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ORIGINAL ARTICLE

Medicine Science 2022;11(1):354-60

Medicine Science International Medical Journal

Factors affecting the length of stay in the intensive care unit of surviving infants with very low birth weight: A cross-sectional study

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Received 27 September 2021; Accepted 07 November 2021
Available online 14.02.2022 with doi: 10.5455/medscience.2021.09.318

Abstract

Low birth weight causing mortality, morbidity, and lifelong disability is an important public health problem. Infants with very low birth have long hospital lengths of stay. The study aims to determine the factors affecting the length of stay of very low birth weight (<1500 g) infants receiving treatment in the tertiary level neonatal intensive care unit (NICU). This descriptive, retrospective and cross-sectional study were conducted with 774 infants who were discharged alive from the NICU between January 01, 2013, and May 30, 2019. Perinatal characteristics, morbidities, and length of stay of the infants were obtained from the electronic records of the hospital. A regression model was built to determine the factors affecting the length of stay of infants in the NICU.The median birth weight of the babies was 1150 (490; 1495) grams and the median gestational age was 205 (161; 261) days. The median length of stay of the infants was found to be 53 days (14; 357). In the regression model, increased birth weight, increased gestational age, application of phototherapy caused the length of stay to decrease, while respiratory distress syndrome, Bronchopulmonary dysplasia, retinopathy of prematurity, necrotizing enterocolitis, non-invasive ventilation, invasive ventilation, and multiple pregnancies had an increasing effect on the length of stay. The length of stay of infants in the NICU can be predicted with the regression model. Thus, it will contribute to more effective NICU use and cost control.

Keywords: Very low birth weight infant, neonatal intensive care unit, length of stay, prematurity, linear regression

Introduction

Preterm birth is not only an important cause of mortality, morbidity, and lifelong disability but also an important public health problem [1-3]. Preterm birth, which is emphasized by the World Health Organization, is defined as the end of pregnancy before the 37th week, with live birth [4]. Regardless of gestational age, babies weighing less than 2500 grams are considered low birth weight (LBW), and babies with a birth weight of <1,500 grams are defined as very LBW (VLBW) [5]. Between 5% and 18% of babies born in 184 countries have LBW, and an estimated one million babies with LBW die [6]. Worldwide, in 2015, 20.5 million babies born with LBW accounted for an estimated 14.6 % of all births [7].

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More than 60% of preterm births, which is a truly global problem, occur in Africa and South Asia [6]. While the rate of LBW babies in Turkey was 12.9% in 2000, it was 11.4% in 2015 [8]. Babies with VLBW account for 1.39% of live births and 51.0% of baby deaths in the USA [9]. It is expressed that the birth weight of the baby is also a strong determinant of mortality and morbidity, and the risk of death increases as the birth weight decreases [10].

The incidence of complications increases in prematures and some of them are Respiratory conditions such as respiratory distress syndrome (RDS), bronchopulmonary dysplasia (BPD), brain injury (BI) such as intraventricular hemorrhage (IVH) and periventricular leukomalacia (PVL), sepsis, retinopathy of prematurity (ROP) [2,11].

The morbidities carried by infants become a source of psychological distress for families and increase the length of stay, the risk of hospital readmission, and the costs [12]. The worse the economic status of the families, the more they are at risk of being affected by these negativities [6]. These morbidities expose infants to additional diagnostic, therapeutic, and surgical interventions [12]. About 85% [from 55% (501-750 grams) to 96% (1250-1500 grams)] of infants with VLBW survive after discharge from hospital [13]. However, those born with LBW have an increased risk of disability that will continue throughout their lives. Some of these are hearing and vision impairments, "wasting, stunting and underweight", executive function issues, attention deficit disorder, low intelligence quotient, cognitive dysfunctions, and chronic problems such as diabetes and obesity that occur in adulthood [6,14-16].

