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Prognosis of Mechanical Ventilation in Very Low Birth Weight Neonates: A Single-Center Study

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ABSTRACT

Background and Aims: Approximately 4–7 percent of all live births are led to a very low birth weight (VLBW) situation where the morbidity and mortality rate are very high. A large number of VLBW newborns in the intensive care unit (ICU) require mechanical ventilation due to various conditions. To reduce mortality in this group, identification of risk factors is important. This study aimed to determine the prognosis of mechanical ventilation in VLBW neonates at Mahdiye hospital in Tehran, Iran.

Materials and Methods: This study is a prospective cohort study. VLBW neonates who consecutively were put on mechanical ventilation during the study period were enrolled. Then, the enrolled neonates were divided into two groups: neonates who died after implementing the ventilator were in group-I and neonates who survived after receiving mechanical ventilation were in group-II. Demographic, clinical, and paraclinical variables were gathered to find out the predictors of mortality of ventilated neonates. The data were analyzed by SPSS software version 21.

Results: During the study period, a total of 177 neonates were ventilated due to different causes. 56% were male with a male to female ratio of 1.27:1. Mean birth weight and gestational ages were 1024.8 ± 247.5 grams and 27.9±2.2 weeks respectively. Out of 177 mechanically ventilated VLBW neonates enrolled for this study, 53% died. Significant factors determining mortality rate were mean weight, mean gestational age, pulmonary hemorrhage, advance resuscitation, and duration of hospital stay ($p<0.05$). APGAR score, gender, Pneumothorax, IVH>II, Sepsis, and Maternal Disease were not significantly associated with mortality in VLBW neonates requiring mechanical ventilation ($P>0.05$).

Conclusion: This study showed that among the analyzed factors weight <1000gm, gestation <28weeks, pulmonary hemorrhage, and complications during ventilation were the most significant predictors of mortality in ventilated VLBW neonates in the intensive care unit.

INTRODUCTION

Recently, the premature birth rate of infants has grown to around 11.1% worldwide which varies from 5% in Northern European countries to 18.1% in parts of Africa, and about 14.9 million preterm newborns are born annually[1, 2] . About one-fifth of babies born in Iran were also preterm, of which 40% were born before 34 weeks of gestation [3]. Despite the advances made in therapeutic approaches, mortality and morbidity rates in VLBW and premature neonates are still remarkable, especially in recent years [4]. Respiratory distress syndrome (RDS) in newborns is one of the most common and deadly complications of premature infants. On the other hand, respiratory disorders are the most common cause of admission of term and preterm infants in the intensive care unit (NICU) [5] and respiratory distress syndrome is the most common cause of respiratory distress in premature infants. Respiratory distress is seen in about 7% of infants [6], with an estimated 24,000 newborns in the United States each year suffering from the disorder[7]. The pathogenesis of the disease is due to the prematurity of alveolar cells which lead to a deficiency in surfactant

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[8, 9]. As a result, the alveolar cells will be clubbed and thus the lung's capacity will be reduced [10]. RDS is characterized by shortness of breaths and cyanosis, which can be seen with nasal flaring, expiratory grant, intercostal muscle retraction, etc. [7]. Also, the risk of developing RDS may increases by up to 5% with decreasing gestational age [11]. This disease has been seen in 60% of infants born before 28 weeks of gestation and affects one-third of infants born between 18-34 weeks of gestation. However, about 5% of newborns with a gestational age of more than 34 weeks also show this disorder[7]. RDS is more common in boys and its prevalence in infants born from diabetic mothers is up to 6 times higher than other infants[12]. Also, the cesarean section before starting labor pain can increase the rate of RDS [13-18]. Different methods have been implemented to improve respiratory symptoms and treatment of respiratory distress in newborns and have been investigated in various studies [11, 19, 20]. The main goal of respiratory distress treatment is to maintain a sufficient volume of the lungs, minute ventilation, and gas transfusion[21]. Here, the standard method of treatment includes artificial respiratory support and surfactant. For respiratory support, mechanical ventilation [22] is the most well-known method for reducing the RDS associated morbidity and mortality [23]. Since mechanical ventilation for the treatment of RDS in preterm infants was introduced [24] To date, not considering the surfactant therapy approval, the selective intubation has been applied as a routine treatment of respiratory failure in extremely low birth weight (ELBW) neonates [25]. In general, mechanical ventilation is undoubtedly one of the key advancements in newborns care. Even at this time when non-invasive respiratory support has attracted much attention, mechanical ventilation is the basis of healing in extremely preterm newborns. The neonatal research network results show that 89% of ELBW infants were exposed to mechanical ventilation on the first day of their birth [26]. About 95% of the surviving infants were also subjected to invasive ventilation during their stay in the hospital. In a study named "surfactant, positive pressure and oxygenation randomized trial" (SUPPORT study), 83% of ELBW infants, who were initially treated with non-invasive methods, required some mechanical ventilation and endotracheal intubation[19]. In another study, entered only 25-28-week-old infants arrived with adequate respiratory capacity at birth, but 46% of neonates with non-invasive respiratory protection ultimately found endotracheal intubation and mechanical ventilation [27]. Immediately after birth, when air-breathing begins in the immature low surfactant lungs, it is known to be critical, since it can quickly and definitively begin the process of lung injury and repair. For a successful transition to extra uterus life, newborns should quickly dry their lungs, remove pulmonary fluid from the airways and maintain the functional residual capacity (FRC), which all contribute to a sharp increase in parenchymal vascular flow. A healthy term infant can quickly pass this transition stage [28], but this does not usually happen in preterm infants. Premature infants may not be able to produce enough pressure to thrash their lungs due to muscle weakness, deficiency of surfactants, and insufficient lung development. The weak respiratory muscles in those infants, cannot keep the air entering into their lungs by itself or positive ventilation pressure. They may also not be able to create adequate negative thoracic pressure to discharge pulmonary fluid into the lungs, lymphatics, and veins. As a result of the subsequent tidal respiration, whether it's self-sustaining or due to positive pressure ventilation, it develops in the airway, which is still partly full of pleural fluid and is partially atelectatic.

