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Evaluation of Short-Term Outcomes of Preterm Infants in 2 Periods: Vermont Oxford Network Results of a Developing Country's Single-Center Level IIIC Neonatal Intensive Care Unit Experience

Aslan Yılmaz[1], Nesrin Kaya[1], Zeynep Alp Ünkar[1], Ersin Ulu[1], Sümeyye Nur Aydın[2], Yıldız Perk[1], Mehmet Vural[1]

[1]Department of Neonatology, İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, İstanbul, Turkey
[2]Department of Public Health, İstanbul University-Cerrahpaşa, Cerrahpaşa Faculty of Medicine, İstanbul, Turkey

What is already known on this topic?

- *The quality of health care provided to newborns and technological advances in neonatal intensive care units over time have contributed to significant improvements in the short- and long-term outcomes of premature newborns.*
- *It is very important to audit and compare local data on clinical outcomes with international standards.*

What this study adds to this topic?

- *In this study, the data of our unit registered in the Vermont Oxford Network system were divided into 2 periods and compared with recent national and international data.*
- *This study encourages the identification of areas that need improvement and the development of quality-enhancing projects in neonatal units.*

ABSTRACT

Objective: This study aimed to compare the short-term outcomes of infants from our level IIIC neonatal intensive care unit in 2 different periods.

Materials and Methods: In this cohort study, data from preterm infants (≤29 weeks and birth weight <1500 g) registered in the Vermont Oxford Network system were divided into 2 periods, the first period between January 1, 2005, and December 31, 2009, and the second between January 1, 2010, and December 31, 2019.

Results: There was no difference in the distribution of preterm infants according to their gestational age subgroups ($P = .169$). Although the survival rate increased significantly in the second period (48.1% vs. 64.3% ($P < .001$), there was no difference in terms of survival without morbidity ($P = .480$). The frequency of antenatal care ($P < .001$), antenatal maternal steroid use ($P < .001$), cesarean section ($P = .025$), and small for gestational age ($P < .003$) increased in the second period. Surfactant treatment in the delivery room ($P < .003$), neonatal intensive care unit ($P < .001$), and nasal continuous positive airway pressure use before intubation as a part of initial resuscitation ($P < .001$), nosocomial infections ($P = .001$), patent ductus arteriosus requiring medical treatment ($P = .011$), and necrotizing enterocolitis ($P = .014$) were significantly more common, but early neonatal sepsis ($P = .002$) and discharge home with only formula ($P = .010$) were less in the second period.

Conclusion: Differences were noted in the prognosis and treatment choices of preterm infants in the same unit between 2 periods. The analysis of neonatal intensive care unit data, through rigorous methods, may provide opportunities for the development of quality improvement projects to improve the quality of health care in developing countries.

Keywords: Mortality and morbidity, preterm infants, quality of healthcare, short-term outcomes

INTRODUCTION

After the establishment of neonatal intensive care units (NICUs) in the early 1970s, the survival rate of very low-birth-weight (VLBW) infants increased from approximately 50% to 80%. Especially in the last 30 years, the increase in the survival rate of VLBW infants has become evident due to developments in perinatal and neonatal intensive care, including antenatal steroids, surfactants, and new mechanical ventilation methods.[1,2] However, the morbidity rate is still high among VLBW infants, especially in developing countries, and many of them develop complications such as sepsis, necrotizing enterocolitis (NEC), bronchopulmonary dysplasia (BPD), intraventricular hemorrhage (IVH), and retinopathy of prematurity (ROP) during their hospital stay.[2,3] These morbidities result in adverse neurodevelopmental

Corresponding author:
Aslan Yılmaz
✉ draslanyilmaz@hotmail.com

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outcomes, long-term hospitalizations, increased risk of hospital readmission, and psychological problems for the family, leading to increased health expenditures.[4]