The study aims to determine the factors affecting the length of stay of very low birth weight (<1500 g) infants receiving treatment in the tertiary level neonatal intensive care unit (NICU).

Materials and Methods

Ethical statement

The research planned as a descriptive, retrospective, and cross-sectional was conducted in a training and research hospital in Ankara, which has one of the biggest tertiary-level NICUs in Turkey. Permission for the study was obtained from Ankara Yıldırım Beyazıt University Ethics Committee (Project Approval Certificate; Ethics Committee Decision meeting date and decision no: 31.07.2019-35) and Medical Specialty Training Board in the hospital where the study was to be conducted.

Data collection

According to the Social Security Institution Healthcare Implementation Communique, the research was planned for infants who were reimbursed. Thus, work was planned according to a standard reimbursement. The population of the study consists of VLBW infants weighing less than 1500 grams, who were hospitalized in the tertiary level NICU between January 01, 2013, and May 30, 2019. During the study period, 1666 the infant had been admitted to NICU. Of these, 892 were not recruited to the study. Reasons for exclusion: Birth weight ≥1500 grams (n=393); died in the NICU (n=305); Dispatch to another facility (n=81); Lack of the electronic epicrisis report (n=63); Different insurance (n=24); Uncertainty of discharge (n=8); Readmission (n=11); Lack of the reimbursement information (n=7). The criteria for exclusion in the study are shown in Figure 1.

In this study, a form was created to collect demographic and clinical data obtained from electronic records. RDS, ROP, sepsis, BPD, BI (IVH+PVL), and NEC were determined as morbidity. In addition, according to birth weights' newborns were separated into four groups: < 750 grams, 750 – 999 grams, 1000 – 1249 grams, and 1250 – 1499 grams.

Morbidities, multiple births, mode of delivery, and applied phototherapy, respiratory treatment, and nutritional treatments were recorded categorically as present or absent. If an infant was treated with invasive ventilation (IV) and/or non-invasive ventilation (NIV) at any time during the hospitalization period, they were marked as receiving respiratory therapy. Therefore, an infant may have received both IV and NIV therapy.

The morbidities determined in infants were collected in 4 groups according to their numbers as the absence of morbidity, 1 morbidity, 2 morbidities, and 3 ≤ morbidities. Apgar score was divided into two groups as ≥7 and <7 according to the 5-minute value. If the 5-minute Apgar score is between 7-10, it is considered reassuring [17].

A multiple linear regression model was built to determine the factors affecting the LOS. Since the LOS variable has a right-skewed distribution, natural logarithm transformation was applied for LOS in comparisons and the obtained values were used [LOS = Ln (LOS)]. The value obtained because of the regression model formula(x) can be calculated as days by using the "base of the natural logarithm be raised to the power of x".

