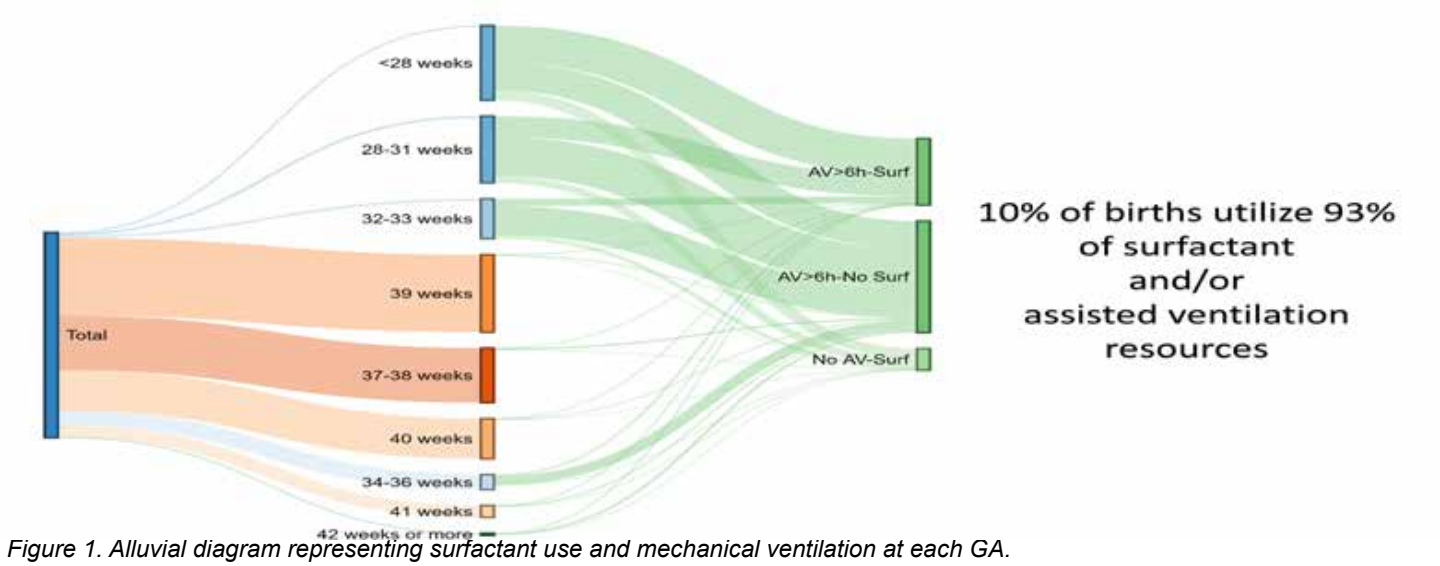

Figure 1. Alluvial diagram representing surfactant use and mechanical ventilation at each GA.

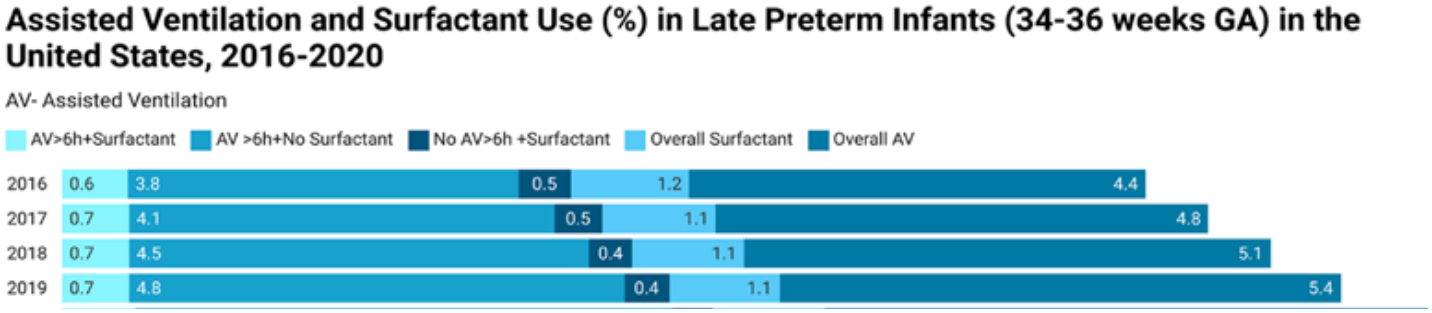

Figure 2. Assisted ventilation and surfactant use in late preterm infants (34-36 weeks GA)

