Umrljivost novorojenčkov na območju Maribora 1997-2008

Neonatal mortality in the Maribor region (1997–2008)

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Izvleček

Namen: *Predstaviti povzetek podatkov o umrljivosti novorojenčkov v 12-letnem vzorcu 24044 novorojenčkov, rojenih na Kliniki za ginekologijo in perinatologijo Univerzitetnega kliničnega centra v Mariboru v obdobju od 1997–2008.*

Metode: *Za študijo smo uporabili podatke kohortnih nizov novorojenčkov iz Nacionalnega perinatalnega informacijskega sistema (NPIS) za obdobje 1997–2008, osnovanih na datumih rojstva in smrti. Univerzitetni klinični center v Mariboru skrbi za populacijo severovzhodne Slovenije, kjer se je v izbranem 12-letnem obdobju rodilo 24044 živorojenih novorojenčkov. Letne kohorte smrti novorojenčkov smo analizirali po gestacijski starosti (GS),*

Abstract

Purpose: *To provide a summary of neonatal mortality data for a group of 24,044 live births in the Maribor Department of Perinatology between 1997 and 2008.*

Methods: *The National Perinatal Informational System (NPIS) cohort files for 1997–2008 were used for this study. Data are presented using cohorts based on dates of birth and death. The University Clinical Center serves the population of northeastern Slovenia, with 24,044 live births in this 12-year period. Yearly cohorts of neonatal deaths were analyzed by gestational age (GA) distribution, birth weight (BW) distribution, age at death, and cause of death.*

Results: *The average neonatal mor-*

porodni teži (PT), po starosti ob smrti in njenem vzroku.

Rezultati: *Povprečna stopnja umrljivosti novorojenčkov v celotni 12-letni preiskovani skupini je bila 2,2 na 1000 živorojenih z GS 28–42 tednov in 4,7 na 1000 živorojenih z GS 22–42 tednov. Najmanjša skupina z izjemno nizko porodno težo (INPT) < 1000 g je bila odgovorna za okoli 50 % vseh smrti novorojenčkov, skupina s PT 1000–1500 g za okoli 20 %, novorojenčki s PT 1500–2500 g za 10 % in novorojenčki s PT > 2500 g za 20 %. Najvišji odstotek smrti novorojenčkov (54 %) so predstavljale smrti zaradi izjemne nezrelosti.*

Zaključek: *Nihanja stopenj umrljivosti novorojenčkov v opazovanih 12 letih so predvsem v letih 1997–2005 v direktni povezavi s številom novorojenčkov z INPT. Toda v zadnjih štirih letih opazovanega 12-letnega obdobja smo, kljub visoki stopnji rojevanja prezgodaj rojenih, priča očitno znižani stopnji umrljivosti novorojenčkov ali boljšemu kazalniku kvalitete perinatalnega varstva. Analiza kazalnikov kvalitete v perinatologiji je obvezni del klinične prakse.*

tality rate in the 12-year investigated group was 2.2 per 1000 live births with a GA of 28-42 weeks and 4.7 per 1000 live births with a GA of 22-42 weeks. The smallest group, with an extremely low birth weight (ELBW; <1000 g), accounted for approximately 50% of all neonatal deaths, newborns weighing 1000-1500 g accounted for approximately 20% of all neonatal deaths, the group with a BW of 1500-2500 g accounted for 10% of neonatal deaths, and newborns weighing >2500 g accounted for approximately 20% of all neonatal deaths. The largest percentage of neonatal deaths was deaths due to immaturity, and represented 54% of all reported deaths during the investigated period.

