

SHORT-TERM OUTCOMES OF VERY LOW BIRTH WEIGHT INFANTS IN RIGA MATERNITY HOSPITAL

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Abstract. *As the preterm birth rate is increasing in most countries, the number of very low birth weight infants (VLBW - birth weight less than 1500 grams) is also growing. VLBW infants are at a high risk of morbidity and mortality, but the adverse outcomes have been decreasing over the last few years due to improvements in the quality of care. The main objective of this research is to determine the risk factors of early neonatal morbidity, rate of survival, frequency of disease and complications in VLBW infants as well as to compare the differences between the years. The data was collected from the Riga Maternity hospital's medical records over a five-year period from 2015 to 2019. A total of 209 VLBW were admitted to the Riga Maternity hospital's intensive care unit, of whom 192 (92.3%) survived to discharge. Over the five years the number of VLBW infants increased almost by half, while the mortality rate fluctuated between the years. Respiratory distress syndrome and sepsis were the two main complications for the infants. More than half (62.5%) of non-survivors died within the first 24 hours after birth with respiratory*

failure being the leading cause. Survival rate was strongly associated with gestational age and birth weight.

Keywords: *morbidity; short-term outcome; very low birth weight.*

Introduction

The main objective of this research is to determine the risk factors of early neonatal morbidity, rate of survival, frequency of disease and complications in VLBW infants as well as to compare the differences between the years.

Premature birth (gestational age <37 weeks) rate has been on the rise over the last few decades (Centers for Disease Control and Prevention, 2022). It is estimated that about 1% of newborns are very low birth weight (VLBW) – weighing less than 1500 g (National Center for Health Statistics, 2012). Babies that weigh less than 1000 g are considered extremely low birth weight (ELBW). The rise in prematurity rates is multifactorial. Some of the factors can be associated with the modern-day tendency of pregnancy later in life, chronic health conditions, such as hypertension or diabetes, insufficient nutrition and obesity, as well as the lack of access to adequate healthcare. Most of the time, the main reason why an infant is born so prematurely is unknown, but there are known risk factors that can affect this, of which the most common are: maternal infection during the pregnancy, substance abuse, young or advanced maternal age, previous preterm birth, multiple pregnancy, as well as being of African-American race and lower socioeconomic status (Pusdekar et al., 2020; Goldenberg, Culhane, Iams, & Romero, 2008; Zhang, Sun, & Zhang, 2021).

Although the number of premature infants has increased, the mortality rate is slowly, but steadily decreasing (WHO, 2022; National Institutes of Health, 2022). Many factors play a role in this; most importantly the quality of care has improved over the years. This includes postnatal surfactant (Coshal et al., 2021) as well as prenatal maternal corticosteroids (Stock, Thomson, & Papworth, 2022) for the premature infant's lung development and magnesium sulfate, which is providing neuroprotective effects to the infant's brain (Chollat & Marret, 2018). Nevertheless, newer medical technologies and equipment, as well as medical staff's appropriate education has had an impact on the survival of premature babies. The involvement of parents in the care of the newborn, especially skin-to-skin "kangaroo care" can also be mentioned as an important factor (Jefferies & Canadian Paediatric Society, Fetus and Newborn Committee, 2012). The choice of delivery also plays a part in the survival of premature infants.

Despite the improvement in the quality of care, VLBW infants are still considered high risk for many reasons. The following are some of the most common short-term problems: infection, respiratory distress syndrome (RDS), intraventricular hemorrhage (IVH), necrotizing enterocolitis (NEC), feeding and weight gain difficulties and many others. All the VLBW infants need specialised care in a neonatal intensive care unit (NICU) setting, most often for several

months. Despite the potential short-term complications, these babies are also at high risk for several long-term problems such as cerebral palsy, developmental delay and even blindness and deafness (Al Hazzani, Al-Alaiyan, Hassanein, & Khadawardi, 2011; Afjeh, Sabzehei, Fallahi, & Esmaili, 2013; Jia et al., 2022).

Literature review

Infections during pregnancy play a significant role in the pathogenesis of preterm birth due to intrauterine inflammatory response (Gao et al., 2021). Young maternal age (<18 years) proved to have a significant correlation with preterm labour and neonatal mortality, conversely, maternal age >35 years was a protective factor for survival (Vilanova et al., 2019) even though other studies consider advanced maternal age as a risk factor for preterm birth. Maternal obesity and smoking also negatively influences babies birth weight and outcome (Günther et al., 2021). The leading cause for preterm birth and neonatal morbidity and mortality is preeclampsia, which also causes 50000 - 60000 pregnancy-related deaths every year worldwide (Amaral, Wallace, Owens, & LaMarca, 2017). Some other studies show that pregnancies affected by maternal hypertension can affect the baby's developmental programming by creating an adverse environment for the fetus (Cunningham & LaMarca, 2018).

