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Original Article:

Study of Early Predictors of Fatality in Mechanically Ventilated Neonates in NICU

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Abstract:
Objective: To evaluate the risk factors associated with fatality in mechanically ventilated neonates using multiple regression analysis**. Design & settings:** Prospective study conducted at Neonatal ICU at New Civil Hospital, Surat – a tertiary care centre, from December, 2007 to May, 2008 for 6 months. **Methods:** Fifty neonates in NICU consecutively put on mechanical ventilator during study period were enrolled in the study. The pressure limited time cycled ventilator was used. All admitted neonates were subjected to an arterial blood gas analysis along with a set of investigations to look for pulmonary maturity, infections, renal function, hyperbilirubinemia, intraventricular hemorrhage and congenital anomalies. Different investigation facilities were used as and when required during ventilation of neonates. Multiple logistic regression analysis was done to find out the predictors of fatality among these neonates. **Results:** Various factors suspected as predictors of fatality of mechanically ventilated neonates were assessed. Hypothermia, prolonged capillary refill time (CRT), initial requirement of oxygen fraction (FiO_2) >0.6, alveolar to arterial PO_2 difference ($AaDO_2$) >250, alveolar to arterial PO_2 ratio (a/A) $\leq$0.25, & oxygenation index (OI) >10 were found statistically highly significant predictors of mortality among mechanically ventilated neonates. **Conclusion:** Hypothermia and prolonged capillary refill time were independent predictors of fatality in neonatal mechanical ventilation. Risk of fatality can be identified in mechanically ventilated neonates
Key Words: Mechanical ventilation, Neonates, Hypothermia, Capillary refill time

Introduction:
Neonatal mortality accounts for nearly two thirds of infant mortality and half of under 5 mortality in India. It is alarmingly high in rural areas.[1] Also, many avoidable handicaps during childhood have their origin in the perinatal period. It is possible to increase neonatal survival and improve the quality of life only through prompt and adequate management of newborn which cannot be thought of without respiratory intensive care and assisted ventilation. Mechanical ventilation has become a must to enhance newborn survival. Babies with perinatal hypoxia and birth asphyxia as well as critically sick babies who develop life threatening apnea or cardiovascular collapse need mechanical ventilation. Neonates with progressive respiratory distress with impending respiratory failure and tiring respiratory muscles, can be supported and saved by assisted ventilation facilities.[2]

The complexity of respiratory therapy is compounded in neonatal critical care, where the unique needs of the neonate, who is immature, fragile, vulnerable and dependent, must be considered constantly. Thus, while the support of ventilation can no longer be viewed strictly as a divine intervention, it remains a formidable challenge, at least for us.[2-4] The objective of the study was to evaluate the risk factors associated with fatality in mechanically ventilated neonates using multiple regression analysis.

Methodology:
A prospective study was carried out in Neonatal Intensive Care Unit (NICU) of Pediatrics department, New Civil Hospital, Surat during December, 2007 to May 2008. The NICU caters to neonates born in the hospital as well as those referred from other hospitals or born at home and transported to the civil hospital directly by relatives, as New Civil Hospital, Surat serves as a tertiary care center for South Gujarat region.

There were 334 NICU admissions during the study period of which those neonates consecutively put on ventilator were enrolled in the study. Exclusion criteria included (1) neonates having major, surgically uncorrectable lethal anomalies, (2) preterm < 28 weeks with severe birth asphyxia, and (3) birth weight < 750 gms were excluded. Total 50 neonates were put on ventilator during study period and were enrolled for the study and none was excluded. All neonates enrolled in the study were classified according to sex, birth weight, gestational age, place of birth. A brief not of antenatal and intranatal history was taken from mothers. A pretested proforma was used to record intricate details of each patient. Informed consent was taken from parents of neonates. The study was conducted in accordance with Helsinki Declaration and after taking approval from human research ethical committee of the Government Medical College, Surat.