Conclusion: *Oscillations in neonatal mortality rates during the 12 years first occurred in 1997-2005 in direct connection with the number of extremely premature newborns. In the last 4 years of the 12 years we observed a new and better quality indicator, i.e., a lower neonatal mortality rate in spite of the increased preterm delivery rate. Analysis of quality indicators in perinatology should be part of routine clinical care.*

INTRODUCTION

The proportion of child deaths that occurs during the neonatal period (38% in year 2000) is increasing, and the Millennium Development Goal for child survival cannot be met without substantial reductions in neonatal mortality (1). Every year an estimated 4 million babies die in the first 4 weeks of life (the neonatal period) and three-quarters of neonatal deaths occur in the first week of life. Indeed, the highest risk of death is on the first day of life (1). Most perinatal deaths occur in preterm infants, and preterm birth is an important risk factor for neurologic impairment. Over the past 20–30 years, advances in perinatal care have improved the outcomes for infants born after short gestation. The number of weeks of completed gestation that defines whether or not a birth is preterm rather than a fetal loss has decreased. This boundary varies internationally from approximately 20–24 weeks. Some classifications of fetal loss, stillbirth, and early neonatal death for these very short gestations may be unreliable.

In recent years, an increased survival of very immature infants has been reported, ranging from 2% to 35% at 23 weeks, between 17% and 58% at 24 weeks, and from 35% to 85% at 25 weeks (2 – 5).

Evaluating the quality of perinatal care at the regional level means assessing the total sum of the resources used, the activities performed, and the results in the area that is served by the regional perinatal center.

The Slovene Perinatal Statistical Database (PERIS) provides important information. At the Maribor Department of Perinatology, as in the remaining 13 obstetrics departments in Slovenia, routine surveys of reproductive health outcomes are performed at regular yearly intervals and data from routine follow-ups in child health care are used for quality assessment purposes.

Clinical quality indicators for monitoring the results have been developed by the American College of Obstetricians and Gynecologists (6). A recent European collaborative effort, the PERISTAT project, which is part of the European Commission's Health Monitoring Programme, has developed indicators of perinatal health. In 2003, a list of recommended indicators was published, together with the figures for the year 2000 for most of the participating countries (7). There are six core indicators for neonatal health, as follows: C2 (neonatal mortality rate by gestational age [GA], birth weight, and plurality); C3 (infant mortality rate by GA, birth weight, and plurality); C4 (distribution of birth weight by vital status, GA, and plurality); C5 (distribution of GA, by vital status and plurality); R2 (Apgar score distribution); and R1 (prevalence of congenital anomalies). There are three indicators of future development, as follows: F1 (causes of perinatal death); F2 (prevalence of cerebral palsy); and F3 (prevalence of hypoxic-ischemic encephalopathy). Outcomes related to the health of babies in the first year of life (specifically, mortality rates) are often used as a measure of the health status of a population or the quality of the perinatal health care system.

MATERIAL AND METHODS

In the cohort epidemiologic study, we used the data from the database of the National Perinatal Information System (NPIS) for 1997–2008 and for the group of 24,044 live births in the Department of Perinatology of the University Clinical Center Maribor during the same period. We formed 1-year cohorts on the basis of the dates of birth and the dates of death between 1 January 1997 and 28 February 2009. Yearly cohorts of deaths were analyzed separately with respect to the distribution according to GA, birth weight (BW), age at death and cause of death.
The definition of terms used are as follows (8): early neonatal mortality (death of a newborn occurring before the 7th day of life); late neonatal mortality (death of a newborn occurring after the 7th day and before the 28th day of life); and neonatal mortality rate (NMR; number of deaths in the neonatal period and in a given year expressed per 1000 live births in the same year).

Table 1. *Absolute number of notifications and neonatal mortality rates for the Maribor region for the 1997-2008 period*

Year	Live births (N)	Deaths at 1st day (N)	Deaths at 2nd-6,9th day (N)	Deaths at 7th-27th day (N)	Neonatal mortality GA ≥22 weeks rate (‰)	Neonatal mortality GA ≥28 weeks rate (‰)
1997	1977	3	6	3	6.6	4.0
1998	1954	3	4	1	3.6	2.6
1999	1848	4	1	2	3.8	1.6
2000	2004	10	4	1	7.5	3.5
2001	1957	2	3	1	3.1	2.0
2002	2021	5	2	2	4.5	2.5
2003	1988	6	4	3	6.5	2.5
2004	1974	2	6	1	4.6	1.0
2005	2060	10	2	1	5.8	2.4
2006	2047	3	1	5	4.4	2.0
2007	1911	3	1	2	3.1	1.6
2008	2303	2	3	1	2.6	0.4
1997-2008	24 044	53	37	23	4.7	2.2