Low-dose dexamethasone (corticosteroid) is a common medication used prenatally to decrease RDS, facilitates extubation and improves survival in premature neonates (Suffolk, Agertoft, Johansen, & Zachariassen, 2019). According to the research, premature newborns exposed to complete prenatal steroid treatment were 1.95 times more likely to survive and 2.74 times more likely to survive without major complications (IVH, bronchopulmonary dysplasia, NEC, retinopathy etc.) (Chawla et al., 2022). Surfactant therapy is effective in the prevention of RDS postnatally (Dumpa & Bhandari, 2018). Caffeine therapy is effective in reducing the apnea of prematurity and has additional benefits, including a reduced need for intubation and respiratory support. (Dobson, Hunt, 2018). Neurologic defects associated with preterm labour often are prevented by magnesium sulfate (MgSO₄) (Bachnas, Akbar, Dachlan, & Dekker, 2021). The controlled trial of magnesium sulfate showed significantly lower rate of cerebral palsy in the study group (Rouse et al., 2008).

The survival rate of VLBW infants in the world differs. For example, in Germany the overall survival rate of VLBW was 89.1% (Jeschke et al., 2016). The best delivery mode for VLBW remains controversial, but cesarean section delivery is becoming more prevalent, especially in early gestational ages (Kardum, Grčić, Muller, & Dessardo, 2018). In the study VLBW infants delivered by cesarean section had a higher survival rate than the newborns delivered vaginally, mainly in infants with birth weight ≤800 g. (AlQurashi, 2020). Research shows that the mean gestational age, birth weight, and Apgar scores

were significantly higher in transferred babies compared with non-survivors among VLBW infants, and respiratory failure was the major factor of mortality among extremely low birth infants (Afjeh et al., 2013). At 22 weeks of gestation mortality was 100%, however the 50% limits of viability were at 25 weeks' gestation or at weight of > 600 g (Abolfotouh, Al Saif, Altwajjri, & Al Rowaily, 2018).

An Australian study proved that the most common cause of death among very preterm infants was major IVH, acute respiratory illnesses and sepsis, while in India the most common death cause was sepsis (Schindler et al., 2017; Jain et al., 2019).

Methodology

Ethics

Anonymity and confidentiality of the data obtained was ensured. The protocol was approved by the Riga Stradins University (RSU) Research Ethics Committee (reference code 6-2/10/85).

Participants and setting

This is a cross sectional study, where the population consisted of all live-born VLBW infants born in Riga Maternity hospital in the 5-year period from 2015 to 2019. The Data was collected from the Riga Maternity hospital's medical records. A total of 266 VLBW infants were born in this period, 57 of them were stillborn (1 was due to a feticide) and 209 were admitted to the hospital's NICU, and enrolled in our study. The data was organised in the following sections: mother's medical history, pregnancy and birth history, anamnesis of the newborn.

Statistics and data analysis

All statistical analyses were performed using IBM SPSS for Windows, Version 27.0. Continuous variables were expressed as the median (Q1-Q3), while categorical variables were expressed as frequency and percentage. Maternal demographic, pre- and perinatal data, and neonatal short-term outcomes up to the time of discharge from Riga Maternity hospital or death were compared between groups of transferred and non-survived infants, and over five years. Continuous variables, including gestational age, birth weight, were compared using the Mann-Whitney U test or the Kruskal-Wallis test. One-minute and five-minute Apgar scores were compared between groups using the Wilcoxon signed rank test. The remaining categorical variables were compared across the study groups using the Chi-square test. A P value < 0.05 was considered as statistically significant. A 95% confidence level was used.

Research results

Demographics

In total 209 VLBW infants were admitted to the Riga Maternity hospital's intensive care unit. Of those 209, 105 (50.5%) were males, 103 (49.5%) females, and the gender of one infant remained unknown.

The most common VLBW infant's mother's characteristics were age of 30 or more (70.7%), higher education (50.2%), married (63.6%), non-smokers (86.6%), and multiparous (66.5%).

During pregnancy, 24.4% of the women were diagnosed with anemia, 30.4% had gestational hypertension, 14.9% had preeclampsia, and 19.2 % had cervical insufficiency. Urinary tract and sexually transmitted infections were encountered in 12.9% of women during pregnancy. Gestational diabetes (GD) occurred in 22.2 % of pregnant women.

Almost a third, 27.0% were diagnosed with oligohydramnios or anhydramnios. Based on the available data, 16.3% (n=34) of the infants were conceived with the help of assisted reproductive technologies. Babies from twin pregnancies accounted for 27.8% of cases.

Cesarean sections dominated the choice of delivery method with 60.4%. Chorioamniotic membrane culture came back positive for 32.1% of women.

The median gestational age of the study population was 29.0 (27.0-30.0) weeks, and the median birth weight was 1120.00 (885.00-1320.00) grams. ELBW neonates made up 37.8% of the study population. The one-minute Apgar score in the median was 6.00 (5.00-7.00), but the five-minute score was 7.00 (6.00-7.00). The maternal and newborn characteristics of the VLBW infants in this study were presented in Table 1.