The morbidity rate of VLBW infants is an essential indicator of intensive care standards and NICU care quality. There have been significant improvements in outcomes for preterm infants over the past few decades.[5] It is crucial to audit and compare local data on clinical outcomes with international standards. One of the largest neonatal databases, the Vermont Oxford Network (VON), has been collecting data on VLBW infants in eligible neonatal units around the world since 1989.[6] It has been reported that different treatment practices among neonatal units cause different mortality and morbidity outcomes. Comparisons between hospitals, regions, and countries provide opportunities to improve healthcare practices.[7] The differences between essential characteristics of mothers and infants, hospital infrastructure, immediate admission to the intensive care unit or referral to another hospital in extremely preterm infants, social factors, race, and differences in clinical care practices may affect survival and morbidity.[8-11] New evidence is constantly emerging in medicine and is translated into practice among healthcare providers, affecting mortality and morbidity outcomes.[12,13]

This study aimed to evaluate the changes in antenatal care rates and short-term survival and morbidity of our unit patients, from a developing country, in 2 periods, by using the data recorded in the VON system.

MATERIALS AND METHODS

Participants and Data

Vermont Oxford Network members register their standardized data in the VON system for infants with a birth weight between 401 and 1500 g or gestational age between 22 weeks and 29 weeks, born at a member hospital, or admitted within 28 days of birth without being discharged home. In this study, the data of preterm infants who had been followed in our unit of İstanbul University Cerrahpaşa-Cerrahpaşa Faculty of Medicine (IUC-CFM) and registered in the VON system with its standardized criteria were used. Our unit is a level IIIC NICU since 2005, which deals with extremely preterm birth and other complex medical or surgical neonatal conditions, also has subspecialties of neonatology, pediatric cardiology, pediatric surgery, pediatric cardiovascular surgery, and ophthalmology.

Data were collected using uniform definitions set in the VON system throughout the working period, and all data were automatically audited for quality and completeness at submission. The data of 288 preterm infants born between January 1, 2005, and December 31, 2009 (first period) and 291 preterm infants born between January 1, 2010, and December 31, 2019 (a second period which coincides with the renovation of the unit), were compared. These 2 periods were chosen for comparison of the unit before and after the renovation. In the second period after the renovation, the number of beds decreased, and the level of our unit and the characteristics of the patients did not change, but the number of nurses per patient increased. Results from 2 periods were evaluated by dividing them into 3 subgroups according to their gestational age (<24 weeks, 24-26 weeks, and 27-29 weeks), and the data for 2 periods were compared. Cases that were referred to the IUC-CFM neonatal unit from external centers and cases that were transferred to another center for any reason were also included in the study.

Ethics approval was obtained from the Ethics Committee of İstanbul University Cerrahpaşa-Cerrahpaşa Faculty of Medicine (IUC-CFM) (approval number: 147975) and this study is conducted in accordance with the Declaration of Helsinki.

Definitions

Definitions for mother and baby characteristics were given in the "Nightingale Data Definitions" guide prepared by VON.[13] Small for gestational age (SGA) was defined as the birth weight percentile <10 for the particular sex and gestational age, using growth charts published by Fenton.[14] Maternal obstetric data included antenatal steroid treatment, multiple pregnancies, gender, Apgar score, and mode of delivery. Antenatal steroid treatment was considered complete if the mother was given intravenous or intramuscular steroids at any time before delivery during pregnancy.

Respiratory distress syndrome (RDS) was defined according to clinical and radiological features within the first 24 hours of life. The length of stay in the hospital was the number of days from the date of admission of the baby until the date of first discharge, transfer to another health institution, or death.[15] Severe intraventricular hemorrhage (IVH) was defined as grade 3 or 4 IVH; severe ROP as stages 3,4, or 5; BPD as additional oxygen use at postmenstrual 36th gestational week; pneumothorax as extra pleural air diagnosed by chest radiograph or needle aspiration; NEC as stage $\geq$2 of Bell's criteria, and nosocomial infection as bacterial or fungal infections that developed after the third day of life with a positive blood culture.[16-20] Patent ductus arteriosus (PDA) was defined with at least one of the findings (left to right or bilateral ductal shunt, systolic or continuous murmur on Doppler echo) and at least 2 of the symptoms (hyperdynamic precordium, throbbing pulses, high pulse pressure, pulmonary vascular occlusion-cardiomegaly, or both). Antenatal steroid use for BPD was defined as steroid therapy used to prevent or treat BPD.[4]

Survival was defined as newborns surviving until discharged alive. Morbidity-free survival was defined as survival without any of the morbidities of severe IVH, periventricular leukomalacia (PVL), BPD, NEC, pneumothorax, or any nosocomial infection.

