

## Factors Affecting the Neonatal Intensive Care Unit Stay Duration in Very-Low-Birth-Weight Premature Infants

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### ABSTRACT

**Introduction:** Improved survival of very low birth weight (VLBW) premature infants requires urgent intensive care, professional nursing and medical care. On the other hand, long hospital stay period imposes emotional and economic burdens on the family and society. Therefore, it is necessary to clarify the most important factors affecting their hospitalization duration to lessen unwanted outcomes of premature birth and to eliminate or relieve the problems. **Methods:** In a descriptive-analytical study, 170 low birth weight premature infants were assessed in a regular daily follow-up in Alzahra Hospital, Tabriz, Iran. Probable factors affecting NICU (neonatal intensive care unit) stay, such as birth age and weight, time of trophic feeding initiation, time of regain birth weight, and duration of parenteral nutrition, were evaluated. Data was analyzed using descriptive statistics and linear regression model in SPSS<sub>14</sub>. Statistical significance was considered at 0.05. **Results:** Mean birth weight and age of infants were  $1310.26 \pm 804.26$  g and  $30.51 \pm 0.34$  weeks, respectively. Duration of NICU stay was  $14.51 \pm 10.12$  days. Intra-uterine growth retardation, positive C-reactive protein (CRP) and blood culture during hospitalization stay, bloody or bile stained gastric remnants, days to regain birth weight, and total enteral nutrition intolerance were the most important factors affecting NICU stay among the studied infants. **Conclusion:** It seems that eliminating risk factors of intrauterine growth retardation during pregnancy, preventing perinatal and nosocomial infections and taking suitable and tolerable feeding strategies will be effective on NICU stay duration in low birth weight premature infants. Therefore, required policies, especially early trophic feeding, are suggested to eliminate the existing difficulties.

### Introduction

Premature birth is one of the direct causes of 27% of 4 million neonatal deaths that annually occur all over the world.<sup>1</sup> Fortunately, in the recent decade, perinatal mortality has significantly reduced in developed countries following the wide advances in received prenatal steroids, surfactant use and respiratory sup-

port. While there have also been widespread advances in neonatal intensive cares and survival rate of very low birth weight (VLBW) infants, reported as approximately 85%, respiratory morbidity and neurological outcomes are still of concern.<sup>2</sup> On the other hand, timely management of labor and neonates, preventing premature birth and low birth weight, prenatal diagnosis and early management of

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congenital anomalies and timely and effective treatment of pregnancy diseases as well as perinatal and nosocomial infections have also affected the decline in perinatal mortality. Advanced neonatal intensive care is of high importance and requires trained staff, advanced devices and high costs of neonatal intensive care unit (NICU) stay.<sup>3</sup>

Hypoxia, ischemia, mental retardation, seizures, intraventricular hemorrhage, hydrocephaly, microcephaly, audio and visual impairments, retinopathy of premature infant, respiratory inadequacies or failures, necrotizing enterocolitis (NEC), malabsorption, cholestatic liver disease, social stress, child abuse, sudden infant death syndrome, increased blood pressure, and nephrocalcinosis are the early and late complications associated with VLBW.<sup>3</sup> On the other hand, nosocomial infections, prolonged NICU stay and treatment costs are the major complications of premature birth. Meanwhile, high rate of problems in premature infants in NICUs causes prolongation of NICU stay process and increased maternal stress.<sup>4-6</sup>

Nutritional strategies are other important factors in caring for premature infants. According to the results of a systematic review study, trophic nutrition significantly reduced number of feeding withdrawal days, time of full intestinal feeding, and the duration of NICU stay.<sup>7</sup> Moreover, education and participation of parents in neonatal care<sup>5</sup> and early discharge of premature infants reduce diseases and disabilities caused in duration of stay and high costs of hospitalization in NICU. Meanwhile, management of apnea as well as methods of feeding premature infants are of the most important factors in decision-making to discharge a premature infant. Subsequently, the possibility of advanced supportive care after discharge, received nutritional supplements, vision and auditory screening after discharge, evaluation of apnea and bradycardia and cardiopulmonary stability can influence the discharge duration. It should be noted that considering the in-

creased survival rate of premature infants and accordingly increased number of infants requiring intensive care, it is tried to minimize the NICU stay length<sup>8</sup> in order to provide intensive care for more premature newborns.

According to the report of the World Health Organization in 2006, the rate of VLBW infants in Iran has been 7%. Moreover, 31% of neonatal mortalities have been due to premature birth.<sup>9</sup> Therefore, it seems that prematurity problems and VLBW infants need to be dealt with and eliminated through required measures. In addition, the rates of nosocomial infections,<sup>10</sup> natural emotional stress incurred in the separation of mother and infant, imposed stress to parents and family and vasomotor retardations and respiratory problems are high in this group of infants.<sup>11</sup> Therefore, caring for such infants imposes large financial and spiritual burdens on family, society and insurance companies. Consequently, accurate determination of factors affecting the NICU stay duration seems essential in order to effectively plan for neonatal health. By recognizing, preventing or controlling such factors, adverse problems caused by premature birth and thus NICU stay are expected to be reduced.