Table 1 Perinatal characteristics (created by the authors)

Perinatal characteristic		N (%)
Maternal age (years)	≤19	3 (1.4)
	20-24	8 (3.8)
	25-29	50 (24.0)
	30-34	72 (34.6)
	35-39	53 (25.5)
	40-44	18 (8.7)
	≥45	4 (1.9)
Maternal education level*	Higher	103 (50.2)
	Secondary	86 (42.0)
	Basic	16 (7.8)
Marital status	Married	133 (63.6)
	Unmarried	76 (36.4)
Use of nicotine	Smokers	28 (13.4)
	Non- smokers	181 (86.6)
Previous abortion*	Yes	94 (45.2)
	No	114 (54.8)
Assisted reproductive technology*	Yes	34 (16.3)
	No	174 (83.7)

Prenatal genetic screening test results*	Low risk	136 (69.7)
	Medium risk	9 (4.6)
	High risk	15 (7.7)
	Unknown results	35 (17.9)
Parity	Primiparous	70 (33.5)
	Multiparous	139 (66.5)
Plurality	Singleton	151 (72.2)
	Twin	58 (27.8)
Type of delivery*	Cesarean	125 (60.4)
	Vaginal	82 (39.6)
Gender*	Male	105 (50.5)
	Female	103 (49.5)
Gestational age (weeks)	<28	66 (31.6)
	28-32	114 (54.5)
	>32	29 (13.9)
Birth weight (grams)	1000-1499	130 (62.2)
	<1000	79 (37.8)
Apgar score at five-minute	<6	38 (18.2)
	≥6	171 (81.8)

*Missing values

Morbidity and complications

The two main complications encountered by the infants were RDS and infection. RDS developed in 133 (63.9%) of infants. Of these infants, 87.8% had received antenatal corticosteroids and 91.7% received surfactant replacement therapy. Respiratory support was used for all the infants with RDS. For 54.1%, non-invasive ventilation was used, while 36.1% received conventional mechanical ventilation (CMV), and 9.8% high-frequency oscillation ventilation (HFOV). Of 133 RDS cases, 10.5% led to death.

In total, 22.6% (n=47) of cases, infection was constituted, with pneumonia being the most common manifestation, forming 46.8% of all infection cases. Among other infection manifestations were sepsis (44.7%), conjunctivitis (19.1%), and meningitis (10.6%).

Other complications in the study group included: 15.5% anemia, 14.9% hemorrhage (including pulmonary, gastrointestinal, *disseminated intravascular coagulation (DIC)*), and 6.3% pneumothorax.

Development of anemia was associated with lower gestational age ($p<0.001$), lower birth weight ($p=0.006$), and five-minute Apgar score ($p<0.001$). From all the anemia cases, 15.6% led to death.

Statistically, hemorrhage was strongly associated with death ($p<0.001$); 25.8% of VLBW infants with hemorrhage did not survive.

Pneumothorax was statistically significantly associated with RDS ($p=0.005$) and the need for respiratory support with CMV ($p<0.001$). From 13 pneumothorax cases, 11 (84.6%) survived till discharge.

Complication rates differ depending on the birth weight (Fig.1). Lower birth weight was significantly associated with anemia ($p=0.006$), infection ($p=0.040$,

especially sepsis $p=0.008$), and RDS ($p<0.001$). In the birth weight group 1000-1249 g there was a significant association with pneumothorax ($p=0.005$). Hemorrhage was equally common across the different birth weight groups.