Statistical Analysis

Statistical analysis was performed using Statistical Package for Social Sciences (SPSS) version 21 software (IBM Corp., Armonk, NY, USA). The conformity of the variables to the normal distribution was evaluated with Kolmogorov–Smirnov and Shapiro–Wilk tests, Q-Q plots, and histogram graphs. As a result of the analysis, normally distributed variables were shown as mean $\pm$ standard deviation, and non-normally distributed variables were shown as median (minimum-maximum). Categorical data were presented with frequency (percentage). Comparisons of 2 groups in continuous data were made with the Mann–Whitney *U* test when the data were not normally distributed. The categorical data were compared with the Pearson chi-square test when the number of observations was sufficient and with Fisher's precision test when the number of observations was insufficient. The correlation between continuous data was evaluated with the Pearson correlation test for those with normal distribution and the Spearman correlation test for non-normally distributed. The relationship between categorical data was examined with the Phi correlation test. $P < .05$ was considered significant.

RESULTS

Patient Groups and Perinatal Demographic Information

There was no significant difference between the 2 periods (2005-2009 and 2010-2019) in terms of the distribution of preterm infants according to their group of gestational age (<24 weeks, 24-26 weeks, 27-29 weeks) ($P = .169$) (Table 1).

In the second period of the IUC-CFM NICU, a significant increase in the frequencies of antenatal care (87.2% vs. 98.1%; $P < .001$), antenatal steroid use (45.1% vs. 75.8%; $P < .001$), cesarean section (70.2% vs. 78.4%, $P = .025$), and SGA births (12.5% vs. 21.8%; $P = .003$) was observed. No difference was noted between the first and second periods in gender, the number of multiple gestations, and cases with 5-minute Apgar scores below 4 (Table 2).

Pulmonary Morbidity

An increase in surfactant treatment at delivery room resuscitation (1.0% vs. 5.5%; $P = .003$) and in the unit (58.3% vs. 77.7%; $P < .001$) was noted in the second period. The rate of nasal continuous positive airway pressure (CPAP) use after resuscitation in the delivery room was found to be higher in the second period (19.9% vs. 56.3%; $P < .001$). There was no difference between the 2 periods concerning the use of oxygen in the delivery room, RDS, pneumothorax, BPD, and being discharged home with oxygen (Table 3).

Other Morbidities

Nosocomial infection (15.8% vs. 30.9%; $P = .001$) and PDA requiring medical treatment (12.7% vs. 21.2%; $P = .011$) and NEC (1.6% vs. 5.7%; $P = .014$) were more common, whereas early bacterial neonatal sepsis (15.4% vs. 6.8%; $P = .002$) was detected less frequently in the second period. There were no differences between the 2 periods regarding fungal infection, severe IVH, and severe ROP (Table 4).

Table 1. Proportions of Infants Born at Different Gestational Ages at IUC-CFM in the First Period (2005-2019) and the Second Period (2010-2019)

Gestational Age (Weeks)	Number (%) of Infants	
	First Period (2005-2009) (n = 288)	Second Period (2010-2019) (n = 291)
<24	12 (4.2)	20 (6.8)
24-26	76 (26.6)	89 (30.5)
27-29	200 (69.4)	182 (62.5)

$P = .169$.
Statistically significant parameters are indicated in bold ($P < .05$).
IUC-CFM, İstanbul University Cerrahpaşa-Cerrahpaşa Faculty of Medicine.

Survival, Morbidity-Free Survival Rates

An increase in survival was noted in the second period of the IUC-CFM NICU compared to the first period (48.1% vs. 64.3%; $P < .001$). There was no difference in terms of morbidity-free survival between the 2 periods.

Discharge Status and Hospitalization Length

When the discharge nutrition patterns of the 2 periods were compared, a decrease in the discharge with exclusive formula feeding was noted in the second period (11.7% vs. 3.6%; $P = .010$). The median hospital stay lengths for the 2 periods were 49 and 62 days, and the mean ± standard deviation of discharge weights was 1879 ± 544 and 2034 ± 481 g.

