Improving clinical outcomes of very low birth weight infants: Implementation of standardized management guidelines in tertiary care hospital in Haryana

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ABSTRACT

Background: Standardized written guidelines and protocols in NICU are known to impact neonatal outcomes and improve survival.

Objective: To study and compare the morbidity and mortality outcomes of very low birth weight (VLBW) neonates before and after introduction of structured approach to standardized management guidelines on four interventions in a tertiary care hospital in North India.

Methodology: Structured approach to standardized management guidelines on four interventions were implemented for VLBW infants in NICU. a) Humidified and Heated High Flow Nasal Cannula (HHHFNC) as the initial mode of ventilator support in preterm VLBW babies. b) Expressed breast milk for feeding preterm VLBW babies and absolutely no formula milk. c) Hand washing and following “Bundle Care Approach” for Central lines as the cardinal cornerstones for maintaining strict asepsis. d) Development and supportive care to be regularly followed. Data was collected prospectively from July 2015 to December 2016 (Intervention Group) and compared with retrospective matched controls from the previous year (July 2014–June 2015) (Control Group).

Results: There was a significant decrease in culture positive sepsis in the intervention group compared to control group (3 (2.97%) CI: 0.006–0.08 vs 11 (19.64%) CI: 0.10–0.32; P = .0004). There was no significant difference in the mortality (5.35% vs 3.96% P = .74) amongst the two groups.

Conclusion: Implementing structured approach to above mentioned interventions in the form of standardized management guidelines for preterm VLBW neonates was associated with significant reduction in culture proven sepsis and mechanical ventilation days without affecting mortality or other co-morbidities.

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1. Introduction

The rate of preterm very low birth weight (VLBW) babies is increasing worldwide, and considerable disparities exist in survival rates and morbidities partly due to varied quality care across countries [1]. As per the World Health Organization (WHO), prematurity and its complications attribute majorly to the demise of children under 5 years of age [2]. Rates of mortality and morbidity are remarkable (30–50% and 20–50%, respectively) in VLBW
infants (VLBW < 1500 g) particularly in extremely low birth weight infants (ELBW < 1000 g) despite recent technological advances [3]. A recent study published from Haryana, India showed that respiratory distress syndrome (RDS), followed by sepsis and birth asphyxia, is the most common cause of mortality in preterm VLBW babies [4].

To combat the most important causes of deaths of preterm VLBW babies, the research team in the hospital has started working on four-point interventions based on evidence and has developed a structured approach for the same. Implementing standardized guidelines and team-based care in the NICU has a positive impact on neonatal morbidity and mortality [5,6]. Standardized guidelines for clinical practice are known to lessen the discrepancies in clinical practice, refine the uniformity of patient care, and hence improve clinical outcomes [7].

A humidified and heated high-flow nasal cannula (HHHFNC) as a primary means of noninvasive ventilation has proven to reduce RDS, chronic lung injury, and overall mortality [8]. As shown in a study by Asad Latif et al., a combination of exclusive maternal milk use and adopting bundle care approach led to reduction in various morbidities, including reduced rate of culture-positive sepsis in VLBW babies [9]. Hospital care costs are reduced by achieving earlier weight gain and time to full enteral feeds by practicing development supportive care, and it also improves neurodevelopment scores at 9–12 months [10]. Although it is universally accepted that noninvasive ventilation, bundle care approach for CLABSI, expressed breast milk for enteral feeding, and development of supportive care have resulted in increased survival of VLBW infants, previous studies still lag the guideline-based structured approach to all these interventions at one time, which is very important for a state like Haryana that is facing high rates of neonatal mortality.

In our unit, we introduced a structured approach to standardized written guidelines toward the management of VLBW neonates. The objective of the study was to study the impact of such standardized management guidelines of four interventions on morbidity and mortality outcomes of VLBW neonates in a tertiary care NICU of North India.

2. Methodology

2.1. Setting, study design, and patient sample

A single-center study was designed to evaluate the impact of standardized protocol-based care on outcomes of VLBW babies. Our NICU unit, situated in an urban metro city of North India, is an academic center accredited with a postgraduate fellowship program having a 20-bedded level III NICU. The hospital has approximately 1000 annual births and average annual NICU admissions of approximately 600. The study was approved by the hospital’s ethics committee.