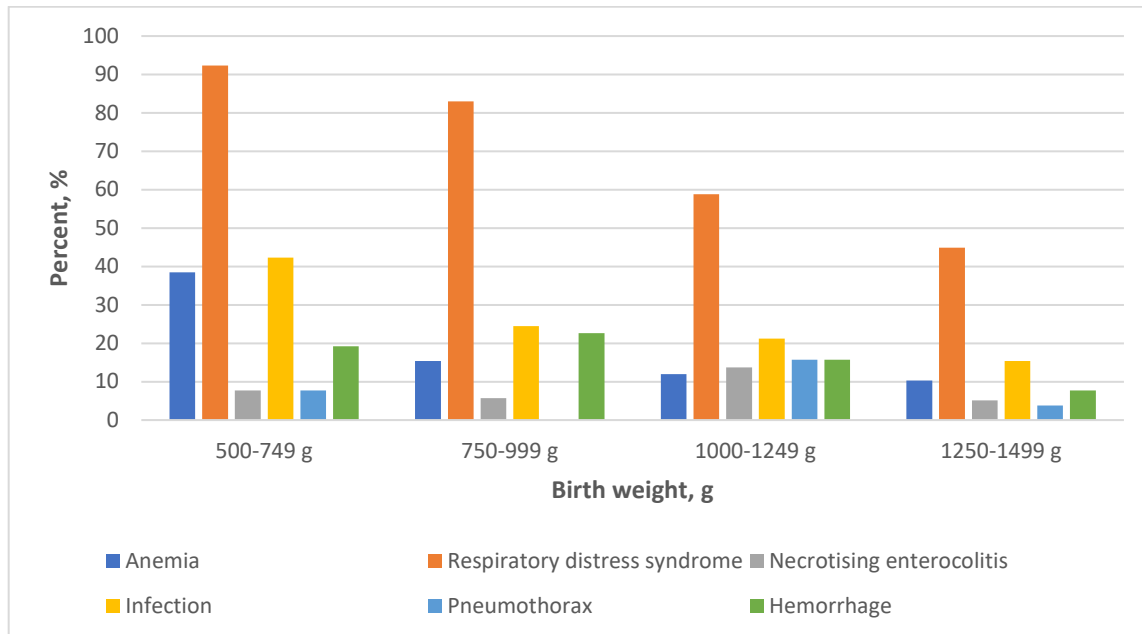


Figure 1 Complications by birth weight (created by the authors)

Risk factors associated with mortality

The study revealed statistically significant maternal, perinatal and neonatal factors associated with mortality (Table 2). One of the neonates was excluded from the analysis of risk factors associated with mortality, as his outcome of survival remained unknown.

Maternal risk factors for mortality in VLBW infants were maternal age of 19 or less ($p=0.011$).

Statistically significant delivery risk factors were positive culture of chorioamniotic membranes ($p=0.028$) and gestational age less than 28 weeks ($p=0.015$). The median gestational age in the transferred group was 29.0 (27.0-30.0) weeks, but in the non-surviving 26.5 (24-28). Statistically, the method of delivery was not significantly associated with neonatal death ($p=0.053$), but vaginal delivery tended to higher mortality.

Neonatal factors associated with a higher mortality were male gender ($p=0.039$), extremely low birth weight ($p=0.035$), and a five-minute Apgar score less than 6 ($p<0.001$). The median birth weight for transferred versus non-survivors was 1148.00 (900.00-1437.00) and 865.00 (642.50- 1112.50) grams respectively. The five-minute Apgar score median was higher 7.00 (6.00-7.00) in the transferred group compared to 4.50 (2.25-7.00) in the non-surviving group.

From the treatment group, risk factors associated with increased mortality were the need for intubation and adrenaline, fluid bolus administration at birth ($p=0.001$), and respiratory support with CMV ($p<0.001$). A significant

observation is that, statistically, non-surviving infants more often did not receive breast milk, antibacterial therapy and caffeine, but were more prone to receiving blood transfusions and surfactant applications than transferred infants. ($p < 0.001$ and $p = 0.002$, respectively). From the transferred infants, 41.7% did not need surfactant applications at all, meanwhile in the non-surviving group, 100% of infants had received at least one surfactant application.

Morbidities and complications associated with mortality were anemia ($p = 0.047$), RDS ($p = 0.041$), hemorrhage ($p < 0.001$), and infections ($p = 0.002$), especially pneumonia ($p < 0.001$). Hemorrhage had the highest mortality rate (25.8%) among complications.

Table 2 Maternal, newborn and perinatal factors between transferred and non-survived individuals (created by the authors)

	Transferred (n=192) N (%)	Non-survived (n=16) N (%)	Total	P value
<i>Maternal</i>				
Maternal age				0.011
– ≤19	1 (0.5)	2 (12.5)	3 (1.4)	
– 20-24	8 (4.2)	0 (0.0)	8 (3.8)	
– 25-29	48 (25.0)	2 (12.5)	50 (24.0)	
– 30-34	63 (32.8)	9 (56.3)	72 (34.6)	
– 35-39	51 (26.6)	2 (12.5)	53 (25.5)	
– 40-44	18 (9.4)	0 (0.0)	18 (8.7)	
– ≥45	3 (1.6)	1 (6.3)	4 (1.9)	
<i>Newborn</i>				
Gender*				0.039
– Female	99 (51.8)	4 (25.0)	103 (49.8)	
– Male	92 (48.2)	12 (75.0)	104 (50.2)	
<i>Pregnancy</i>				
Gestational age (weeks)				0.015
– <28	56 (29.2)	10 (62.5)	66 (31.7)	
– 28-32	108 (56.3)	6 (37.5)	114 (54.8)	
– >32	28 (14.6)	0 (0.0)	28 (13.5)	
Birth weight				0.035
– 1000-1499 (VLBW)	123 (64.1)	6 (37.5)	129 (62.0)	
– <1000 (ELBW)	69 (35.9)	10 (62.5)	79 (38.0)	
<i>Delivery</i>				
Delivery mode*				0.053
– Cesarean	118 (62.1)	6 (37.5)	124 (60.2)	
– Vaginal	72 (37.9)	10 (62.5)	82 (39.8)	