These conditions lead to poor distribution of the tidal volume in the parts of the predominant lung, which can cause "Volutrauma", even if the tidal volume is in physiologic ranges [29].

Despite the advances and less invasive methods used to help RDS infants with VLBW, many neonates still require mechanical ventilation from the beginning or after the failure of other methods. There is still insufficient information to decide on the best time for initiating mechanical ventilation and non-invasive methods in many infants. Therefore, in this study, we decided to study the risk factors of the mechanical ventilation of newborn infants, and thus reduce the ambiguity in this field.

MATERIALS and METHODS

In this descriptive-analytic prospective cohort study, all infants of VLBW (birth weight less than 1500 gr) with RDS born in Mahdieh Hospital for two years, requiring birth-resuscitation in the delivery or operating room, were included in the study. Sampling was non-random, continuous, and available. Then, the variables studied such as infant sex, birth weight, gestational age at birth, pre-birth steroid intake, birth APGAR, resuscitation type, frequency of receiving surfactants, and mechanical ventilation outcome gathered in forms designed by researchers. The method of data collection was observation and examination method. The data were analyzed using SPSS software version 21. A confidence interval of 95% was used to express the accuracy of the estimates. Statistical analysis was performed using Chi-square, Fisher's exact test, t-test, and Pearson correlation coefficient. In all tests P-value of <0.05 considered as significant. The study was approved with the ethical code ir.sbmu.retech.rec.1395.508.

RESULTS

This study was performed on all neonates weighing less than 1500 grams at birth at Mahdieh hospital for 2 years. Therefore,

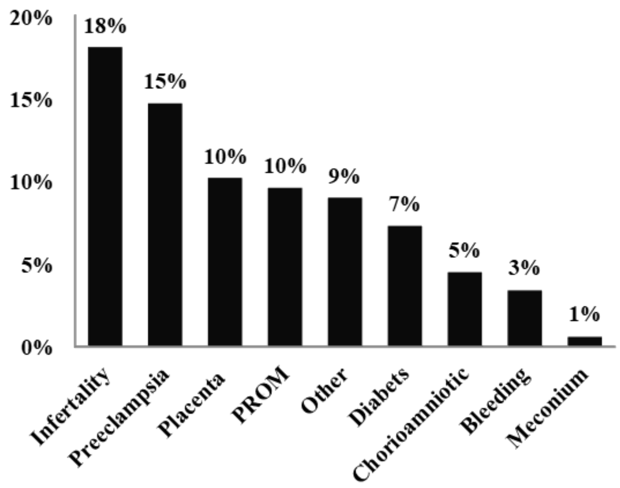

Diagram 1. Frequency distribution of pregnancy and maternal problems in newborns with birth weight less than 1500 gr.

177 neonates were enrolled in the study. The purpose of this study was to determine the mechanical ventilation prognosis in the VLBW infants of Mahdieh hospital. 99 neonates (56%) were male and 78 neonates (44%) were female. The mean gestational age was 27.9 ± 2.2 weeks with a range of 23-35, the mean birth weight of newborns was 1024.8 ± 247.5 g with a range of 470-1500 g, the mean of the first minute Apgar score was 5.8 ± 2. 3 with a range of 9-0 and the mean of the fifth minute Apgar score was 7.4 ± 1.9 with a range of 2-10. A total of 41 neonates (23%) were born with normal vaginal delivery and 136 neonates (77%) by cesarean section of which 156 neonates (88%) in Mahdieh hospital and 21 newborns (12%) were born in another center. 105 newborns (59%) were single, 62 infants (35%) were twins, 9 cases (5%) triple, and one (1%) was a quartet. 95 newborns (54%) received basic resuscitation and 82 neonates (46%) got an advanced type. The maternal complications during pregnancy are presented in Diagram 1. Infertility (18%) and pre-eclampsia (15%) were the most common complications. Also, 55% of infants had patent ductus arteriosus (PDA), 45% sepsis, 26% retinopathy of prematurity (ROP), and 18% pneumothorax. Diagram 2.