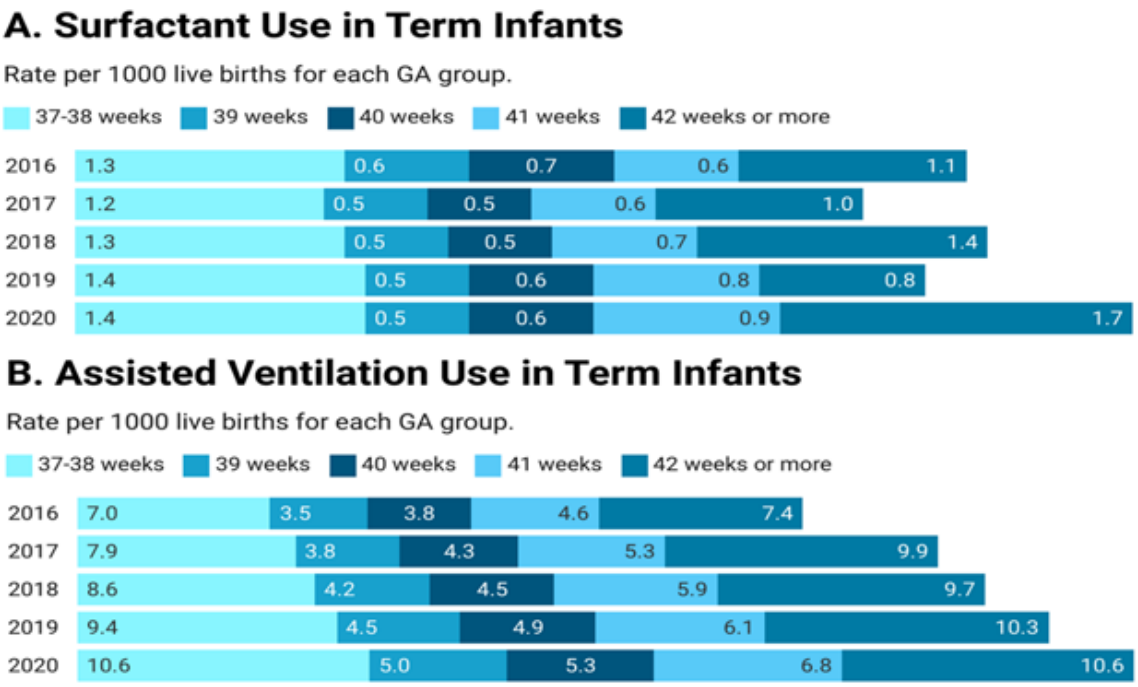

Figure 3. Surfactant and Assisted ventilation use rates per 1000 live births in term newborns.

Assisted Ventilation and Surfactant Use by Race.

Category	Assisted Ventilation	Surfactant
	OR (95% CI)	OR (95% CI)
White	Ref	Ref
American Indian or Alaska Native	1.29 (1.24-1.33)	1.26 (1.18-1.34)
Asian	0.67 (0.66-0.68)	0.57 (0.55-0.59)
Black or African American	1.30 (1.28-1.30)	1.49 (1.46-1.50)
Native Hawaiian or Other Pacific Islander	1.19 (1.12-1.26)	0.97 (0.86-1.1)*
More than one race	1.16 (1.13-1.18)	1.14 (1.10-1.19)

*OR- Odds Ratio; * p=not significant*

Table 1. Assisted ventilation and surfactant use by race, 2016-2020.

Assisted ventilation and Surfactant Use.

	Surfactant	Assisted Ventilation
	Rate per 1000 live brithss	Rate per 1000 live births
Race		
White	4.5	15.1
American Indian or Alaska Native	5.7	19.4
Asian	2.6	10.2
Black or African American	6.7	19.5
Native Hawaiian or Other Pacific Islander	4.4	17.9
More than one race	5.2	17.4
Sex		
Female	4.3	14.0
Male	5.3	17.1

Table 2. Assisted ventilation and surfactant use rates by sex and race, 2016-2020.

ventilation. Our findings align with those from recent studies conducted by the Vermont Oxford Network, which reported a 2.6-fold increase in the provision of continuous positive airway pressure among infants born between 30-36 weeks GA during the years 2011 to 2020 (10). In our study, we identified a 6% decrease in surfactant use and a 30% increase in the use of any form of mechanical ventilation among late preterm infants (34-36 GA). Other epidemiological studies, such as the one by Donda et al., also confirmed similar trends of consistently increased use of noninvasive mechanical ventilation among preterm infants (<34 weeks GA) during the years 2003 to 2014 (11). Similarly, a cohort study based on two large national datasets demonstrated a consistent increase in the use of noninvasive mechanical ventilation among preterm infants <35 weeks GA (12). Our study, encompassing all live births, aimed to shed light on the population-level use of surfactant therapy and mechanical ventilation.

However, it is essential to acknowledge the limitations of this study, such as the inability to differentiate noninvasive and invasive ventilation data due to the lack of standardized modes of ventilation in birth certificate data. Moreover, large administrative databases like CDC-WONDER are susceptible to misclassification of variables and inaccurate documentation. Despite these limitations, the strength of this study lies in its use of a large national dataset obtained from standardized and validated data sources providing valuable insights into the population-level use of surfactant therapy and mechanical ventilation.

"While overall surfactant use rates remained stable over the past few years, the implications of increasing evidence and popularity of MIST and less invasive surfactant administration (LISA) (13) remain to be seen. Consistent adherence to practice guidelines for surfactant administration among preterm infants (14, 15) may optimize outcomes and reduce costs. "

While overall surfactant use rates remained stable over the past few years, the implications of increasing evidence and popularity of MIST and less invasive surfactant administration (LISA) (13) remain to be seen. Consistent adherence to practice guidelines for surfactant administration among preterm infants (14, 15) may optimize outcomes and reduce costs. Recognizing the ongoing pursuit of personalized care for premature infants is crucial to individualizing therapeutic approaches, incorporating gestational age, lung maturity, and other clinical considerations. Collaborative research efforts, technological innovations, and an improved understanding of prematurity's pathophysiology hold the potential to optimize surfactant use, refine mechanical ventilation strategies, and embrace personalized care approaches that can significantly improve outcomes and quality of life for premature infants.

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