Resuscitation at birth				
– Yes, basic	169 (88.0)	8 (50.0)	177(85.1)	<0.001
– Yes, advanced	23 (12.0)	8 (50.0)	31 (14.9)	
Apgar score at five-minute (mean)				
– <6	29 (15.1)	9 (56.3)	38 (18.3)	<0.001
– ≥6	163 (84.9)	7 (43.8)	171 (81.7)	
Positive chorioamniotic membrane culture*	44 (29.7)	8 (61.5)	52 (32.3)	0.028
<i>Treatment</i>				
Antibacterial therapy*	190 (99.5)	13 (81.3)	203 (98.1)	0.001
Caffeine	148 (77.1)	4 (25.0)	152 (73.1)	<0.001
Surfactant therapy*	114 (59.4)	15 (100.0)	129 (62.3)	0.002
Breast milk feeding*	172 (94.0)	3 (60.0)	175 (93.1)	0.039
Respiratory support				
– None	6 (3.1)	0 (0.0)	6 (2.9)	<0.001
– Non-invasive ventilation	132 (68.8)	0 (0.0)	132 (63.5)	
– Mechanical ventilation	46 (24.0)	9 (56.3)	55 (26.4)	
– HFOV	8 (4.2)	7 (43.8)	15 (7.2)	
Transfusions*	51 (26.7)	12 (80.0)	63 (30.6)	<0.001
<i>Complications</i>				
Anemia*	27 (14.1)	5 (35.7)	32 (15.5)	0.047
RDS	119 (62.0)	14 (87.5)	133 (63.9)	0.041
Hemorrhage	23 (12.0)	8 (50.0)	31 (14.9)	<0.001
Infection	38 (19.8)	9 (56.3)	47 (22.6)	0.002

*Missing values

Mortality and survival rate

The overall survival rate till discharge from the neonatal intensive care unit was 92.3% (n=192), for ELBW it was statistically significantly lower (87.3%). A total of 16 neonates passed away. All 192 surviving patients were later transferred to the Children's Clinical University Hospital. More than half (62.5%) of non-survivors died within the first 24 hours after birth, and another 37.5% (n=6) passed away in the first seven days of life.

The mortality rate decreased with increased gestational age (p=0.015) (Fig.2), birth weight (p<0.001) (Fig.3), and Apgar score (p<0.001). The leading cause of death was intrauterine pneumonia 43.8% (7 out of 16) and tear of the

cerebellar tentorium 25.0% (4 out of 16). Other important death causes included sepsis, hypoxic-ischemic encephalopathy, pulmonary hypoplasia and hemorrhage, as well as congenital anomalies incompatible with life. For two infants the parents refused pathological examination, thereby the cause of death remains unknown.

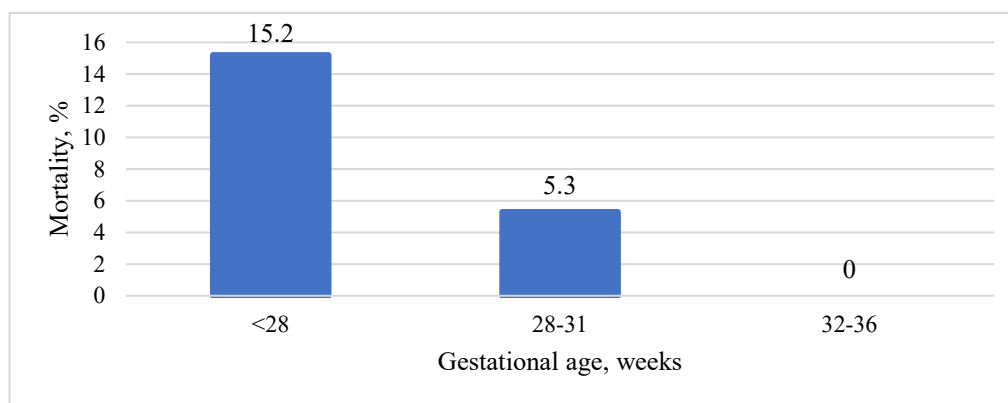


Figure 2 Mortality rate by gestational age group (created by the authors)

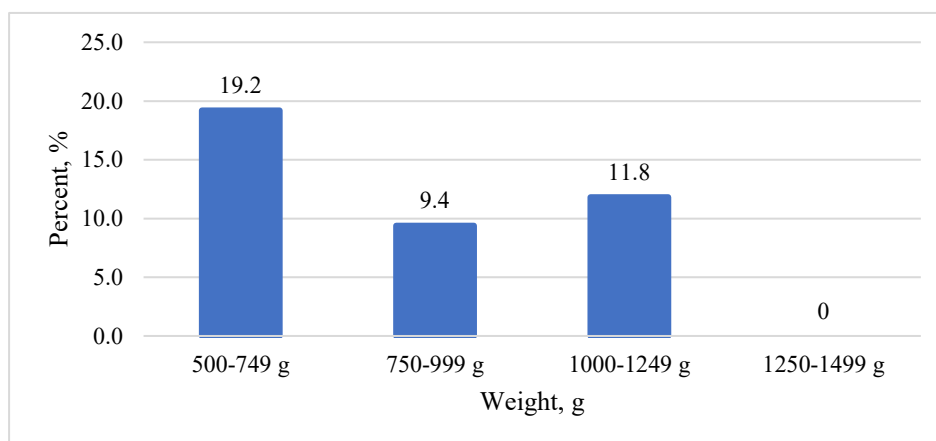


Figure 3 Mortality rate by weight group (created by the authors)

Differences between years

VLBW infant numbers in the year 2015, 2016, 2017, 2018 and 2019 were 31, 43, 44, 37, and 54, respectively. Annually there were on average 42 ± 9 neonates born weighing less than 1500 g, overall, the number of VLBW infants increased over the five years almost by half (from 31 infants in 2015 to 54 in 2019).