Table 2. Number of neonatal deaths analyzed by gestational age

Gestational age (weeks)	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
< 28	5	2	4	8	2	4	8	7	7	5	3	5
28 - 31	2	1	1	4	0	3	4	2	2	3	1	0
32 - 36	3	2	2	1	2	2	0	0	2	0	1	0
≥ 37	3	3	0	2	2	0	1	0	1	1	1	1

Table 3. Neonatal mortality rate (‰) computed by birth weight (Maribor region, 1997-2008)

Birth weight (g)	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
< 1000	2.5	1.0	2.7	4.0	1.0	2.0	4.0	4.1	2.9	2.4	1.6	2.2
1000-2499	2.0	0.5	1.1	2.5	1.0	2.5	2.0	0.5	2.4	1.5	1.0	0.0
≥ 2500	2.0	2.0	0.0	1.0	1.0	0.0	0.5	0.0	0.5	0.5	0.5	0.4

RESULTS

This report provides a summary of neonatal mortality data for the Maribor region for 1997–2008, computed by age on the day of death (Table 1), GA (Table 2 and Fig. 2), BW (Table 3 and Fig. 1), and by the causes of neonatal death (Fig. 3).

From the investigated group of 24,044 live births, 53 newborns died on the first day of life, 37 in the first week of life, and 23 newborns died in the late neonatal period. Thus, the early NMR in our study represented approximately 80% of the total neonatal mortality for this period, and the highest risk of death was also on the first day of life (Table 1 and Fig. 4).

The higher number of extremely premature and live births with BWs of 1000–1500 g in the years 2000, 2003, 2004, and 2005 is directly reflected in the higher early NMR (Fig. 4). In the years 2006, 2007, and 2008 we observed that change took place; a higher number of premature and live births with BWs of 1000-1500 g has persisted and the NMR was lower. It is also evident that approximately 50% of all neonatal deaths are newborns with BWs < 1000 g and GAs < 28 weeks (Figs. 1 and 2 and Table 2).

BW is also a major determinant of neonatal mortality in the Maribor design. Low birth weight (LBW) includes infants with intrauterine growth restriction and infants born preterm. In 2005, for example, the proportion of births that were LBW or very low birth weight (VLBW) was 8% and 1.5%, respectively, and the proportion of neonatal deaths that occurred in these groups was 80% and 60%, respectively (Fig. 2).

The largest percentage of neonatal deaths was due to immaturity (GS < 28 weeks and BW<1000 g), representing 54% of all reported deaths in the investigated period, followed by deaths due to prematurity (GS 28 ≥ weeks and BW = 1000-2499 g; intracranial haemorrhage and sepsis) representing 19%, deaths classified as congenital malformations (19%), and deaths from different perinatal causes (perinatal asphyxia and meconium aspiration syndrome, 8%; Fig. 3).

DISCUSSION

In recent years, the results of the Center of Disease Control (CDC) analyses showed a rise in the NMR from 4.5 to 4.7 deaths per 1000 live births for the 2001–2002 period (9). This study suggested that the rise in the NMR was due to an increase in the percent-