DISCUSSION

In this cohort study, we aimed to present the short-term results of our unit, especially survival and survival without morbidity, in 2 periods, before and after our neonatal care renewal. Our study has some limitations as there are many factors affecting mortality and morbidity in NICUs. The main finding of our study is the increase in survival in the second period. We assume that the increased survival in the second period and as a result, decreased number of patients per nurse is one of the main factors that may lead to the main result of our study. Consistent with the results of our study, in a comprehensive review, the effect of the patient-per-nurse ratio on mortality was emphasized, and in a recent prospective study, nurse workload was found to be associated with missed nursing care.[21,22] In addition, changes in practice over time in our neonatal unit and their possible effects are discussed under separate headings below.

Perinatal Features

In our study, the frequency of antenatal care and antenatal steroid use increased over time (Table 2). The prospective study by Tyson et al[23] in preterm gestation between 22 and 25 weeks reported that antenatal steroid use, female gender, singleton birth, and higher birth weight were associated with increased survival and decreased morbidity. It was shown that even a short internal between antenatal corticosteroid administration and birth was effective in increasing the survival.[24] Similar to previous studies, our results support the relationship between antenatal steroid use and rates of survival.

In this study, we observed an increase in the frequency of SGA in the second period (Table 2). In a recently published national study from Turkey, the incidence of SGA under 31 weeks of gestation was reported to be similar to our second-period results.[25] Small for gestational age infants are at high risk for other complications such as prematurity, neonatal asphyxia, hypothermia, hypoglycemia, hypocalcemia, polycythemia, sepsis, and death.[26] Another comprehensive study published in 2021 showed that birth weight, SGA, female sex, multiple gestations, and less invasive resuscitation are independent risk factors for neonatal outcomes.[27] We hypothesized that despite the increase in SGA in the second period, the decrease in the mortality rate and the constant morbidity was due to the improved care conditions in our unit over time.

It has been reported that delivery by cesarean section below 26 weeks of gestation is associated with a decrease in mortality.[28] However, Kim et al[29] found in a recent national cohort

Table 2. Demographic Features and Perinatal Information of the Infants Born at IUC-CFM in the First Period (2005-2009) and the Second Period (2010-2019)

		Gestational Age, Week				
	Period	**<24**	**24-26**	**27-29**	**Total**	***P***
Male	1st	6/12 (50)	41/76 (53.9)	109/200 (54.5)	156/288 (54.2)	.502
	2nd	13/20 (65)	41/89 (46.1)	95/181 (52.5)	149/290 (51.4)	
Multiple gestations	1st	5/12 (41.7)	27/76 (35.5)	67/200 (33.5)	99/288 (34.4)	.06
	2nd	8/20 (40)	21/89 (23.6)	50/182 (27.5)	79/291 (27.1)	
Antenatal care	1st	10/11(90.9)	47/65 (72.3)	154/166 (92.8)	211/242 (87.2)	**<.001**
	2nd	19/19 (100)	83/83 (100)	162/167 (97.0)	264/269 (98.1)	
Antenatal steroid	1st	0/11 (0)	24/65 (36.9)	81/157 (51.6)	105/233 (45.1)	**<.001**
	2nd	5/18 (27.8)	61/80 (76.3)	125/154 (81.2)	191/252 (75.8)	
Cesarean section	1st	4/12 (33.3)	39/76 (51.3)	157/197 (79.7)	200/285 (70.2)	**.025**
	2nd	5/20 (25.0)	61/89 (68.5)	162/182 (89.0)	228/291 (78.4)	
Apgar 5-min <4	1st	6/12 (50.0)	7/68 (10.3)	19/180 (10.6)	32/260 (12.3)	.331
	2nd	12/20 (60)	22/89 (24.7)	10/181 (5.5)	44/290 (15.2)	
SGA	1st	1/11 (9.1)	9/76 (11.8)	26/200 (13.0)	36/287 (12.5)	**.003**
	2nd	3/19 (15.8)	21/89 (23.6)	39/181 (21.5)	63/289 (21.8)	

Data are given as number/total (percentage). Statistically significant parameters are indicated in bold ($P < .05$).
IUC-CFM, İstanbul University Cerrahpaşa-Cerrahpaşa Faculty of Medicine; SGA, small for gestational age.