Analysing maternal factors and complications during the pregnancy (Fig.4), a tendency of growing numbers of GD during the years was found. In 2015 5.3% of women were diagnosed with GD, while in 2019 this number has risen to 42.9%. Other maternal factors and common complications during the pregnancy did not have statistically significant differences.

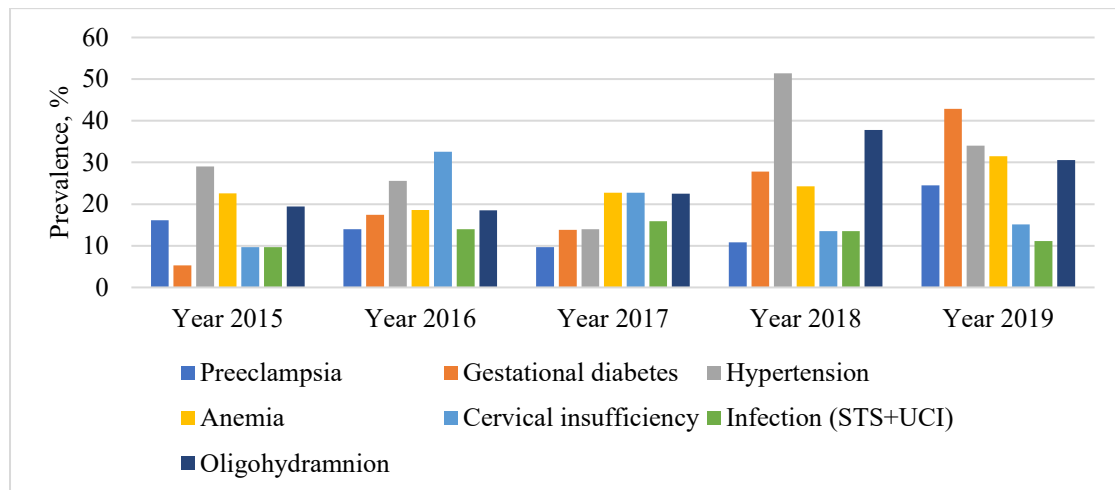


Figure 4 *Prevalence of pregnancy complications across five years (created by the authors)*

In total, antenatal steroids were administered for 88.8% infants, of which 83.5 % got a complete course. There was not a statistically significant difference between the years. In addition, neuroprotection with magnesium sulfate was administered to 53.1% of neonates. Neuroprotection significantly increased from 2015 to 2019 (respectively from 12.9% to 83.0%, $p < 0.001$). The increase started in 2017.

Starting from 2015, the number of vaginal deliveries decreased each year (from 48.4% in 2015 to 28.8% in 2019) and cesarean section became the more frequently chosen of delivery methods. There is also a statistically significant difference in delivery type by gestational age throughout the years, where vaginal delivery was preferred for premature pregnancies less than 28 gestational weeks ($p < 0.001$). Therefore, vaginal deliveries accounted for the majority of deliveries (64.6%) among gestational weeks less than 28, while for gestational age > 32 weeks cesarean section was the primary choice. In the gestational age group 28-32 weeks, there was a significant tendency to deliver vaginally in 2018, compared to other years ($p = 0.010$). Proportion of cesarean section by gestational age in weeks and year can be viewed in Figure 5.