## Materials and methods

In a descriptive-analytic study, regular daily follow-up (practical examination of infants and referring to nursing reports and records) was performed to evaluate probable effective factors on NICU stay among 170 VLBW infants admitted in NICU of Alzahra University Hospital in Tabriz, Iran from September 2009 to May 2010. The sample size for each effective factor was calculated using Power and Sample Size Software. Considering maximum type I of 0.05 and 80% power and a 2-day difference in the number of required days to reach the initial weight at the time of birth, the largest sample size was estimated as 156 infants. Finally, 170 infants were studied due to the possibility of sample loss. The study was approved by the Ethics Committee

and the Research Council of Tabriz University of Medical Sciences. It was also accepted as a research project. Informed consents were obtained from the parents who promised to participate and cooperate in the study by delivering breast milk to the NICU. They also agreed for further cooperation after discharge, if necessary.

Infants were included if they weighted 1000-1500 grams and had a gestational age of 31-26 weeks (according to last menstrual period (LMP) or early pregnancy ultrasound). Infants with major congenital anomalies, severe asphyxia and those who were referred from other hospitals (due to nosocomial infections, hypothermia after birth and lack of appropriate treatment) were excluded from the study.

Some characteristics of infants that may have affected the duration of NICU stay, such as birth age and weight, Apgar score at the first and fifth minutes, need for resuscitation after birth, received surfactant, the result of blood culture at the time of labor and during hospitalization, neonatal feeding type, time of trophic feeding initiation, time of regain birth weight, duration of intravenous feeding, initial positive C-reactive protein (CRP) and duration of stay, suspected and confirmed NEC, affecting factors in nutritional tolerance and the number of required days for total enteral nutrition tolerance, were recorded. After random sampling (through a table of random numbers), the data was collected by a researcher-made questionnaire whose validity was confirmed by faculty members of Tabriz University of Medical Sciences using content validity method. The reliability of the questionnaire was confirmed by a pilot study with a Cronbach's alpha coefficient of 80%.

Daily follow-up, including important clinical outcomes and recorded items in nursing reports and disease fact sheets, was performed for all infants until discharge while the parents were present. The amount and initiation time of breastfeeding through the enteral feeding via catheter by bolus method, which was the selective method in the NICU of Alzahra Hospital, were determined during

the daily visits by a physician. Feeding tolerance before every nutritional meal by the previous remained food in stomach (by aspiration of gastric secretions), bloody or bile stained gastric remnants, vomiting, abdominal distention or tenderness, the number of bowel movements, bloody stool or diarrhea, the number of feeding withdrawal, apnea and the possibility of NEC were evaluated. In case of the abovementioned symptoms, the items were recorded in the feeding tolerance special forms by the feeding nurse. Then the physician was informed to make the appropriate decision for continuing feeding. For infants suspected to NEC, enteral feeding was stopped and abdominal radiography was performed. NEC was diagnosed based on lack of feeding tolerance with lethargy, body temperature imbalance and gas in intramural and portal vein in abdominal radiograph. Cases of sepsis were diagnosed considering combined clinical and laboratory signs (positive blood culture and lumbar puncture). The incidence of sepsis seven days after the labor was considered as late sepsis. Weights of infants were measured daily in a certain hour. Measured weights were recorded in special forms. The time of regaining initial birth weight was determined. The duration of NICU stay from birth to discharge, duration of intravenous feeding and intravenous catheter, as well as health outcomes such as sepsis and NEC were also recorded.

The discharge criteria included satisfactory weighting with total enteral nutrition, maintaining body temperature and no medical problems confirmed by a pediatrician.

The data was analyzed in SPSS<sub>14</sub> using independent t-test, chi-square and linear regression tests. P values less than 0.05 were considered as statistically significant.

## Results

Mean birth weight and gestational age of infants were  $1310.26 \pm 804.26$  g and  $30.51 \pm 0.34$  weeks, respectively. Duration of NICU stay was  $14.51 \pm 10.12$  days. While singletons and twins constituted 66.5% (113 infants) and

27.6% (47 infants) of the infants, respectively, others were triplets or more. The fluid and caloric intake rate was similar for both groups. Thirteen infants (7.6%) had intra uterine growth retardation (IUGR). Trophic nutrition had begun for 124 infants (72.2%) in the first 48 hours after birth. Preeclampsia and multiple-birth were the most common causes of premature delivery in mothers (Table 1).