The four-point methodology on the below-mentioned interventions was established on the basis of review of literature. Dominic Wilkison et al. [8] concluded that a high-flow nasal cannula has the same success rates in preventing chronic lung disease and mortality rates as those of other forms of noninvasive support in preterm infants. Antonio Di Mauro et al. [11] also suggested that nasal high-flow therapy seems to be effective as the first respiratory support with mild RDS. Smith Joan Renaud [12] identified guidelines on enteral feeding of preterm VLBW babies, which states that human milk is the recommended source of nutrition for VLBW babies, which significantly impacts lactation rates. Naomy PO Grady et al. [13] developed guidelines for reducing intravascular catheter-related infections, which emphasizes on strict hand washing and bundle care approach in neonatal units. Mary Coughlin [10] constructed a development care model directed to ameliorating the morbidities associated with prolonged and stressful hospital stay. Hence, we combined all the strong lines of evidence and developed a four-point methodology (Fig. 1) to be followed in our unit, and we hypothesized that implementing this methodology will decrease the mortality and morbidity of preterm VLBW babies.

![Fig. 1. Four point methodology for standardized management guidelines.](image)
a) A humidified and heated high-flow nasal cannula (HHHFNC) to be considered as the initial mode of ventilator support in preterm VLBW infants with respiratory distress [8,11,14,15].
b) Expressed breast milk for feeding preterm VLBW infants and absolutely no formula milk [12].
c) Hand washing and following “Bundle Care Approach” for central lines as the cardinal cornerstones for maintaining strict asepsis [13,16].
d) Development supportive care to be regularly followed while managing preterm VLBW infants to control environmental stressors, i.e., minimal handling, prone positioning, kangaroo mother care, clustering of care, dim lights, and low noise environment [10,17].

2.2. Protocols for interventions

A) A humidified and heated high-flow nasal cannula (HHHFNC) or “High Flow” (Fig. 1).
1. An air-oxygen blender (Biomed), a humidifier (MR850; Fisher & Paykel NZ TM), a disposable circuit (RT 330-A; Fisher & Paykel NZ TM) and an “Optiflow” nasal cannula (Fisher & Paykel NZ TM).
2. The initial settings of flow of 5 L/min and FiO2 of 21% — increased by 1 L/min until a maximum of 8 L/min and FiO2 by increments of 5% as needed.
3. Weaning was attempted by reducing FiO2 by 2% and flow by 0.5 L/min as guided by blood gas analysis and clinical response.
4. Trial of stopping the support was given when flow was weaned to 2 L/min or less at an FiO2 of <25%.
5. For babies with persistent respiratory distress with FiO2 requirement >40% at flow of 8 L/min, a surfactant was given through the INSURE technique (Intubate, Surfactant, Extubate).
6. Mechanical ventilation was performed for babies with poor respiratory efforts or not maintaining vitals and saturations even with maximum high flow support.

B) Expressed breast milk (EBM):
1. Policy of strict use of EBM was adopted.
2. Counseling of mothers for providing EBM was started from before delivery at the time of admission to the hospital and also immediately after the birth stating the benefits of breast milk for their babies.
3. Galactogogues (Domperidone) were used for mothers who did not lactate well

C) Maintaining strict asepsis with primary focus on hand washing and following “Bundle Care Approach” for central lines [16].
1. Strict hand-washing protocols were laid and followed during the study period. Both didactic and video presentations and then live demonstrations were given to all doctors and nursing staff in the NICU. Regular audits and surprise checks were performed to ensure adherence to hand-washing protocols.
2. PICC Line care — The bundle care approach was adopted for central line placements to prevent central line-associated bloodstream infection (CLABSI) [13,18]. (See Appendix). Bundle checklists were pasted on the baby files, and daily audits were conducted until the line was removed.