A total of 166 infants (94%) received surfactant at least one time, 75 infants (42%) twice and 19 infants (11%) received three times. The number of cases of surfactant receiving by age of infants per hour is summarized in Table 1.

Findings of the type of respiratory support showed that 11 neonates (6%) received only mechanical ventilation and 166 newborns (94%) received both mechanical ventilation and surfactant. The type of respiratory support and its duration are summarized in Table 2.

The mean hospitalization days of infants were 28 ± 2.8 days with a range of 0.03 to 157 days. The average weight of newborns at discharge was 1270 ± 425 g, with a range of 450- 2350 g. A total of 93 neonates died (53%) of which 68 neonates (73%) died due to respiratory failure and 9 newborns (10%) died due to sepsis. The mean and standard deviation of the demographic and clinical variables of the neonates in terms of outcome are summarized in Table 3. There was a statitically significant difference between the mean gestational ages, birth weight, and hospitalization days with neonatal outcomes.

The demographic and clinical variables of neonates are summarized in Table 4. There was a statistically significant difference between the gestational age, birth weight, number of receiving surfactants, pulmonary hemorrhage, and hospitalization days with neonatal outcomes.

DISCUSSION

Various studies have been carried out to determine the best time of respiratory support for VLBW infants with respiratory distress. Besides, the in-time benefit-harm assessment in managing these patients has been investigated. In a retrospective cohort, the effect of two different approaches in the labor room on the amount of endotracheal intubation and mechanical ventilation and short-term morbidity in ELBW infants were compared. In this study, ELBW infants that were not mechanically ventilated had less morbidity (including bronchopulmonary dysplasia (BPD), intraventricular hemorrhage, and periventricular leukomalacia). Also, a per case intubation strategy for ELBW infants was more effective than the intubation of all newborns with short symptoms of respiratory distress [30]. It

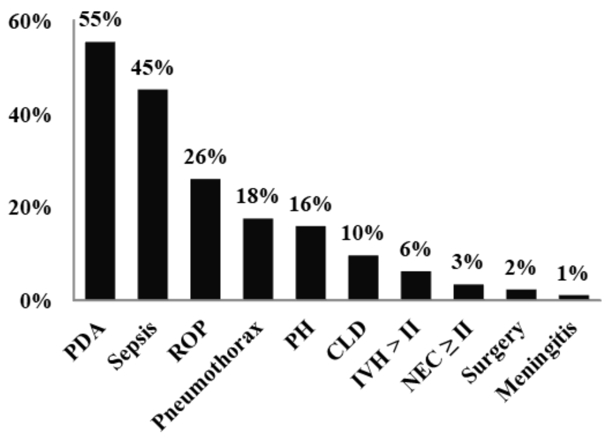

Diagram 2. Frequency distribution of infantile problems in newborns with birth weight less than 1500 gr.

Table 1. Frequency distribution of the surfactant therapy rate by the age in newborns with birth weight less than 1500 gr.

Age(Hour)	Surfactant		
	I	II	III
<2	88 (53%)	1 (1%)	0 (0%)
2-6	69 (42%)	0 (0%)	0 (0%)
6-24	7 (4%)	54 (31%)	6 (32%)
>24	2 (1%)	20 (11%)	13 (68%)
total	166 (94%)	75 (42%)	19 (11%)

Table 2. Frequency distribution of type of respiratory support by its duration in newborns with birth weight less than 1500 gr.

Duration (hour)	Type of respiratory support	
	Mechanical Ventilation	MV and Surfactant
<3	10 (91%)	122 (74%)
4-7	1 (9%)	17 (10%)
8-14	0 (0%)	9 (6%)
15-28	0 (0%)	17 (10%)
>28	0 (0%)	0 (0%)
total	11 (6%)	166 (94%)

Table 3. The mean and standard deviation of the demographic and clinical variables of the neonates in terms of outcome in newborns with birth weight less than 1500 gr.

Variables	Treatment outcome		P-value
	Survived	Death	
Gestational age (week)	28.7±0.2	2.1±27.2	<0.001
Birth weight (gr)	239±1125	220±934	<0.001
1st minute Apgar	2.2±6.1	2.3±5.5	0.055
5th minute Apgar	1.8±7.7	2.0±7.2	0.054
Hospitalization days	22.7±50.0	13.3±7.9	<0.001

Table 4. Frequency distribution of demographic and clinical variables of neonates in terms of outcome in newborns with birth weight less than 1500 gr.