All admitted neonates were subjected to an arterial blood gas analysis along with a set of investigations to look for pulmonary maturity, infections, renal function, hyperbilirubinemia, intraventricular hemorrhage and congenital anomalies. Neonates were kept on pressure limited time cycled ventilators (Drager Babylog 8000 Plus) in the NICU. Different investiga-

tion facilities were used as and when required during ventilation of neonates.

(A) Criteria for initiating mechanical ventilation [5-7]

(a) Clinical criteria:

1. Respiratory distress like tachypnea (>60 breathing/minute), nasal flaring, grunting, severe chest indrawing

2. Central cyanosis like cyanosis of oral mucosa/ SPO_2 < 85% on O_2 through hood or with CPAP at FiO_2 > 0.6

(b) Laboratory criteria:

1. Severe hypercapnia like

- pCO_2 > 60 mmHg in early RDS with pH < 7.2,
- pCO_2 > 70 mmHg in resolving RDS with pH < 7.2

2. Severe hypoxemia like pO_2 < 40-50 mmHg on O_2 through hood or with CPAP at FiO_2 > 0.6

3. Blood gas scoring system: Score ≥ 3

Score	0	1	2	3
pO_2 (mmHg)	> 60	50-60	< 50	<50
pH	> 7.3	7.2-7.29	7.1-7.19	< 7.1
pCO_2 (mmHg)	< 50	50-60	61-70	> 70

(B) Criteria for initiating weaning from mechanical ventilation [5-7] (i.e. when the patient can undergo extubation readiness test)

(a) Subjective criteria:

- underlying disease process is improving as judged clinically
- adequate gas exchange
- improving respiratory mechanics
- absence of any condition that poses an undue burden on respiratory muscles
- patient capable of sustaining spontaneous ventilation as ventilatory support is decreased

(b) Objective criteria:

- alertness
- breathing without distress
- normal heart rate & blood pressure without pressure support
- no sedatives, analgesics, neuromuscular blockers
- normal electrolytes
- endotracheal secretions nil or < 1 ml 6 hourly
- hemoglobin > 13 g/dl
- Gases:
  - pO_2 ≥ 60 mmHg & SPO_2 ≥ 90% with FiO_2 ≤ 0.4 & PEEP ≤ 5
  - pO_2 / FiO_2 ≥ 150
  - pCO_2 ≤ 50 mmHg
  - pH > 7.2

(C) Criteria for successful extubation readiness test

(a) Subjective criteria:

- No change in mental status
- No onset / worsening of dyspnoea
- No diaphoresis
- No signs of respiratory distress

(b) Objective criteria:

- SPO_2 > 90 %
- pH > 7.32
- pO_2 > 50 mmHg
- pCO_2 rise ≤ 10 mmHg
- Respiratory rate rise ≤ 50 %

(D) Monitoring of neonates on Ventilators and DOs

All type of monitoring was done as per the requirement of neonates on ventilator including various investigations like blood sugar, serum electrolytes, hemoglobin, Arterial Blood Gas Analysis (ABGA) (1 hourly for 1st six hours, 2 hourly for next 6 hours and then 4 hourly or as needed), X ray chest after each tube change, endotracheal tube tip culture and sensitivity and tracheal aspirate culture and sensitivity at each tube change, blood urea & serum creatinine twice weekly. A detailed charting of every change in ventilatory parameters was done till the patient was on ventilator. All neonates were nebulized, suctioned and given chest physiotherapy. The complications anticipated were clinically suspected and confirmed by investigations.

Adjunctive treatment was given simultaneously as per the requirements and nutritional support was maintained by nasogastric feeding. Feeding was omitted 12 hours before planned extubation. Neonates not able to tolerate nasogastric feeds were given parenteral nutrition. The patients were given trials of Extubation Readiness Test and weaned according to above mentioned criteria. Patients were monitored for signs of clinical deterioration after extubation.

Data Analysis

The data was entered in MS excel and analyzed using chi square test and multiple logistic regression analysis by using Epi Info software.

Results:

Total 50 neonates were enrolled during the study period. Table 1 shows characteristics of mechanically ventilated neonates. Birthweight ≤ 2000 grams and gestational age ≤ 34 weeks was in 20 neonates, majority (94%) neonates were kept on IPPV mode of mechanical ventilation.