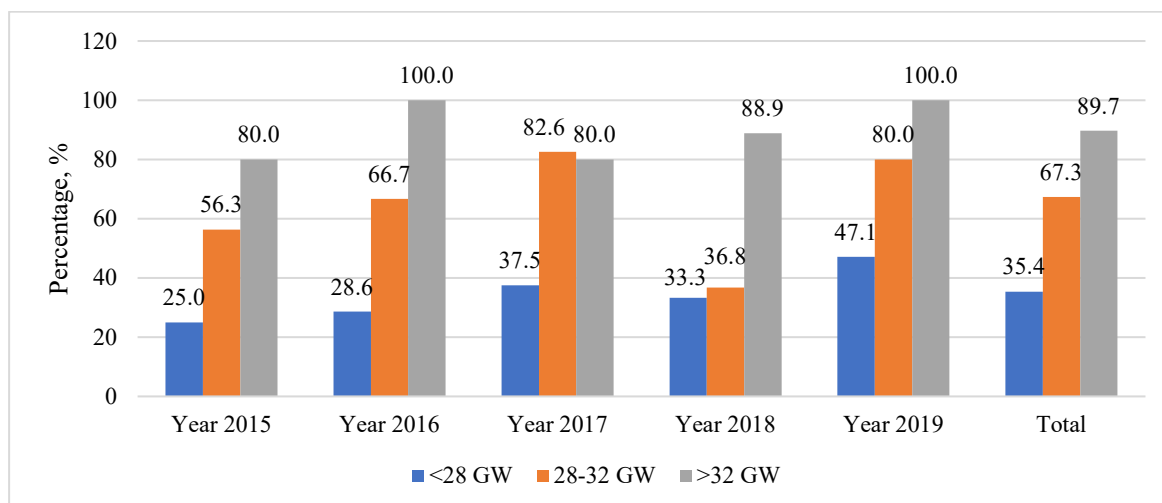


Figure 5 *Proportion of Cesarean section by gestational age in weeks and year* (created by the authors)

Neonatal factors (gender, birth weight, gestational age and Apgar scores) were similarly distributed over the years. The mortality rate fluctuated between the years, but it did not statistically significantly change (Fig.6). The highest mortality rate was seen in 2018 13.5%, and the lowest was 2.3% in 2016 ($p=0.277$). One-third (31.3%) of all neonatal deaths of the study population (5 out of 16) occurred in the year 2018, when intrauterine pneumonia, hemorrhage and tear of the cerebellar tentorium were the leading causes of death. All infants in 2018 died in the first 24 hours of their life.

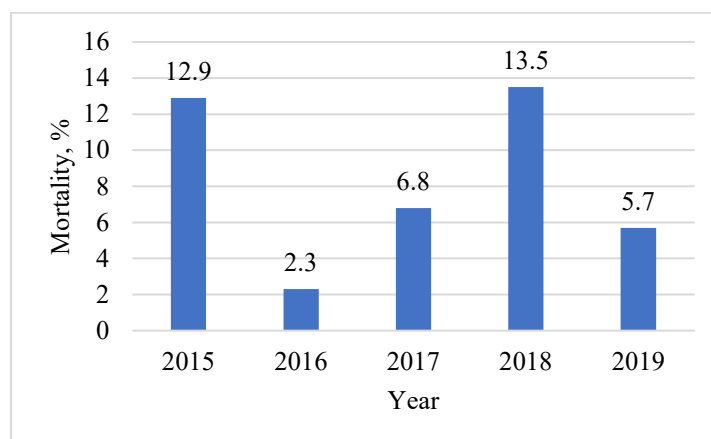


Figure 6 *Mortality rate by the year* (created by the authors)

Caffeine treatment differs over the years. Statistically, more infants in 2016 were given caffeine than in 2018 ($p=0.032$). Lower vitamin K usage was seen in 2015. The respiratory support rate increased significantly from 2015 to 2019 ($p=0.018$). In 2015, 29.0% of neonates did not get any kind of respiratory support, but in 2019 this number steadily decreased to 9.3%.

Table 3 Treatment and complication differences between years (created by the authors)

	2015 n=31 (%)	2016 n=43 (%)	2017 n=44 (%)	2018 n=37 (%)	2019 n=54 (%)	Total (N=) (%)	P value
Resuscitation at birth							
– Yes, basic	24 (77.4)	41 (95.3)	34 (77.3)	32 (86.5)	47 (87.0)	178 (85.2)	0.117
– Yes, advanced	7 (22.6)	2 (4.7)	10 (22.7)	5 (13.5)	7 (13.0)	31 (14.8)	
Antibacterial therapy*	30 (96.8)	43 (100.0)	43 (97.7)	36 (97.3)	52 (98.1)	204 (98.1)	0.910
Vitamin K	29 (93.5)	43 (100.0)	44 (100.0)	35 (94.6)	54 (100.0)	205 (98.1)	0.022
Caffeine	19 (61.3)	37 (86.0)	32 (72.7)	22 (59.5)	43 (79.6)	153 (73.2)	0.032
Surfactant therapy*	18 (60.0)	28 (65.1)	27 (61.4)	20 (54.1)	36 (66.7)	129 (62.0)	0.786
Breast milk*	24 (82.8)	38 (90.5)	36 (97.3)	31 (100.0)	47 (94.0)	176 (93.1)	0.076
Respiratory support*							
– None	0 (0.0)	1 (2.3)	0 (0.0)	4 (10.8)	1 (1.9)	6 (2.9)	0.289
– Non-invasive ventilation	20 (64.5)	31 (72.1)	27 (61.4)	23 (62.2)	31 (58.5)	132 (63.5)	
– Mechanical ventilation	7 (22.6)	10 (23.3)	15 (34.1)	6 (16.2)	17 (32.1)	55 (26.4)	
– HFOV	4 (12.9)	1 (2.3)	2 (4.5)	4 (10.8)	4 (7.5)	15 (7.2)	
Transfusions* (m=3)	9 (30.0)	9 (21.4)	16 (36.4)	8 (21.6)	21 (39.6)	63 (30.6)	0.215
Complications							
– RDS*	20 (64.5)	28 (65.1)	29 (65.9)	21 (56.8)	35 (66.0)	133 (63.9)	0.905
– Anemia*	5 (17.2)	8 (18.6)	9 (20.5)	1 (2.7)	9 (17.0)	32 (15.5)	0.206
– Pneumothorax	3 (9.7)	3 (7.0)	1 (2.3)	1 (2.7)	5 (9.4)	13 (6.3)	0.461
– Hemorrhage	4 (12.9)	7 (16.3)	8 (18.2)	4 (10.8)	8 (15.1)	31 (14.9)	0.906
Infection	8 (25.8)	7 (16.3)	10 (22.7)	9 (24.3)	13 (24.1)	47 (22.5)	0.862
– Meningitis	2 (6.5)	1 (2.3)	0 (0.0)	0 (0.0)	2 (3.7)	5 (2.4)	0.322
– Pneumonia	3 (9.7)	3 (7.0)	5 (11.4)	6 (16.2)	5 (9.3)	22 (10.5)	0.751
– Sepsis	6 (19.4)	3 (7.0)	5 (11.4)	2 (5.4)	5 (9.3)	21 (10.0)	0.400
– Conjunctivitis	1 (3.2)	2 (4.7)	2 (4.5)	1 (2.7)	3 (5.6)	9 (4.3)	0.986
Overall survival rate until transferred*	27 (87.1)	42 (97.7)	41 (93.2)	32 (86.5)	50 (94.3)	192 (92.3)	0.277