D). Developmental and supportive care [10,17]:
1. Low noise/dim light environment:
   a) The NICU environment was kept as quiet as possible by following 45 dB as the upper limit of sound according to the American Academy of Pediatrics (AAP) guidelines.
   b) Lights were kept at dim levels.
   c) Minimizing opening and closing of incubator doors. OR
   d) If under open care systems — kept in a separate room away from older neonates.
   e) Alarms were responded to as soon as possible preferably within 10 s
   f) Bedside conversations were avoided/minimized.
2. Minimal handling, prone positioning, “nesting” (keeping the neonate in a cloth pouch supported from all sides), and clustering of care were done.
3. Early, frequent, and prolonged skin-to-skin contact.
4. Nonpharmacological support (sucrose, breast milk, containment) was provided for any invasive procedures in the NICU.

Data of all VLBW infants admitted to the hospital from July 2015 to December 2016 (intervention group: 18 months) were collected prospectively and compared and analyzed with those of the retrospective control group during the 12-month period from July 2014 to June 2015 (control group: 12 months).

Baseline demographic and perinatal data were collected in a predesigned Excel sheet, that is, gestational age: birth weight; gender; whether inborn or outborn; maternal age; maternal complications such as pregnancy-induced hypertension (PIH), antepartum hemorrhage (APH), gestational diabetes mellitus (GDM), and chorioamnionitis; mode of delivery; antenatal steroids; Apgar score at 1 min; and rates of RDS, patent ductus arteriosus (PDA), culture-proven sepsis, intraventricular hemorrhage (IVH), periventricular leukomalacia (PVL), retinopathy of prematurity (ROP), and bronchopulmonary dysplasia (BPD) were noted. RDS was defined as respiratory difficulty including tachypnea, retractions, grunting, nasal flaring, and need for oxygen or pressure-positive support for more than 6 h in the first 24 h. Culture-positive sepsis was defined as signs and symptoms of sepsis along with the microorganism identified in aerobic blood culture with the sensitivity pattern. BPD was defined as the physiological need for oxygen for at least 28 days after birth, and the severity was graded according to respiratory support required at 36 weeks PMA, by the criteria of Walsh et al. [19].

The primary outcomes were preterm VLBW death rate; survival rates; and rates of RDS, BPD, ROP, necrotising enterocolitis (NEC), IVH, PDA, and culture-proven sepsis in the two groups. The secondary outcomes were length of hospital stay, number of days on mechanical ventilator, and number of days on high-flow cannula.

2.3. Research team

The core team comprised two neonatologists, one pediatrician, and one nursing incharge. Didactic sessions, video demonstrations, and hands-on training were given by the research team to all the other doctors and nursing staff of the department for using these above-mentioned guidelines one month before the commencement of the intervention period, i.e., for the whole month of June 2015. Scheduled classes were held for 1 h during each working day of June 2015.

2.4. Statistical analysis

Relevant prenatal, perinatal, and postnatal data were collected in a predesigned Excel sheet. Categorical data were reported as count and percentage, while continuous data reported as mean±standard deviation (SD) or range. Pearson chi-square test/Fisher exact test was applied to test the variables with nominal/
categorical data. P-value less than .05 was considered as significant at 95% confidence levels. Logistic regression analysis was applied to determine predictors of mortality. SPSS version 18.0 software was used to analyze the data. After commencing of the intervention period, all the data were analyzed and reviewed quarterly.

3. Results

There were 56 VLBW babies in the control group from July 2014 to June 2015 and 101 babies in the intervention group from July 2015 to December 2016. Antenatal, natal, and postnatal parameters were well matched between the two groups, except for 2 parameters, namely, cesarian section rate and mean APGAR scores at 1 min, both being more in the control group (Table 1).

There was remarkable reduction in culture-positive sepsis in the intervention group compared to that in the control group (3.297%) CI: 0.06–0.08 vs. 11 (19.64%) CI: (0.10–0.32); p: 0.0004 (Fig. 2), which is a consequence of following strict hand-washing and bundle care approach (insertion bundle, maintenance bundle, and hub care bundle) during the intervention period (See Appendix). Klebsiella was positive in the blood culture samples of five babies, six babies were positive for E. coli, and three were positive for Pseudomonas.