Variable		Treatment outcome		P-value
		Survived (84)	Death (93)	
Gender	Female	36 (43%)	42 (45%)	0.764
	male	48 (57%)	51 (55%)	
Gestational age (week)	<28	27 (32%)	55 (59%)	0.001
	28-30	32 (38%)	25 (27%)	
	≥ 30	25 (30%)	13 (14%)	
Birth weight (gr)	≤ 750	5 (6%)	15 (16%)	<0.001
	751-1000	26 (31%)	49 (53%)	
	1001-1250	25 (30%)	20 (21%)	
	1251-1500	28 (33%)	9 (10%)	
1st minute Apgar	<6	31 (37%)	48 (52%)	0.069
	≥ 6	53 (63%)	45 (48%)	
1st minute Apgar	<6	10 (12%)	19 (20%)	0.156
	≥ 6	74 (88%)	74 (80%)	
Neonatal problems	pneumothorax	10 (12%)	21 (23%)	0.075
	pulmonary hemorrhage	5 (38%)	23 (54%)	<0.001
	IVH > II	5 (6%)	6 (6.5%)	1.0
	sepsis	40 (48%)	40 (43%)	0.549
Maternal problems		50 (60%)	52 (56%)	0.650
Resuscitation	basic	52 (62%)	43 (46%)	0.050
	advanced	32 (38%)	50 (54%)	
Surfactant Intake	once	48 (62%)	43 (49%)	0.042
	twice	26 (33%)	30 (34%)	
	three times	4 (5%)	15 (17%)	
Hospitalization Days	<1	0 (0%)	69 (74%)	<0.001
	1-4	10 (12%)	19 (20%)	
	4-6	24 (29%)	1 (1%)	
	6-8	19 (23%)	2 (2%)	
	>8	31 (37%)	2 (2%)	

is shown that infants who need intubation have a lower gestational age, birth weight, and 1st minute Apgar than others. Newborns who are intubated in the delivery room have a higher risk of increased oxygen demand. In summary, the per-case VLBW neonatal respiratory protection strategy is the best remedy [31].

In another study neonates with a gestational age of fewer than 28 weeks were included. In a group, the CPAP was used for 56% of infants in the delivery room and 22% did not need intubation or mechanical ventilation. In the latter group, all infants were intubated from the beginning. Similarly, less CPAP was used and the mean airway pressure (MAWP) was higher in the first four weeks of life. Mortality and moderate to severe BPD were similar in both groups at week 36, while at week 40, oxygen demand was higher in the latter group [32]. invasive ventilation using the endotracheal tubes is one of the most commonly used therapeutic interventions in preterm newborns with respiratory failure. RDS is seen in about 50% of preterm infants with an age of fewer than 30 weeks. Mechanical ventilation using surfactant is the standard RDS treatment method. Nonetheless, mechanical ventilation is associated with complications as BPD[33]. Various studies that compared mechanical ventilation types did not show a difference in BPD levels. The best method for ventilating premature infants with RDS should be started in the delivery room and based on the infant's conditions, have the least invasion and the least intubation time should be included [34]. It is worth mentioning that early nasal CPAP has had no significant effect on the reduction of mortality or BPD compared to intubation. Even though the CPAP may contribute to a higher incidence of pneumothorax, fewer infants have needed oxygen at day 28 and fewer days of intubation [19, 27].

A study on VLBW neonatal early respiratory protection techniques showed that VLBW and ELBW infants are at risk for death or complications such as chronic pulmonary disease. The Standard treatment for pulmonary failure, mechanical ventilation at birth, can lead to barotrauma, volutrauma, pulmonary edema, infection, and inflammation[33]. Different therapeutic strategies have been introduced to reduce these complications. In this study, the use of mechanical ventilation, NCPAP and surfactant therapy in the neonates of VLBW and ELBW were compared and it was shown that a per case support should be provided for respiratory protection of premature VLBWs [35].

Multiple studies have examined the incidence, predictors, and outcomes of the CPAP failure in preterm infants. In a study, CPAPs were unsuccessful in 65 out of 297 infants who received CPAP (22%), so that CPAP failure was more pronounced in neonates with low gestational age. This study showed that CPAP failure in newborns was due to unrecognized respiratory distress, with FiO2≥0.3 in the first hour of life predicted and associated with other complications [36].

CONCLUSION

Identification of the risk of death in neonates with mechanical ventilation is essential for early intervention, reducing mortality and even triage, in collections with limited resources. Weighing less than 1000 grams, age less than 28 weeks of gestation, and pulmonary hemorrhage, prognosticated mortality in neonates under mechanical ventilation.

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