No infants were excluded from the study due to lack of compliance with the nutritional

protocol, death or medical conditions such as NEC, gastrointestinal surgery and secondary cerebral hemorrhage. Feeding method using syringe pump (intervals) was performed only in one infant in the delayed group due to continuous feeding intolerance. Hypoglycemia occurred more than 3 times in 9 infants (6.3%). In addition, 2.4% of infants experienced some extent of intracranial hemorrhage during their stay. Other demographic and clinical characteristics of the infants and mothers are summarized in Table 1.

**Table 1.** Demographic and clinical characteristics of mothers and premature infants with very low birth weight (VLBW)

Characteristics	n (%)
Sex	Female Male
Gravidity and Parity Rate	1 <sup>st</sup> pregnancy 2 <sup>nd</sup> pregnancy 3 <sup>rd</sup> or more pregnancy
Labor type	Vaginal Cesarean
Cause of premature delivery	Preeclampsia Multiple pregnancy Premature rupture of membrane Detachment Other causes

**Table 2.** Factors affecting the length of NICU stay in infants with very low birth weight (VLBW)

Probable factors	Results	P-value	Beta coefficient
The time of regaining initial birth weight (day)	15.51 ± 6.23	< 0.001	0.49
Total enteral nutrition intolerance	5.30 ± 11.08	0.08	0.23
Perinatal birth weight	1310.26 ± 804.26	0.92	0.005
Perinatal gestational age	30.51 ± 0.34	0.36	-0.04
Time of intravenous feeding (day)	10.55 ± 5.53	0.26	0.10
First minute Apgar score	6.63 ± 0.61	0.40	0.04
Fifth minute Apgar score	1.26 ± 8.26	0.98	0.004
Number of days for feeding withdrawal	1.36 ± 0.64	0.68	-0.03
Resuscitation support	65 (38.2)	0.99	0.001
Use of surfactant	40 (23.5)	0.87	0.01
Vomiting	12 (7.1)	0.34	0.05
Gastric residual volume	48 (28.2)	0.98	-0.001
Abdominal distension	2 (1.2)	0.74	0.02
Positive blood culture during stay	12 (7.1)	0.001	0.30
Bloody or bile stained gastric remnants	2 (1.2)	0.001	0.23
Intrauterine growth retardation	13 (7.6)	0.007	0.15
Positive CRP during stay	6 (3.5)	0.001	0.21
Initial positive CRP	7 (4.1)	0.70	0.02
Initial positive blood culture	0	-	-
Suspected NEC	2 (1.17)	0.98	0.001
Confirmed NEC	0	-	-

CRP: C-reactive protein; NEC: Necrotizing enterocolitis

Values are presented as mean ± SD or number (%)

The relations between possible factors affecting the duration of NICU stay including birth age and weight, Apgar scores at the first and fifth minutes, resuscitation after birth, received surfactant, IUGR, perinatal blood culture results during stay, type of feeding, initiation of trophic feeding, regaining initial birth weight, length of intravenous feeding, initial positive CRP, length of NICU stay, suspected NEC, factors effective on feeding tolerance (vomiting, retention of residual enteral contents more than 30% by previous feeding, bloody or bile stained gastric remnants, abdominal distention), and number of days required to tolerate enteral nutrition with the dependent variable were assessed. The factors were then entered into a linear regression model. Finally, IUGR, positive CRP and blood cultivation during hospital stay, bloody or bile stained gastric residual following enteral feeding, and number of days required to regain initial birth weight were found to be effective on NICU stay (Table 2).

## Discussion

Hospitalization in NICU can be discussed in terms of health, family, economic and social dimensions. Since premature infants lack balance and coordination between different body systems, they may face multiple diseases. Thus, a team of medical and nursing specialists and excessive attention of parents and caregivers are definitely required. Approximately 30-50% of VLBM infants are believed not to be able to cope with school works despite normal intelligence quotient (IQ) at the age of 7. Moreover, 24% of VLBM adults have neurological/sensory disabilities (auditory, visual, cerebral palsy and cognitive impairments)<sup>3</sup> which confirms the continuation of premature complications and requirement for more services and future costs. On the other hand, high costs of NICU stay would cause higher stress for anxious families. The society and insurance companies would also be influenced.<sup>12</sup>

Therefore, searching for appropriate strategies to solve this problem seems necessary.