study that cesarean section did not improve survival or morbidity in low-birthweight infants. In our study, the cesarean section rate increased, as well as improved survival rate, in the second period (Tables 2 and 5). Advances in neonatal intensive care have increased preterm infants' survival rates. Survival rates of VLBW infants in developed countries are reported to be around 85%-90%.[30,31] However, studies from developing countries have shown a lower survival rate of around 66%-74%.[32-34] In a recent national study from Turkey on VLBW infants, the total survival and survival without major morbidity (defined as severe IVH, NEC, BPD, and severe ROP) were reported to be 78% and 48%, respectively.[25] In the second period of our study, the survival rate was similar to that reported from developing countries and lower than the national study, although the mean gestational age of the cases was higher (≤32 weeks) than in our study. Our survival rate in the first period was lower than in the second period (Table 5). We speculate that this amelioration could be related to the improvement of health care in our unit over time (such as the use of antenatal steroids, surfactant treatment, nasal CPAP, and an increase in the number of nurses per patient involved in patient care). These evidence-based interventions are consistent with those suggested in large meta-analyses to reduce mortality among low birthweight neonates in low-and middle-income countries.[35]

Our study detected that second-period hospital stay durations (49 vs. 62 days) in the whole population (including the

Table 3. Pulmonary Morbidities According to Gestational Age at IUC-CFM in the First Period (2005-2009) and the Second Period (2010-2019).

		Gestational Age, Week				
Outcome	**Period**	**<24**	**24-26**	**27-29**	**Total**	***P***
Initial resuscitation oxygen	1st	12/12 (100)	73/74 (98.6)	178/196 (90.8)	263/282 (93.3)	.128
	2nd	15/29 (75.0)	83/89 (93.3)	154/172 (89.5)	252/281 (89.7)	
Initial resuscitation surfactant	1st	1/12 (8.3)	0/75 (0)	2/199 (1.0)	3/286 (1.0)	**.003**
	2nd	5/20 (25.0)	5/89 (5.6)	6/182 (3.3)	16/291 (5.5)	
Surfactant use any time	1st	8/12 (66.7)	38/68 (55.9)	108/184 (58.7)	154/264 (58.3)	**<.001**
	2nd	15/20 (75.0)	72/85 (84.7)	122/164 (74.4)	209/269 (77.7)	
Nasal CPAP use before intubation in the delivery room	1st	0/9	9/67 (13.4)	42/180 (23.3)	51/256 (19.9)	**<.001**
	2nd	0/18	41/82 (50.0)	107/163 (65.6)	148/263 (56.3)	
RDS	1st	8/9 (88.9)	55/68 (80.9)	137/181 (75.7)	200/258 (77.3)	.070
	2nd	16/18 (88.9)	73/82 (89.0)	133/165 (80.6)	222/265 (83.8)	
Pneumothorax	1st	1/9 (11.1)	7/66 (10.6)	8/177 (4.5)	16/252 (6.3)	.883
	2nd	1/18 (5.6)	6/82 (7.3)	9/165 (5.5)	16/265 (6.0)	
BPD	1st	0	6/17 (35.3)	14/92 (15.2)	20/109 (18.3)	.201
	2nd	0	15/40 (37.5)	28/133 (21.1)	43/173 (24.9)	
Oxygen at discharge home	1st	0	0/14 (0)	1/89 (1.1)	1/103 (1.0)	.276
	2nd	0	3/39 (7.7)	2/129 (1.6)	5/168 (3.0)	

Data are given as number/total (percentage). Statistically significant parameters are indicated in bold ($P < .05$).
BPD, bronchopulmonary dysplasia; CPAP, continuous positive airway pressure; IUC-CFM; İstanbul University Cerrahpaşa-Cerrahpaşa Faculty of Medicine; RDS, respiratory distress syndrome.

Table 4. Other Neonatal Morbidities According to Gestational Age at IUC-CFM in the First Period (2005-2009) and the Second Period (2010-2019).