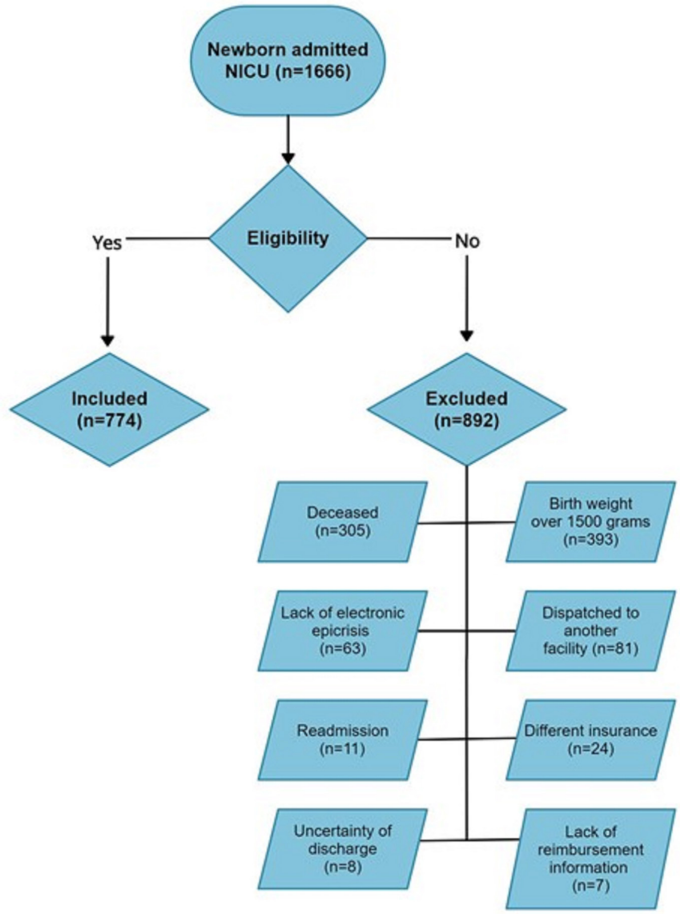

Figure 1. Recruit model: Exclusion criteria from the study

Statistical analysis

IBM SPSS Statistics for Windows 21.0 (IBM Corp. Released 2012. Armonk, NY: IBM Corp) was used for statistical analysis and calculations. The p-value of <0.05 was considered statistically significant. The conformity of the numeric variables to the normal distribution was evaluated by the Shapiro Wilk test. In the representation of the descriptive statistics of the variables, the appropriate values from the median (minimum; maximum), mean ± standard deviation, and number (percentage) were given. Pearson's chi-square test was used for categorical variables in statistical analyses, Kruskal-Wallis test was used for more than two independent group comparisons, and Mann Whitney U test was used for two independent group comparisons. When there is a significant difference, Bonferroni correction was used in pairwise comparisons. Correlation between numerical variables was analyzed and interpreted with Spearman's rho correlation coefficient.

The effects of the variables on LOS were analyzed by the stepwise regression method. The probability of the variable to be entered into the regression model at each step was 0.05, and the probability of being removed from the regression was 0.10. Spearman's rho non-parametric correlation coefficient was evaluated in the analysis of the correlations between independent variables to analyze the presence of multiple correlations. The problem of heteroscedastic was analyzed visually with a scatterplot.

Limitations of the study

Our research is a single-center and single-level study. This research has been evaluated only from the point of view of the paying institution.

Results

A total of 774 discharged infants with VLBW (BW<1500g) deemed appropriate were included in this study, which was accounted for 46.5% of infants accepted in the NICU in the study period (Figure 1.) and focused on the length of stay of infants with VLBW. The mothers who gave birth to babies with the highest VLBW were in the 20-29 age group (n=399; 51.6%). The rate of mothers who gave birth for the first time is 38.5% (n=298). While 19.1% of the babies were born with vaginal delivery (n=148), 81.8% (n=625) were born as a result of a singleton pregnancy. Regarding their birth weights, they were born in the range of 1250-1499 grams at most (n=283; 36.6%) and they were born ≥203 Day (≥29 Weeks) (n=463; 59.8%) regarding gestation age (GA). 49.5% (n= 383) of these babies were female and 50.5% (n=391) were male.

The median LOS was found to be 53 (14; 214) in females (mean: 58.86 ± 28.74), 54 (17; 357) in males (mean: 59.11 ± 28.53) and 53 days (14; 357) [(mean: 58.99 ± 28.62)] in total. There was no statistically significant difference between the LOS of females and males (p>0.05). When the statistical significance of the difference between the LOS of the birth weight groups was evaluated, no statistically significant difference was determined between the group of < 750 grams [median: 102.5 days (61; 357)] and the group of 750 – 999 grams "[median: 75.5 days (45; 214)]. The group of 1000 – 1249 grams [median: 55 days (14; 174)], and the group of 1250 – 1499 grams [median: 38 days (17; 94)] had a statistically significant LOS difference both among themselves and the other two groups (p<0.001). When the statistical significance of the difference between LOS of the GA groups was evaluated, there was no statistically significant difference between the group of <175 Days (25 Weeks) [median: 109 days (82; 357)] and the group of 175 – 188 Days (25-26 Weeks) [median: 82.5 days (39; 214)]. The group of 189 – 202 Days (27 – 28 Weeks) [median: 63.5 days (24; 155)] and the group of ≥203 Days (≥29 Weeks) [median: 44 days (14; 138)] had a statistically significant difference both among themselves and the other two groups (Table 1).