Feeding intolerance problems due to premature gastrointestinal system may cause temporary cessation of feeding, prolongation of total enteral nutrition intolerance and accordingly prolongation of intravenous feeding and NICU stay.<sup>7</sup> In the present study, among the factors affecting feeding tolerance, bloody or bile stained gastric remnants due to previous residual food was of the most important causes of stay prolongation. Thus, the infants with blood or bile tolerance at the time of aspiration due to nutritional problems or suspected NEC, faced with cessation or interruption of subsequent nutrition. Such issue could make the progression of feeding absorption even slower. On the other hand, the required time for tolerating total enteral nutrition had a direct association with duration of stay which can be interpreted in correlation with the problems of feeding tolerance. It seems that initiation of enteral feeding with small amounts of breast milk on the first days after birth can be helpful. A review study by Tyson et al. found 42% reduction in duration of stay following the early enteral feeding and appropriate nutritional tolerance.<sup>13</sup> The results of our previous study<sup>14</sup> also showed that infants with enteral nutrition intolerance<sup>7</sup> had more prolonged NICU stay.

Bacterial colonization and nosocomial infections are also considered as affective factors in prolongation of hospital stay. Prolonged hospitalization, procedures (catheter, lumbar puncture catheter of bladder) and lack of full observation of sanitary norms, as well as lack of breastfeeding (intravenous feeding) on early days after birth would make infants susceptible to infection. In the present study, positive CRP and blood culture during stay were the causes of prolonged NICU stay. It is obvious that eliminating factors for nosocomial infections would effectively shorten the hospitalization

process. Significant reductions have been reported in confirmed sepsis cases and sepsis markers of breastfeeding following breastfeeding which are attributed to immunological and antimicrobial properties of breast milk.<sup>15-17</sup> For instance, similar to our previous study,<sup>14</sup> lower cases of sepsis in infants receiving trophic nutrition have been reported to lead to earlier discharge.<sup>18-20</sup> However, unfortunately, very little information exists about this risky subject in caring for premature infants. In fact, the exact time of feeding initiation is not clear despite its major and prolonged clinical outcomes particularly NEC.

Presence of parents beside their infants has also been reported as an effective factor on NICU stay duration reduction.<sup>21</sup> However, mothers could only meet their infants in the NICU of Alzahra University Hospital while day and night accommodations were provided after the infants were transferred. Therefore, this factor was not mentioned as effective in the present study.

Perinatal age and weight and required time to regain initial weight are the important indices for discharge<sup>22</sup> which can be increased by prematurity and IUGR. They may also prolong weighting process.<sup>23</sup> In the present study, although we expected perinatal weight and age to be determinants of NICU stay duration, there were no statically significant correlations in this regard. Such finding might have been due to the selection of infants at a certain age and weight range. Further studies are thus needed to evaluate a combination of VLBM and LBM infants.

In addition, infants with IUGR or those who took longer time to regain their initial birth weight experienced more prolonged NICU stay. Combination of prematurity and IUGR is a chronic and multifactor process which requires appropriate measures even before pregnancy.<sup>24</sup> Various studies confirmed faster rate of weighting after birth by using early trophic nutrition which can cause reduction of stay duration.<sup>7,14</sup> Furthermore, comprehensive cares before and during preg-

nancy would result in a safe labor and would therefore prevent chronic diseases. Decreasing mothers' stress is also considered as an important step toward reduction of IUGR cases.<sup>24</sup>

Need for respiratory supports and diversity of respiratory problems associated with premature respiratory tract in infants are the most important causes of NICU hospitalization.<sup>25</sup> Although the participated infants in this study required surfactant due to their first and fifth minute Apgar scores, no significant correlations were found among these factors and duration of NICU stay. Such finding might have resulted from the inclusion criteria, i.e. infants with severe perinatal asphyxia retransferred from other hospitals had no chance to enter the study due to the risk of infections, hyponatremia and lack of identical primary cares. Therefore, the studied infants had relatively proper first and fifth minute Apgar scores. On the other hand, all deliveries were performed in Alzahra University Hospital with pediatric assistants present in the labor room during the delivery. Therefore, infants were immediately transferred to NICU after primary measurements and received surfactant, if necessary. Considering the optimal status of receiving respiratory cares in the shortest possible time, lack of such a relationship can be partly confirmed.

## Conclusion

Considering the urgent need of infants, families and the society for shortening the premature infant hospitalization as much as possible, implementing different interventions can be effective on survival rate of infants by eliminating prenatal infection factors as well as nosocomial infections. Paying higher attention to prenatal cares, informing parents about the high risk of infection, training parents with strategies to cope with nosocomial infections, improving nutritional cares in terms of early breastfeeding, and promoting prenatal cares to reduce IUGR cases are among the mentioned interventions. Finally, similar studies using infants with extremely

low birth weight (ELBW) are recommended to be performed in different age and weight groups to evaluate the inabilities resulted by prematurity of such group of infants.

## Limitations

Since mothers did not have the chance to stay in the NICU, suburban mothers had difficulties transferring their breast milk to the hospital. Therefore, infant formula milk was inevitably used for their infants.

## Ethical issues

None to be declared.

## Conflict of interest

The authors declare no conflict of interest in this study.

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