Further, there was a significant decrease in the number of days on mechanical ventilator (1.19 days (CI: 0.27–2.1) vs. 3.36 (CI: 2.27–4.44); p: 0.002), while at the same time, number of days on HHHFNC was increased in the intervention group (4.03 days (range 2.62–5.44) vs. 2.2 days (range 1.01–3.38), p: 0.049) (Fig. 3) when the rates of RDS in both groups were almost the same (Table 2).

Policy of strict use of expressed breast milk was adopted [12]. Galactogogues (Domperidone) were used for mothers who did not lactate well, which resulted in a decrease in culture-positive sepsis in the intervention group as mentioned above (Fig. 2). Although there was a decrease in the number of VLBW babies with NEC in the intervention group, it was not statistically significant (P = .096) (Table 2).

We used develop supportive care in the form of minimal handling, prone positioning, Kangaroo mother care, clustering of care, low noise/dim lights; therefore, comorbidities such as BPD, NEC, I VH, retinopathy of prematurity, PDA were statistically insignificant in both groups (Table 2). Notably, the duration of NICU stay in the intervention group was more likely because neonates in the intervention period were discharged at a higher mean discharge weight than those in the control period (Table 2).

There was no significant difference in mortality (5.45% vs. 4.26%; P = .74) or survival 94.55% vs. 95.7% between the two groups (Fig. 4). While applying logistic regression, gestational age was found to be the only parameter predicting mortality in both groups.

4. Discussion

Guideline-based management strategies have shown to have beneficial effects in improving the outcomes of VLBW neonates [5–7]. As part of interventional study, we studied the impact of adopting standardized management guidelines in four different aspects of neonatal care and compared the intervention time period with that of matched retrospective controls in the past 1 year.

The number of babies with culture-positive sepsis was reduced from 19.64% in the control group to 2.97% in the intervention group. Such significant drop in sepsis rate can be attributed to the combined effect of maintaining strict asepsis, adopting “Bundle Care Approach” for central lines, and use human milk only. This low rate of culture-positive sepsis in the intervention group is comparable to blood culture-positive rate of VLBW babies in a study by National Institute of Child Health and Development (NICHD) [20]. A previous study has demonstrated the role of using “Bundles” for controlling CLABSI [18]. In one study, the zero-sepsis rate for 1000 days was achieved and was attributed to adopting the “Bundle care approach.” [21] In another study by Asad Latif et al., the combined use of exclusive maternal milk and adopting Bundle care approach led to reduction in various morbidities including reduced rate of culture-positive sepsis in VLBW babies [8].

El-Mohandes et al. and Hylander et al. showed that consuming maternal milk results in decreased rates of sepsis among LBW infants compared to those of infants fed with preterm formula only [22,23]. Favorable outcomes were also reported by Schanler and coworkers in terms of reduced rate of sepsis and NEC in VLBW infants who were given at least 50 ml/kg of maternal milk daily compared with preterm formula [24]. In addition to decreasing rates of late-onset sepsis, NEC, ROP, and human milk have also resulted in providing benefits by reducing a number of rehospitalizations in the first year and improving neurodevelopment outcomes in preterm VLBW infants [25].

The other significant finding is the reduction in number of days on mechanical ventilation (from mean 3.4 to 1.2 days (p: 0.002) and at the same time an increase in number of days on CPAP/HHFNC in the intervention group. This is because HHHFNC was adopted as the primary mode of ventilation in spontaneously breathing neonates in the intervention group even in the smallest of neonates and were put on invasive ventilation only when HHHFNC trial failed. Dominic Wilkinson et al., using HHHFNC as the primary mode of ventilation, suggested a decrease in ventilator-induced lung injury (VILI), chronic lung disease (CLD), and overall mortality [8]. Based on evidence, HHHFNC is similar to other forms of noninvasive ventilation in preterm infants when efficacy was compared [15]. In some recent trials, however, HHHFNC as the primary mode was been found to be inferior to nasal CPAP, although equal to CPAP as post-

Table 1
Baseline demographic, perinatal and neonatal characteristics of preterm VLBW babies of control and intervention group.