It was determined that there was no statistically significant effect on LOS whether the pregnancy was multiple or singleton (p>0.05). Babies born by Cesarean section (median: 53 (18; 357)) had a statistically significant shorter LOS than babies born by vaginal delivery (median: 59 days (14; 214) (p<0.001).

While 21.6% (n=167) of the infants included in the study had no morbidity, 41.5% (n=321) of the infants had at least one morbidity. Babies without morbidity had a statistically significant shorter LOS than babies with morbidity (p<0.001), and LOS increased as the number of morbidities increased. In addition, each of the morbidity groups (from no morbidity to 3≤ more morbidities) had a statistically significant LOS difference among the others (p<0.001). Those with an Apgar score of ≥7 [median: 51 days (17; 214)] had a shorter LOS with a statistically significant difference than those with <7 [median: 75 (14; 357)] (p<0.001) (Table 1).

A high and negative correlation was determined between LOS and BW (rho=-0.780; p<0.001). A moderate and negative correlation was determined between LOS and GA (rho=-0.692; p<0.001). A moderate and positive correlation was determined between LOS and Morbidity number (rho=0.616; p<0.001). (Table 1).

The most common morbidity was RDS (n=540; 69.8%), while the least common morbidity was BI (n=32; 4.1%). Regarding morbidities, the median longest LOS was respectively BPD 89 days (42; 357), NEC 80 days (36; 174); ROP 73 days (32; 214), sepsis 69 days (14; 357), BI 69 days (36;137), and those without morbidity compared to those with morbidity (p<0.001) , those who did not receive nutrition (p=0.004), IV and NIV treatment, compared to those who received (p<0.001), those who received phototherapy compared to those who did not have a lower LOS with a statistical significance (p=0.018) (Table 2).

While 142 (18.3%) infants did not receive respiratory treatment, 202 (26.1%) infants received both IV and NIV treatment. The Median LOS of infants who received both respiratory treatments was 74.5 days (14; 357) (mean: 77.30 ± 35.05), the median LOS of infants who did not receive any respiratory treatment was found to be 36 days (17; 102) (mean: 38.69±13.37). The difference in LOS between both groups was statistically significant (p<0.001).

Logarithmic transformation was applied to the dependent variable of LOS and the mean of Ln(LOS) was 3.98±0.43 (median= 3.97 (2.64; 5.88)). In the linear regression model built to assess the effects of clinically predicted variables to influence LOS, the model was significant (F= 211.316, p<0.001), its explanatory was 73.1%, and the constant coefficient of the model was 6.123 (p<0.001). While all other variables are constant, 1 gram increase in birth weight causes a decrease of -0.001 units in LOS, a one-day increase in gestational age causes a decrease of -0.006 units in LOS, administration of phototherapy causes a decrease of -0.062 units in LOS. The descriptors of the variables in the model are given in Table 3. RDS, BPD, ROP, NEC, NIV, IV, and multiple pregnancies have been shown to have an increasing effect on LOS. The formula for the regression model is shown below (1).

Displayed equation

(LOS=6.123-0.001 x BW-0.006 x GA(day)-0.062 x Fototerapi+0.266 x BPD+0.105 x NIV+0.060 x IMV +0.141 x NEK+0.076 x ROP+0.065 x Multiple Birth+0.062 x RDS) (1)

In our study, it was determined that there was a very high level of the positive and significant relationship between LOS and reimbursement amount (rho= 0.966; p<0.001). The reimbursement method applied by the Social Security Institution has a great impact on this relationship. The application of the Social Security Institution is a fee for service for the first and last day, and per day for the other days [18].