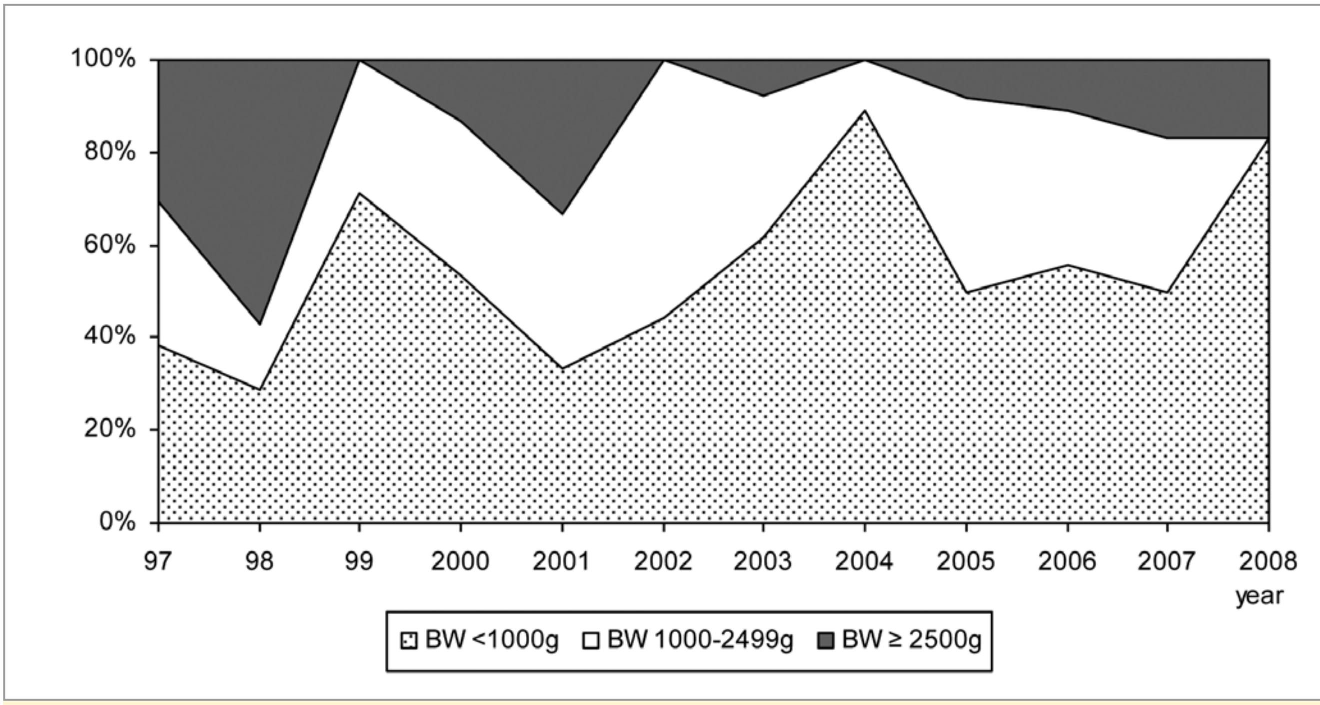

Figure 1. *Distribution of neonatal deaths by birth weight (BW), 1997-2008.*

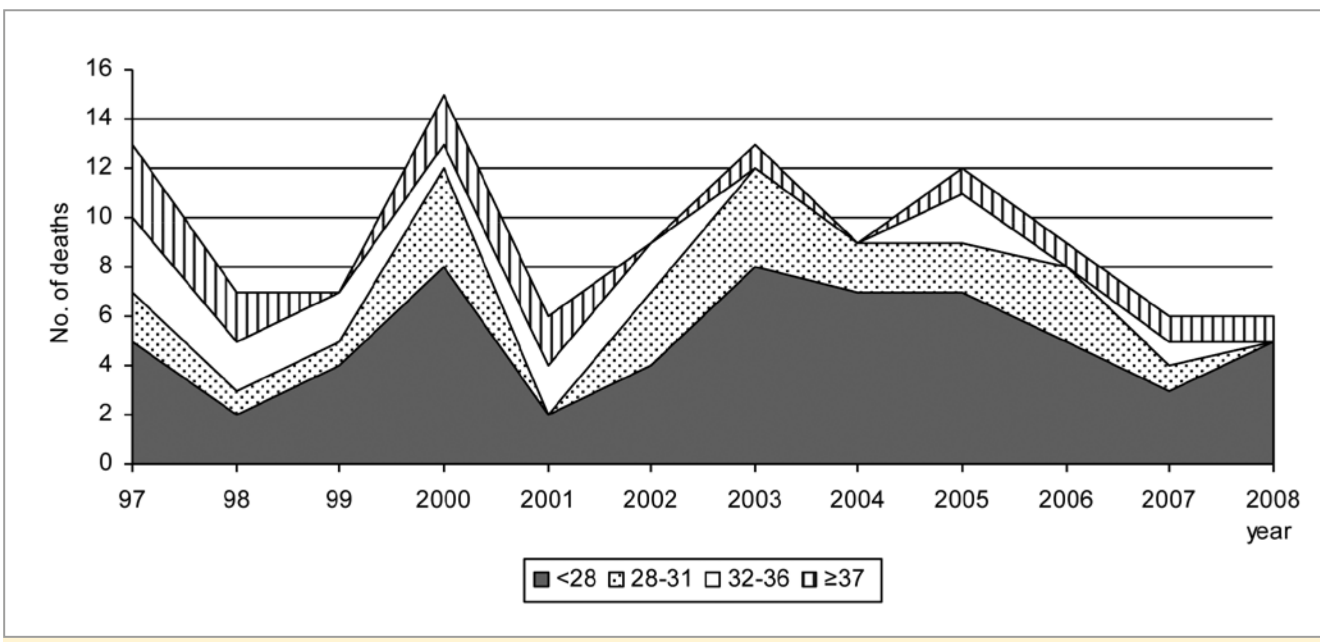

Figure 2. *Graphical presentation of neonatal deaths analyzed by gestational age (GA).*

age of infants born preterm (< 37 weeks) and infants with LBW (10). The Maribor statistical analysis of NMR in the past 12 years showed a similar connection between the higher number of extremely premature and live births with BWs between 1000 and 1500 g in the years 2000, 