Outcome	Period	Gestational Age, Week <24	24-26	27-29	Total	*P*
Early bacterial sepsis	1st	2/9 (22.2)	8/67 (11.9)	29/178 (16.3)	39/254 (15.4)	**.002**
	2nd	2/18 (11.1)	9/82 (11.0)	7/163 (4.3)	18/263 (6.8)	
Nosocomial Infection	1st	0	4/29 (13.8)	21/129 (16.3)	25/158 (15.8)	**.001**
	2nd	0	19/60 (31.7)	48/154 (31.2)	67/217 (30.9)	
Fungal infection after day 3	1st	0	2/29 (6.9)	4/129 (3.1)	6/158 (3.8)	.397
	2nd	0	3/60 (5.0)	2/154 (1.3)	5/217 (2.3)	
NEC ≥2	1st	0	1/66 (1.5)	3/177 (1.7)	4/252 (1.6)	**.014**
	2nd	0	5/82 (6.1)	10/165 (6.1)	15/265 (5.7)	
PDA	1st	0	6/65 (9.2)	26/177 (14.7)	32/251 (12.7)	**.011**
	2nd	0	24/81 (29.6)	32/165 (19.4)	56/264 (21.2)	
Severe IVH	1st	0	7/31 (22.6)	18/107 (16.8)	25/140 (17.9)	.978
	2nd	0	16/52 (30.8)	9/87 (10.3)	25/141 (17.7)	
Severe ROP	1st	0	5/15 (33.3)	7/70 (10.0)	12/85 (14.1)	.239
	2nd	0	8/36 (22.2)	6/117 (5.1)	14/153 (9.2)	

Data are given as number/total (percentage). Statistically significant parameters are indicated in bold ($P < .05$).
IUC-CFM; İstanbul University Cerrahpaşa-Cerrahpaşa Faculty of Medicine; IVH, intraventricular hemorrhage; NEC, necrotizing enterocolitis; PDA, patent ductus arteriosus; PVL, periventricular leukomalacia; ROP, retinopathy of prematurity.

non-surviving neonates) and discharge weights (1879 ± 544 vs. 2034 ± 481 g) for surviving patients were increased. It has been reported that intrauterine growth retardation, C-reactive protein and blood culture positivity, feeding intolerance, and retardation in weight gain cause delayed discharge day.[36] A change in the discharge approach (increase in the number of NICU beds in the country and less need to empty beds for the new patients) for preterm infants over time or more additional problems may be a reason.

Pulmonary Morbidities

In our study, the increases in the frequency of antenatal care, antenatal steroid use, nasal CPAP use in the delivery room, and surfactant treatment in the second period align with the current approach as suggested in the current RDS guidelines.[37] In a recent study from China, surfactant treatment under 31 weeks of gestation was reported to be 65%.[24] We observed a non-significant increase in RDS frequency (Table 3) in the second period and the rates were close to those reported in

Table 5. Overall Survival, Morbidity-Free Survival Rates, and Feeding Status at Discharge According to IUC-CFM in the First Period (2005-2009) and the Second Period (2010-2019).

Outcome	Period	Gestational Age, Week <24	24-26	27-29	Total	*P*
Survival	1st	0	15/69 (27.5)	105/177 (59.3)	124/258 (48.1)	**<.001**
	2nd	0	41/89 (46.1)	146/182 (80.2)	187/291 (64.3)	
Survival without morbidities	1st	0	9/61 (14.8)	71/145 (49.0)	80/218 (36.7)	.480
	2nd	0	16/89 (18.0)	82/182 (45.1)	98/291 (33.7)	
Discharge (home) human milk only	1st	0	1/14 (7.1)	33/89 (37.1)	34/103 (33.0)	.218
	2nd	0	12/39 (30.8)	56/129 (43.4)	68/168 (40.5)	
Discharge (home) formula only	1st	0	3/14 (21.4)	9/89 (10.1)	12/103 (11.7)	**.010**
	2nd	0	2/39 (5.1)	4/129 (3.1)	6/168 (3.6)	
Discharge (home) human milk and fortifier/ formula	1st	0	10/14 (71.4)	46/89 (51.7)	56/103 (54.4)	.799
	2nd	0	25/39 (64.1)	69/129 (53.5)	94/168 (56.0)	

Data are given as number/total (percentage). Statistically significant parameters are indicated in bold ($P < .05$).
IUC-CFM; İstanbul University Cerrahpaşa-Cerrahpaşa Faculty of Medicine.

the national study (77%).[25] In our study, surfactant treatment increased in the second period (Table 3) and was in harmony with the national study results. The national neonatal resuscitation program, RDS guidelines, and regularized treatment strategies are probably contributing to the increase in surfactant use.