Table 1. Variables associated with length of stay

	n (%)	Median (min; max)	Z, χ2	p
Length of stay	774 (100)	53 (14; 357)		
Gender				
Female	383 (49.5)	53 (14; 214)	-0.702	0.483
Male	391 (50.5)	54 (17; 357)		
Birth weight (rho=-0.780; p<0.001) *		1150 (490; 1495)		
< 750 grams	30 (3.9)	102.5 (61; 357)[a]	435.932	<0.001
750 – 999 grams	186 (24.0	75.5 (45; 214)[a]		
1000 – 1249 grams	275 (35.5)	55 (14; 174)[b]		
1250 – 1499 grams	283 (36.6)	38 (17; 94)[c]		
Gestation age (rho=-0.692; p<0.001)*	774 (100)	205 (161; 261)		
<175 Days (<25 Weeks)	15 (1.9)	109 (82; 357)[a]	298.555	<0.001
175 – 188 Days (25-26 Weeks)	86 (11.1)	82.5 (39; 214)[a]		
189 – 202 Days (27 – 28 Weeks)	210 (27.1)	63.5 (24; 155)[b]		
≥203 Days (≥29 Weeks)	463 (59.9)	44 (14; 138)[c]		
Mode of delivery				
Cesarean section	626 (80.9)	53 (18; 357)	-3.436	0.001
Vaginal delivery	148 (19.1)	59 (14; 214)		
The number of morbidities (rho=0.616; p<0.001) *				
No morbidity	167 (21.6)	38 (17; 102)[a]	296.028	<0.001
1 morbidity	321 (41.5)	50 (14;138)[b]		
2 morbidities	175 (22.6)	64 (22;157)[c]		
3≤ morbidities	111(14.3)	87 (32;357)[d]		
Morbidity				
Absence	167 (21.6)	38 (17; 102)	-11.757	<0.001
Presence	607 (78.4)	59 (14; 357)		
1 Minute Apgar score (n=656; 84.8%)		6 (1; 10)*		
5 Minute Apgar score (n=656; 84.8%))		8 (3; 10)		
≥7	572 (87.2)	51 (17; 214)	-6.129	<0.001
<7	84 (12.8)	75 (14; 357)		
Maternal age	774 (100)	28 (15; 47)		
Gravida	774 (100)	2 (1; 11)		
Multiple births				
Absence	625(81.8)	53 (14; 357)	-1.636	0.102
Presence	149 (19.2)	54 (25; 165)		

(a, b, c, d: the length of stay is similar between groups containing the same letter (P>0.05 with Bonferroni correction))
* Correlation with hospitalization day

Table 2. Length of stay according to morbidities and treatments

Variables	Absence		Presence		Z	p
	n (%)	Median (min; max)	n (%)	Median (min; max)		
Morbidity						
Bronchopulmonary dysplasia	708 (91.5)	51 (14; 174)	66 (8.5)	89 (42; 357)	-9.987	<0.001
Necrotizing enterocolitis	757 (97.8)	53 (14; 357)	17 (2.2)	80 (36; 174)	-3.390	0.001
Retinopathy of prematurity	542 (70.0)	47 (14; 357)	232 (30.0)	73 (32; 214)	-13.816	<0.001
Sepsis	629 (81.3)	50 (17; 214)	145 (18.7)	69 (14; 357)	-8.168	<0.001
Brain injury	742(95.9)	53 (14;357)	32 (4.1)	69 (36;137)	-4.031	<0.001
Respiratory distress syndrome	234 (30.2)	42.5(14;138)	540 (69.8)	59 (18; 357)	-9.493	<0.001
Other treatment						
Phototherapy	228 (29.5)	56 (18; 357)	546 (70.5)	52 (14; 188)	-2.364	0.018
Total parenteral nutrition	61 (7.9)	45 (19; 155)	713 (92.1)	54 (14; 357)	-2.905	0.004
Invasive ventilation	572 (73.9)	49 (17; 214)	202 (26.1)	74.5(14;357)	-11.853	<0.001
Non-invasive ventilation	142 (18.3)	36 (17;102)	632 (81.7)	59 (14;357)	-11.608	<0.001
Both (invasive and non-invasive ventilation) respiratory treatments	142(18.3)	36(17;102)	202(26.1)	74.5(14;357)	14.689	<0.001