| S. No. | Variables | Control group (N = 56) | Intervention group (N = 101) | P Value |
|-------|-----------|------------------------|-----------------------------|---------|
| 1     | Maternal age in year: mean (95%CI) | 27.9 (27.24–28.62) | 28.5 (27.8–29.2) | .22 |
| 2     | Weight in gms: Mean (95%CI) | 1231 gm (1169.6–1294.2) | 1248 gm (1207.6–1288.8) | .66 |
| 3     | Gestational age wks mean (95%CI) | 30.6wk (30.1–31.2) | 30.9wk (30.37–31.5) | .44 |
| 4     | PHN n (%) | 7 (12.5%) | 11 (10.89%) | .76 |
| 5     | APH n (%) | 5 (8.93%) | 6 (9.4%) | .48 |
| 6     | Chorioamnionitis n (%) | 2 (3.57%) | 0 | .056 |
| 7     | Antenatal steroids n (%) | 18 (32.14%) | 32 (31.68%) | .95 |
| 8     | LSCS n (%) | 48 (85.71%) | 67 (66.34%) | .008 |
| 9     | Sex (F) n (%) | 27 (48.21%) | 42 (41.58%) | .42 |
| 10    | Inborn n (%) | 21 (37.5%) | 40 (39.6%) | .79 |
| 11    | APGAR scores at 1 min mean (95%CI) | 7.1 (6.87–7.31) | 6.5 (6.15–6.82) | .003 |
| 12    | GDM n (%) | 3 (5.36%) | 2 (1.98%) | .24 |
extubation support with evidence of less nasal trauma and reduced pneumothorax [26,27]. Hence, the role of HHHFNC as the primary mode is not well established yet in current literature.

Fig. 2. Culture positive sepsis in control group (19.64%) and intervention group (2.97%) (P = .0004).

Fig. 3. Number of days of high flow therapy in control group (2.2 days) and intervention group (4.03 days) (P = .049). Number of days of mechanical ventilation in control group (3.36 days) and intervention group (1.19 days) (P = .002).

Table 2

| S No. | Variables          | Control group (N = 56) mean (95%CI) | Intervention group (N = 101) mean (95%CI) | P value |
|-------|--------------------|-------------------------------------|------------------------------------------|---------|
| 1     | Duration of stay   | 18.1 (13.7–22.4)                    | 24.7 (20.62–28.75)                       | .02     |
| 2     | Discharge weight   | 1508 gm (1454 gm–1607 gm)           | 1743 gm (1657–1846 gm)                   | .0017   |
| 3     | RDS                | 83.99                               | 80.5                                     | .15     |
| 4     | IVH (grade 3 or 4) | 0                                   | 1 (0.99)                                 | .45     |
| 5     | BPD                | 3 (5.36)                            | 2 (1.98)                                 | .24     |
| 6     | NEC                | 3 (5.36)                            | 1 (0.99)                                 | .096    |
| 7     | ROP                | 2 (3.97)                            | 10 (9.9)                                 | .485    |
| 8     | PDA                | 5 (8.92)                            | 3 (2.97)                                 | .62     |

RDS-Respiratory distress syndrome, BPD- Bronchopulmonary dysplasia, NEC- Necrotising enterocolitis, ROP- Retinopathy of prematurity, PDA- Patent ductus arteriosus

The mean duration of stay of babies in the NICU in the control group was lesser than that in the intervention group, 18.07 days vs. 24.68 days. This can be attributed to the fact that discharge weight criteria in the control group were quite variable (mean: 1503 g with 95% CI (1454 – 1607 g) while a higher discharge weight criterion was kept in the intervention period and was strictly adhered to (mean: 1743 g (95% CI: 1657–1846 g)), which led to prolonged stay.
However, there were no other changes in the team, equipment, or management protocols apart from these four interventions in the two groups. Other morbidities such as BPD, NEC, and ROP were marginally less in the intervention group during the study period primarily because of a decrease in invasive ventilation and using expressed breast milk as the only feed. The rate and severity of NEC and retinopathy of prematurity have been reduced by maternal milk feeding in VLBW infants [28]. One baby in the intervention group developed IVH, while none developed in the control group. All these morbidities, however, did not reach statistical significance. There is enough published evidence to suggest that interventions such as EBM for feeding, minimally invasive ventilation, and development supportive care have positive outcomes in reducing the above-mentioned morbidities [29].