Prenatal and postnatal infections, ventilation strategies causing lung damage, oxidative stress, malnutrition, and genetic factors have been reported as BPD-related risk factors.[38-40] In the study by Koc et al[25], the frequency of BPD under 31 weeks of gestation was 27.3%. In our study, although statistically not significant, the frequency of BPD increased in the second period (Table 3) but was still lower in a more premature population (≤29 weeks) compared to the national study. In addition, although we noted an increase in survival, there was no difference between the 2 periods in terms of BPD and being discharged with oxygen. We suppose that the stability in BPD frequency in the presence of increased survival may be related to the improvements in the quality of health care provided to this group of patients with the more widespread use of gentle ventilation practices, permissive hypercapnia, and volume-controlled ventilation in our unit. We noted an increase in nasal CPAP use before intubation in the second period (Table 3), which supported the tendency of our non-invasive ventilation strategies.

Other Neonatal Morbidities

Low 5-minute Apgar score, need for resuscitation, chorioamnionitis, premature rupture of membranes, group B streptococcal colonization, and preterm delivery are considered to be the risk factors of early neonatal sepsis.[41] We supposed that the decrease in early neonatal sepsis (Table 4) in the second period could be related to increased prenatal care (Table 2) and infrastructure development in the NICU. Insufficient breastfeeding, total parenteral nutrition, catheterization, prolonged intensive care stays, and surgical procedures are reported to be the risk factors for nosocomial infection in neonatal units.[42] In the national study by Koc et al.[25] the frequency of culture-positive late neonatal sepsis was found to be 22.7% under 31 weeks of gestation. Our study observed that the frequency of nosocomial infections increased in the second period (Table 4). We thought that the increase in nosocomial infections might be related to a more extended stay in the neonatal unit in the second period (49 vs. 62 days) together with increased survival. In addition, it was taken into account that the need for a central catheter would increase with the increase in survival. The invasive fungal disease is a challenging problem in NICUs, affecting 10% of VLBW preterm neonates, and is associated with high morbidity, mortality, and late neurodevelopmental impairment.[43,44] In our study, the frequency of fungal infections in both periods (Table 4) was found to be lower than those that had been reported.[43] We suppose that the low fungal infection rates were related to our unit's rational antibiotic treatment strategies.

In a recent multicenter study, the frequency of PDA requiring medical treatment under 29 weeks of gestation was reported to be 43%;[42] Koc et al[25] reported a 28% frequency for premature gestation under 31 weeks. In a recent national prospective study evaluating preterms between 246/6 and 286/7 weeks of gestation, the frequency of moderate-to-large PDA was found to be 46% (544/1193) and medical treatment was applied to 76% of these babies.[45] In our study, although the rate of PDA requiring medical treatment increased in the second period from 12.7% to 21.2%, it was still lower than the national and international results reported. We supposed that the increased availability of bedside echocardiography examination in our unit after 2010 was associated with the increase in the detection of PDA requiring treatment.

The most important risk factors associated with the development of NEC are formula feeding, PDA, umbilical catheterization, chorioamnionitis, birth asphyxia, intrauterine growth retardation, primary infection, anemia, transfusion, circulatory disorders, treatment with H2 receptor blockers, and hyperosmolar agents.[46] In a recent study by Gupta et al[47] examining short-term results of VLBW infants, the frequency of NEC was reported to be 15.2%. Koc et al[25] found a frequency of 10.7% for stage 2 and above NEC under 31 weeks of gestation age in a national recent study. In our study, stage 2 and higher NEC frequency increased significantly in the second period (Table 4). Although our mortality rate was close to the national study results, the frequency of NEC was much lower. We think the lower incidence of NEC in our unit might be related to the importance provided to breastmilk feeding and the rational use of antibiotics. We also showed that the frequency of discharge by exclusive formula feeding decreased (Table 5) in the second period, which is compatible with our breastfeeding policy. An increase in NEC frequency in the second period may be related to increased survival rates, higher SGA incidence, and increased nosocomial infection rates.