Table 3. Multiple linear regression analysis results

Length of stay	β^	SE(β^)	%95 CI for β^		Std. β^	t	p
			Lower bound	Upper bound			
Constant	6.123	0.134	5.860	6.386		45.692	<0.001
Birth weight (gram)	-0.001	0.000	-0.001	-0.001	-0.485	-20.492	<0.001
Gestation age (day)	-0.006	0.001	-0.007	-0.005	-0.237	-9.428	<0.001
Bronchopulmonary dysplasia	0.266	0.030	0.206	0.325	0.172	8.782	<0.001
Noninvasive ventilation	0.105	0.023	0.059	0.151	0.096	4.505	<0.001
Invasive ventilation	0.060	0.021	0.020	0.101	0.061	2.917	0.004
Phototherapy	-0.062	0.018	-0.097	-0.028	-0.066	-3.516	<0.001
Necrotizing enterocolitis	0.141	0.056	0.032	0.250	0.048	2.532	0.012
Retinopathy of prematurity	0.076	0.020	0.036	0.116	0.081	3.750	<0.001
Multiple births	0.065	0.020	0.025	0.106	0.060	3.193	0.001
Respiratory distress syndrome	0.062	0.019	0.024	0.100	0.067	3.225	0.001

Model: n= 774, p=10, R^2= 0.735, $\bar{R}^2$= 0.731, Durbin Watson d= 1.788, F= 211.316, p<0.001

Discussion

The median BW of all infants included in our study was determined as 1150 (490; 1495) grams. 3.9% (n=30) of these babies < 750 grams, 24% (n=186) between 750 – 999 grams, 35.5% (n=275) between 1000 – 1249 grams, 36.6% (n=283) between 1250 – 1499 grams are in the group. In another study, it has been reported that 20% of infants (n=87) were <750 grams, 26% (n=112) were between 750–999 grams, 24% were between 1000–1249 grams, and 30% (n=127) were between 1250-1499 grams [19]. Results of living infants with VLBW (n=211) in another study: It has been reported that 3 babies were between 490–749 grams, 29 babies between 750–999 grams, 72 babies between 1000–1249 grams, 107 babies between 1250–1499 grams [20].

When the genders of the infants born in our study were evaluated, 50.5% were considered male. In other studies, the male gender was reported as 53% [21] 52% [22], 51.9% [23].

656 infants in this study had 1-minute and 5-minute Apgar scores (84.8% of all infants included in the study). The median Apgar score was 6 (1; 10) at the 1-minute 8 (3; 10) and the 5-minute. Apgar score in other studies was reported 5.9±2.3 at 1-minute, 7.7±1.9 at 5-minute [24]; the mean score was 7 (1–8) at 1-minute,

8 (3–9) at 5-minute [25], and the median was 8 (7–9) at 5-minute [23].

In this study, 69.8% (n=540) of VLBW infants have RDS, 30.0% (n=232) have ROP, 18.7% (n=145) have sepsis, 8.5% (n=66) have BPD, 4.1% (n=32) have BI, 2.2% (n=17) have NEC. In other study: RDS was found to be 7.3% (n=14), IVH was 9.4% (n=18), NEC was 16.8% (n=32), sepsis was 27.3% (n=52), BPD was 4.2% (n=8) [25]. In another study: 10.9% (n=23) BPD, 14.2% (n=30) ROP, 11.4% (n=24) PVL were found [20].