Table 1 Characteristics of mechanically ventilated neonates

Characteristics	No. (n=50)	%
Sex		
Male	36	72
Female	14	28
Birth weight (in grams)		
< 750	0	0
750-1000	5	10
1001-1500	6	12
1501-2000	9	18
2001-2500	15	30
>2500	15	30
Gestational age (in weeks)		
<28	0	0
28-30	2	4
30-32	6	12
32-34	11	22
34-36	4	8
>36	27	54
Place of delivery		
Home	12	24
Civil Hospital	26	52
Other Hospital	12	24
Mode of delivery		
Vaginal	42	84
Cesarean	8	16
Mode of mechanical ventilation		
IPPV	47	94
CPAP	1	2
CPAP + IPPV	2	4

Table 2 shows various parameters like indications, clinical features, complications, and immediate outcome of mechanically ventilated neonates. Pneumonia & septicemia, apnea, & meconium aspiration syndrome were the most common indications for mechanical ventilation.

Respiratory distress was most common clinical feature followed by recurrent apnea & severe birth asphyxia among mechanically ventilated neonates. Pulmonary hemorrhage was most common complication of mechanically ventilated neonates. Forty two percent neonates were successfully weaned, while 46% neonates were expired during mechanical ventilation and 12% neonates went on discharged against medical advice.

Table 2 Various parameters of neonates on mechanical ventilation

Parameters	No. (n=50)	%
Indications		
Apnea	7	14
Severe Birth Asphyxia	6	12
Respiratory Distress Syndrome	6	12
Meconium Aspiration Syndrome	7	14
Pneumonia & Septicemia	15	30
Aspiration Pneumonia	4	8
Pulmonary Hemorrhage	4	8
Others	1	2
Clinical Features		
Respiratory distress	33	66
Recurrent Apnea	8	16
Severe Birth Asphyxia	4	8
Convulsions	3	6
Not taking feed	2	4
Vomiting	2	4
Frothy discharge from mouth	2	4
Jaundice	1	2
Bleeding manifestations	1	2
Complications		
No complication	23	46
Sepsis	5	10
Pulmonary hemorrhage	10	20
Shock	6	12
Intraventricular hemorrhage	2	4
Ventilator associated pneumonia	2	4
Pneumothorax	1	2
Immediate outcome		
Successfully weaned without complications	14	28
Successfully weaned with complications	6	12
Successfully weaned but later expired	1	2
Discharge against medical advice	6	12
Expired on weaning	23	46

Logistic regression analysis of those predictors of mortality found statistically significant on univariate analysis was shown in table 3. Various parameters were studied to assess their association with mortality among mechanically ventilated neonates. Hypothermia, prolonged capillary refill time (CRT), initial requirement of oxygen (FiO_2) > 0.6, alveolar to arterial PO_2 difference ($AaDO_2$) > 250, alveolar to arterial PO_2 ratio (a/A) ≤ 0.25, & oxygenation index (OI) > 10 were found statistically highly significant predictors of mortality among mechanically ventilated neonates.

Table 3 Logistic regression analysis of early predictors of fatality among mechanically ventilated neonates

Parameter	Group 1	Fatality No. (%)	Total No.	Group 2	Fatality No. (%)	Total No.	P value
Birthweight	≤ 2000 gms	10 (50)	20	> 2000 gms	13 (43.3)	30	>0.05
Gestational age	≤ 34 weeks	10 (50)	20	> 34 weeks	13 (43.3)	30	>0.05
Mode of delivery	Vaginal	17 (40)	42	Cesarean	6 (75)	8	>0.05
Temperature	Hypothermia	18 (72)	25	Normal	4 (16)	23	<0.001
Capillary refill time	Prolonged	21 (65.6)	32	Normal	2 (11.1)	18	<0.001
Heart rate	Tachycardia	19 (45.2)	42	Bradycardia/ No activity	4 (80)	5	>0.05
Respiratory rate	Tachypnea	17 (47.2)	36	Irregular/absent respiration	4 (80)	5	>0.05
Initial FiO_2	≤ 0.6	13 (32.5)	40	> 0.6	10 (100)	10	<0.001
$AaDO_2$	≤ 250	2 (7.4)	27	> 250	21 (91.3)	23	<0.001
a/A	≤ 0.25	20 (91)	22	> 0.25	3 (10.7)	28	<0.001
O.I.	≤ 10	16 (37.2)	43	> 10	7 (100)	7	<0.01
V.I.	≤ 30	16 (41)	39	> 30	7 (63.6)	11	>0.05