Prenatal steroid administration, intrauterine transport of the fetus to NICU, delivery by elective cesarean section, maintaining normothermia, avoiding fluctuations in cerebral blood flow, and optimal ventilation methods are reported to reduce the risk of IVH.[48] In 2 recently published multicenter studies, the frequency of severe IVH under 29 weeks of gestation was reported to be 10.2% and 13.1%.[49,50] In a multicenter, comprehensive study from Turkey evaluating the data of VLBW infants, severe IVH under 31 weeks was reported to be 6.3%.[25] In our study, there was no difference between the 2 periods (Table 4), and severe IVH was detected above the international rates reported. We think that we should develop new strategies to reduce the rates of IVH.

In a multicenter US study conducted on newborn units between 2008 and 2012 in infants under 29 weeks of gestation, the frequency of ROP was reported to be 56% and the frequency of severe ROP was 12%.[51] In a recent US study (2010-2015), the incidence of ROP and treated ROP in premature infants, less than 28 weeks at birth, was reported to be 67% and 29.7%, respectively.[52] In 2 different multicenter studies conducted in Turkey, the frequency of severe ROP under 31 weeks of gestation was found to be 12.8% and another one under 29 weeks of gestation was found to be 15.1%.[25,53] Lower body weight, SGA, increased total days under oxygen treatment, late-onset sepsis, high frequency of erythrocyte transfusions, and insufficient weight gain were determined as independent risk factors for severe ROP in infants with birth weight ≤ 1500 g in a prospective, multicenter study conducted in Turkey.[54] In our unit, during both periods, severe ROP was detected much less frequently than in recent national and international studies. We also found that the frequency of severe ROP regressed (Table 4) in the second period. We supposed that using oxygen titration meticulously to target saturation and increasing the frequency of antenatal steroids, surfactant treatment, and non-invasive ventilation effectively reduced our ROP frequency.

Survival and Survival Without Morbidities

This study evaluated the single-center short-term results of a level IIIC neonatal unit in a developing country with a per capita income of 9000 dollars.[55] The last 15-year data of the IUC-CFM neonatology unit was evaluated in 2 periods, the first period (2005-2009) and the second period (2010-2019) after the renovation of the unit. The improvement in survival without an increase in short-term morbidity in the second period was considered the most important outcome of our study. In recent similar studies, an increase in survival incidence has been reported, but the incidence of short-term morbidities associated with prematurity has remained constant.[3,31,56] Studies have shown that survival is very low below 25 weeks of gestation, and short-term morbidity is high in survivors.[57,58] A recent study evaluated the factors that increase the chance of neonatal survival. Gestational age, birth weight, SGA birth, female gender, multiple pregnancies, and less-invasive resuscitation were found to be independent risk factors.[25] In our study, survival rates below 24 weeks of gestation were 0% in both periods. Because of the above discussions, we believe that improvements during the second period in antenatal care, increase in antenatal steroid treatment, surfactant administration, cesarean delivery, SGA birth, nasal CPAP application in the delivery room before intubation, as well as the decrease in the frequency of early bacterial sepsis, were associated with increased survival in the second period. In addition, changes in treatment approaches between 2 periods, infrastructure improvements, and the increase in the number of nurses per patient involved in patient care were possible reasons that might affect survival in our study.

The main limitation is the cohort type of study, which can never rule out all confusing situations.[59] In this study, the most effective factors such as antenatal steroids, surfactant treatment, nasal CPAP, and the increase in the number of nurses per patient involved in patient care could not be distinguished among the factors that increase survival. It seems to be the only study in the literature to compare homogeneously stored long-term data of very low-birth-weight newborns in a NICU during 2 periods. The results of this study will guide us in developing our policies to provide better health care for our premature newborns.

CONCLUSIONS

Our single-center study observed that survival increased over time, and the short-term morbidity did not change. In addition, antenatal care, antenatal steroid use, delivery room surfactant, and nasal CPAP use were more common than in previous years, and the number of patients per nurse decreased. Taking part in a multicenter network helps the medical staff of NICUs to observe the evaluation of their units in real time and compare their results with the rest of the world. This is a very crucial benefit for this very vulnerable population of newborns.

Ethics Committee Approval: The study was approved by the Ethics committee of İstanbul University Cerrahpaşa-Cerrahpaşa Faculty of Medicine (approval number: 147975).

Informed Consent: Informed consent was obtained from the patients included in this study.

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