2002, and 2005, and reflected the higher NMR in the same years (Fig. 4). The results of our analyses of live births between 1997 and 2008 showed that greater than two-thirds of deaths in the neonatal period were newborns with BWs <2500 g

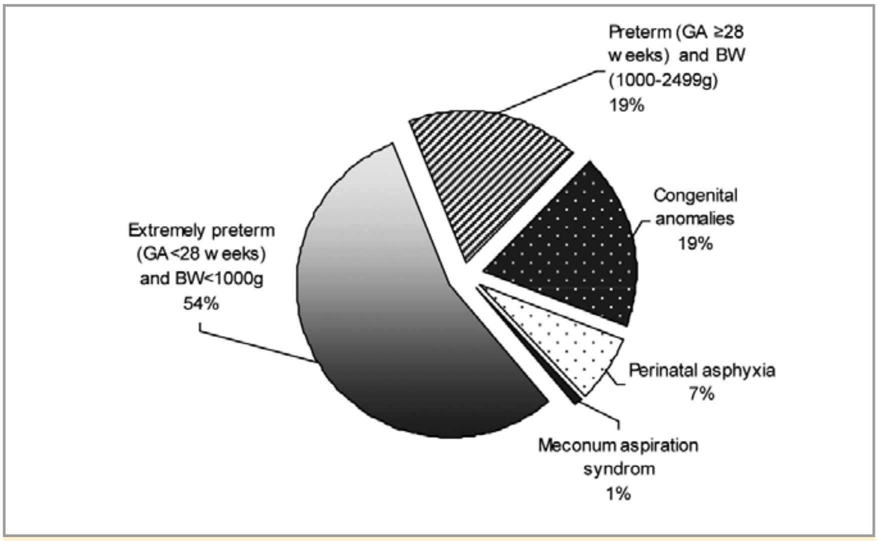

Figure 3. *Causes of neonatal death in the investigated group(Maribor region, 1997-2008).*

and these deaths occurred early (before 7 days of age). This increase was primarily driven by an increase in the birth rate of infants with BWs <1000 g.