In this study, the median LOS of infants with VLBW was 53 (14; 357), while in other studies it was reported to be 97.4±57.0 [21], 72.35±35.74 days [19]. When the effect of morbidities on LOS was evaluated, the medians of the LOSs from longest to shortest were determined as follows: 89 (42; 357) in BPD, 80 (36; 174) in NEC, 73 (32; 214) in ROP, 69 (14;357) in sepsis, 69 (36; 137) in BI, 59 (18;357) in RDS. In another study, LOS was found as follows according to morbidities: BI 97.3±45.7 days, NEC 87.4±32.3, BPD 94.4±31.4, Late-onset sepsis 83.4±38.8 days [19]. In the same study, it was found that the presence of morbidity and number of morbidities being more than one, and low BW and low GA increased LOS [19].

It has been reported that morbidities such as NEC, ROP, and PVL are more common in infants with late-onset sepsis, they need mechanical ventilation more, and their hospital LOS is longer [26]. It has been expressed that the possibility of IV and NIV treatment is increased in infants with ROP compared to infants without ROP, in addition to morbidities such as RDS, IVH, perinatal infection, etc. [27].

In our study, 92.1% (n=713) of infants received TPN treatment and the median LOS of these infants was 54 (14; 357) days. Because VLBW infants are immature, they need very high energy for growth and metabolic needs [28]. Infants with VLBW are usually low in weight at discharge because they do not get enough of the protein, energy, mineral, and vitamin sources they need [29,30]. It has been reported in the early period "aggressive" feeding of preterm infants by a peripheral or central route can reduce postnatal growth retardation in the short term and may give good results especially for brain and cognitive functions in the long term [28,31].

In this study, 26.1% (n=202) of the infants have applied IV and the median LOS of these infants was determined as 74.5 (14; 357) days. In other studies, this rate is 70% [24], 79% [32].

As a result of multiple pregnancies, prematurity and complications related to prematurity are seen with an increased frequency [33]. In a study, it was shown that mean birth weight is lower, prematurity is higher, and intrauterine growth retardation is more in twins [34]. In addition to these, BPD, IVH, NEC, and ROP are among the most important morbidities of prematurity [3,11].

In our study, it has been shown that there is an inverse relationship between birth weight, gestational age, number of morbidity babies, and LOS. Besides, the increase in LOS causes an increase in reimbursements.

A multiple linear regression model was established to determine the factors affecting the LOS and it was found to be significant. In the model, it was found that the increase in birth weight and gestational age and the administration of phototherapy had a decreasing effect on LOS and it has been determined that BPD, NIV, IMV, NEC, ROP, RDS, and multiple pregnancies have an increasing effect on LOS.

With the built regression model, the length of stay of infants with VLBW admitted to the NICU can be predicted. This prediction will provide very important conveniences for planning in NICUs where expensive services are provided. Increases in LOS also increase hospital costs. In other studies, an increase in birth weight and gestational age has a decreasing impact on costs, while a decrease in birth weight and gestation period has an increasing impact on costs [19,35].

There is a correlation between VLBW and the incomes of the countries [6]. Some, but not all, of the determining causes of VLBW can be prevented [10]. Although a significant number of resources are spent to keep babies with LBW alive, these babies are faced with very serious and various problems that will most likely affect their lives negatively in the future and have high economic and social costs. For these reasons, health policies should be developed to reduce VLBW births.

Acknowledgements
This article was produced from data collected during MA's master's thesis study.

Conflict of interests
The authors declare that they have no competing interests.

Financial Disclosure
All authors declare no financial support.

Ethical approval
Permission for the study was obtained from Ankara Yildirim Beyazit University Ethics Committee (Project Approval Certificate; Ethics Committee Decision meeting date and decision no: 31.07.2019-35) and Medical Specialty Training Board in the hospital where the study was to be conducted.

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