Favorable outcomes were demonstrated when environmental sensory overstimulation is reduced in preterm infants. Neuroprotective strategies such as skin-to-skin contact and family-oriented care for hospitalized preterm infants can be adopted to achieve this goal [30]. Providing the neonate with developmentally supportive positioning (prone positioning) is essential, as it influences neuro-motor and musculoskeletal development and also improves thermo-regulation, facilitates sleep, and maintains integrity of skin, thereby optimizing growth and brain development [31,32]. Physiological and behavioral alterations are observed in preterm infants for several minutes who are frequently handled in a day for various reasons [10]. This was the reason to practice clustering of care in the intervention period.

5. Conclusion

It was a single-center before-and-after study with limited sample size with retrospective controls and therefore has its inherent limitations. However, the adoption of a structured approach to these interventions as part of standardized management means that prospective data will be available on an ongoing basis in future and thus may provide more insights into the role of such interventions on outcomes.

Evidence-based guidelines and adherence to written NICU-specific guidelines are known to impact outcomes in preterm neonates. Standardized guidelines on specific interventions as mentioned elsewhere may have a positive impact on culture-positive sepsis and number of days on mechanical ventilation.

In our study, we found a significant reduction in culture-proven sepsis and mechanical ventilation days after implementing the structured approach toward standardized management guidelines for preterm VLBW neonates without affecting mortality or other comorbidities.

Conflict of interest

None.

Source of funding

None.

Author contribution

SA: Carried out the actual research project and drafted the manuscript. PY: Carried out the actual research and contributed to the manuscript. HB: Contributed in designing the study and proof reading. AST: Contributed in statistical analysis and drafting the manuscript. MM: Contributed in preparation of results and drafting the manuscript. MRG: Carried out prospective part of research and drafting of manuscript. AJ: Implementation of policies of the project, team training and collection of data. RA: Conceptualized the research based Quality initiative, looked over the project, edited and finalized the manuscript.

Disclaimer

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CHECKLIST: INSERTION BUNDLE

A) Establish a central line kit or cart to consolidate all items necessary for the procedure.
B) Perform hand hygiene with a hospital-approved alcohol-based product or an antiseptic-containing soap before and after palpating insertion sites and after inserting central lines. Use maximum barrier precautions (including gowns, surgical mask, sterile gloves, cap, and large sterile drape).
C) Disinfect skin with an appropriate antiseptic (2% chlorhexidine, 70% alcohol) before catheter insertion.
D) Minimize the number of access ports
E) Keep connecting ports with UVC/UAW away from diaper area.
F) Use either a sterile transparent semipermeable dressing or sterile gauze to cover the insertion site.
G) Prefer upper limb veins over lower limb veins
H) Ensure the catheter tip at proper location
I) No blood strains around the catheter site

CHECKLIST: MAINTENANCE BUNDLE

A) Establish a central line kit or cart to consolidate all items necessary for the procedure.
B) Perform hand hygiene with a hospital-approved alcohol-based product or an antiseptic-containing soap before and after accessing a catheter or before and after changing the dressing.
C) If the dressing is damp, soiled, or loose, change dressing antiseptically and disinfect the skin around the insertion site with an appropriate antiseptic.
D) Develop and use intravenous tubing setup and changes.
E) Maintain aseptic technique when changing intravenous tubing and when entering the catheter including “scrub the hub.”
F) Daily review the catheter necessity with prompt removal when no longer essential.

CHECKLIST: HUB CARE BUNDLE

A) Cleanse hands with soap and water.
B) Put on gloves
C) Establish a sterile field under access port
D) Place syringes on the edge of the sterile field
E) Scrub access port with chlorhexidine for 10 s and allow to dry.
F) Pick up a syringe keeping the tip sterile.
G) Attach the syringe to a hub keeping the connections sterile.
H) Administer flush solutions keeping the connections sterile.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcledpro.2020.000000.

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