*Missing values

Median length of hospital stay over the five-year period was 6 days (Q1-Q3; 6-7). However, the distribution of hospital stay days was not the same across the years ($p < 0.001$). Earlier discharges were seen in 2019, compared to 2016 and 2017 when infants used to stay longer in the NICU.

Discussion

This study provides a new insight on neonatal care in Latvia's largest maternity hospital during a 5-year period. As the birth weight and gestational age increased, the mortality rate decreased, which is consistent with other studies of VLBW infants (Abolfotouh, Al Saif, Altwaijri, & Al Rowaily, 2018; Afjeh, Sabzehei, Fallahi, & Esmaili, 2013). Of the risk factors for increased mortality, the study proved that a young maternal age (<19 years) and positive chorioamniotic membrane culture proved to be significant. From the infant's data, being of male gender, having a 5-minute Apgar score <6 and extremely premature gestational age were significant factors, which is also proven by other studies (Jain et al., 2019; Jeschke et al., 2016). The most important factors from the treatment were the need for advanced resuscitation at birth, respiratory support with CMV, blood transfusions and surfactant applications, which may also indicate that these

newborns were in a more severe state. Non-survivors received significantly less breastmilk, therapy with antibiotics and caffeine, which could be explained by their serious condition and the need to focus on life-saving therapy options.

Complications and morbidities that lead to death were infection, anemia, RDS and hemorrhage, which are also proven by other studies as one of the most frequent ones (Jeschke et.al., 2016; Kardum, Grčić, Muller, & Dessardo, 2018).

We found that during the years 2014-2019, 7.7% of the total 209 VLBW infants did not survive till discharge. While the mortality rate decreased from 2015 to 2019, there was a rapid increase in the year 2018. While the underlying cause is unknown, there are some possible factors that could affect it. In the year 2018 various characteristics differed from other years such as the choice in delivery method - vaginal delivery was chosen more often. Although opinions differ, some studies show that vaginal delivery, particularly for extremely premature infants, has a higher percentage of adverse outcomes (AlQurashi, 2020; Kardum, Grčić, Muller, & Dessardo, 2018). Of all the years, 2018 had the highest number of cerebellar tentorium tears, which could be caused by the delivery process. Compared to 2016, 2018 1-minute Apgar scores were significantly lower as well as all non-survived infants died within the first 24 hours in 2018, which could indicate that the newborns had a more severe condition already at birth. Another factor that could have an impact on the mortality rate is caffeine usage - it was significantly lower than in other years. Furthermore, the use of caffeine is associated with reduced neonatal morbidity (Abdel-Hady, Nasef, Shabaan, & Nour, 2015). Looking from the mother's medical history during the years, there was a rapid increase in GD incidence and gestational hypertension, and both diseases have a higher risk for various complications for the newborn. On the treatment side we found an increase in the usage of ventilation support and antenatal neuroprotection with magnesium sulfate throughout the years, which are important factors in the reduction of the mortality rate (Rouse et al., 2008).

Our study results show that the VLBW infants survival rate has improved due to several developments in the quality of care in Latvia, which corresponds to the total worldwide tendencies, but that early and adequate prenatal care in preterm labour and choice of delivery plays a very important part for the survival of these infants (WHO, 2022; National Institutes of Health, 2022).

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