Discussion:

There were reports on the risk factors associated with fatality in mechanically ventilated neonates using multiple regression analysis to establish risk factors for fatality with adjustment for potential confounders. Mechanically ventilated neonates have a high fatality [8-10]. The fatality is even higher in the small number of tertiary referral neonatal units receiving out born neonates [11]. In present study, more than half of the neonates were destabilized at admission with reference to cardiac activity, temperature, respiration, tissue perfusion & metabolically. Similar findings were reported by other authors [8-11].

The causes of respiratory insufficiency requiring mechanical ventilation included pneumonia (38%), apnea (14%), meconium aspiration syndrome (14%), hyaline membrane disease (12%), central respiratory depression and pulmonary hemorrhage. In contrast, several studies have reported hyaline membrane disease [8, 9, 12] or apnea [11] as most common indications for mechanical ventilation.

Complications of mechanical ventilation among neonates included pulmonary hemorrhage (20%), sepsis (12%), circulatory disturbances (12%), intraventricular hemorrhage (4%), ventilator associated pneumonia (4%) & pulmonary air leak (2%). Sepsis and pneumonia were the most common complications encountered which was closely followed by pulmonary air leaks in other studies [13-15]. Out of 44 mechanically ventilated neonates, 52.3% died and 47.7% survived. Nangia S et al [8] reported 46.5% overall survival, Singh M et al [10] had reported 55.5% overall survival, Maiya PP et al [14] had 48.8% overall survival among mechanically ventilated neonates.

The present study highlights the hypothermia, prolonged CRT, $AaDO_2 > 250$, $a/A \leq 0.25$, oxygenation index > 10, and initial $FiO_2 > 0.6$ as significant independent predictors of fatality in mechanically ventilated neonates. FiO_2 requirement reflects the severity of respiratory failure. All oxygen indices like OI, $AaDO_2$, and a/A depend on it [16]. Birthweight ≤ 2000 gms and gestational age ≤ 34 weeks reported as independent predictors of mortality by Mathur NB et al [11] in their study. In contrast, present study showed no such association with fatality of neonates.

Hypothermia was found as a main predictor of fatality among mechanically ventilated neonates in present study. Essential New Born Care (ENBC) includes care of body temperature of newborn to prevent hypothermia as it is one of the main risk factor for early neonatal mortality. Hypothermia can be prevented easily by providing Kangaroo Mother Care (KMC), a technique with minimum care and precautions and can be given by any adult person. Before and during referral of neonates to hospital for mechanical ventilation, care was not taken for prevention of hypothermia. So, present study highlights that fatality among mechanically ventilated neonates may decline by preventing hypothermia.

There were some limitations in present study like; neonatal pulmonary function testing was not possible so the dynamics of respiration was not judged, ventilator used does not have facilities like internal nebulization, pre & post suction oxygenation & inspiratory hold, and all risk factors were not taken in the regression model because of sample size.

Conclusion:

Risk of fatality can be identified in mechanically ventilated neonates. Measures put forward for favorable outcome of mechanically ventilated neonates includes, (1) early institution of mechanical ventilation before complications and organ damage set in, (2) thermoregulation – as 72% of the hypothermic neonates died with hypothermia in present study being a significant predictor of mortality, (3) acid base balance – 84% neonates were metabolically unstable, increasing the mortality risk, (4) circulation – as mortality in the neonates with prolonged CRT was 65.5%, being statistically significant predictor of mortality, & (5) establishment of proper network of neonatal services, preventing hypothermia by KMC before and during referral & transport of neonates.

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None.

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