The NMR is a sensitive measure of health during the perinatal period. When analyzed by GA and BW, the NMR provides a good comparative measure of outcome and is associated with the extent of early neonatal care. The number of weeks of completed gestation that defines whether or not a birth is preterm rather than a fetal loss has decreased. This boundary varies internationally from approximately 20 – 24 weeks (11). Some classifications of fetal loss, stillbirth, and early neonatal death for these very short gestations may be unreliable. Slovenia accepted this definition of the limit for viability at 22 weeks gestation from the European Association of Perinatal Medicine in the year 2000, also accepting the problems with the definition (i.e., whether or not a birth at 22 weeks gestation is a fetal loss or a preterm birth).

After a precise analysis of all deaths in this period, and particularly the analysis of deaths in the first hours of life, we can conclude that two or three infants were born each year at the limit of viability, as recently defined by the WHO and the European Association of Perinatal Medicine as completed 22 weeks gestation. Biological survival will depend not just on the presence of a given organ, but on its functional maturation, a sequential evolution often referred to as the "developmental windows." Alveolarization, which is essential for survival, is a process that includes ana-

Table 4. *Comparison of neonatal mortality rates between the Maribor region and England, Wales, and Northern Ireland (2000–2003)*

Year of birth	Maribor region, Slovenia 2000-2003		England, Wales and Northern Ireland 2000-2003	
	Frequency of live births	Neonatal mortality ratea	Frequency of live births	Neonatal mortality ratea
2000	2004	3.5	625,642	3.89
2001	1957	2.0	616,322	3.65
2002	2021	2.5	617,299	3.59
2003	1988	2.5	642,899	3.66

a Rate per 1000 live births (≥28 weeks)

Sources: PERIS 1997-2005

Confidential Enquiry into Maternal and Child Health (CEMACH), 2000, 2001, 2002, 2003 tomic, physiologic, and biochemical differentiation starting from approximately 24 weeks gestation, progressing until term. "Viability," according to some authors and in our opinion, would therefore be approximately 24 weeks gestation (12).

Table 4 shows a comparison between NMRs (per 1000 live births with a GA ≥ 28 weeks) in the Maribor region in 2000 - 2003 and in England, Wales, and Northern Ireland during the same period (13). The results are somewhat better for the Maribor region; thus, this quality indicator of neonatal care in Maribor, and in all of Slovenia, is at the European level. The WHO data for NMRs in other European countries in 2001 - 2002 are as follows: Germany, 2.7‰; France, 2.8‰; Switzerland, 3.6‰; Austria, 2.8‰; Greece, 3.5‰; Norway, 3.0‰; Finland, 2.1‰; Italy, 3.4‰; and Slovenia, 3.0‰. The European average is 3.2‰ (14). The first European Perinatal Health Report (17) showed wide variation between European countries in NMRs (1.6–5.7 ‰) in 2004. In addition, these countries had different patterns of early and late neonatal deaths. New member states of the European Union had high early and high late NMRs, while in other countries patterns of either low early with high late or high early and low late rates were observed (17). Variation in NMRs between countries may also reflect differences in policies between European countries related to the resuscitation of babies at the limit of viability (18). The second European Perinatal Health Report (2010) showed that NMRs ranged from 1.2 per 1000 live births in Iceland to 1.8 per 1000 in Slovenia, 4.5 per 1000 in Malta, and 5.5 per 1000 in Romania. Between 61% and 85% of all neonatal deaths in European countries occurred during the early neonatal period. Babies born before 28 weeks gestation or with a BW < 1000 g accounted for approximately 40% of all neonatal deaths. Slightly greater than one-quarter of the deaths were of term babies (last European data report; 19).

Graphical presentation of distribution of neonatal deaths in Maribor by BW is an obvious demonstration of oscillations in mortality rates, which until the year 2005 are in direct connection with the yearly number of extremely premature newborns with BWs < 1000 g and GAs <28 weeks (Fig. 4). In the years 2006, 2007, and 2008 we observed that change took

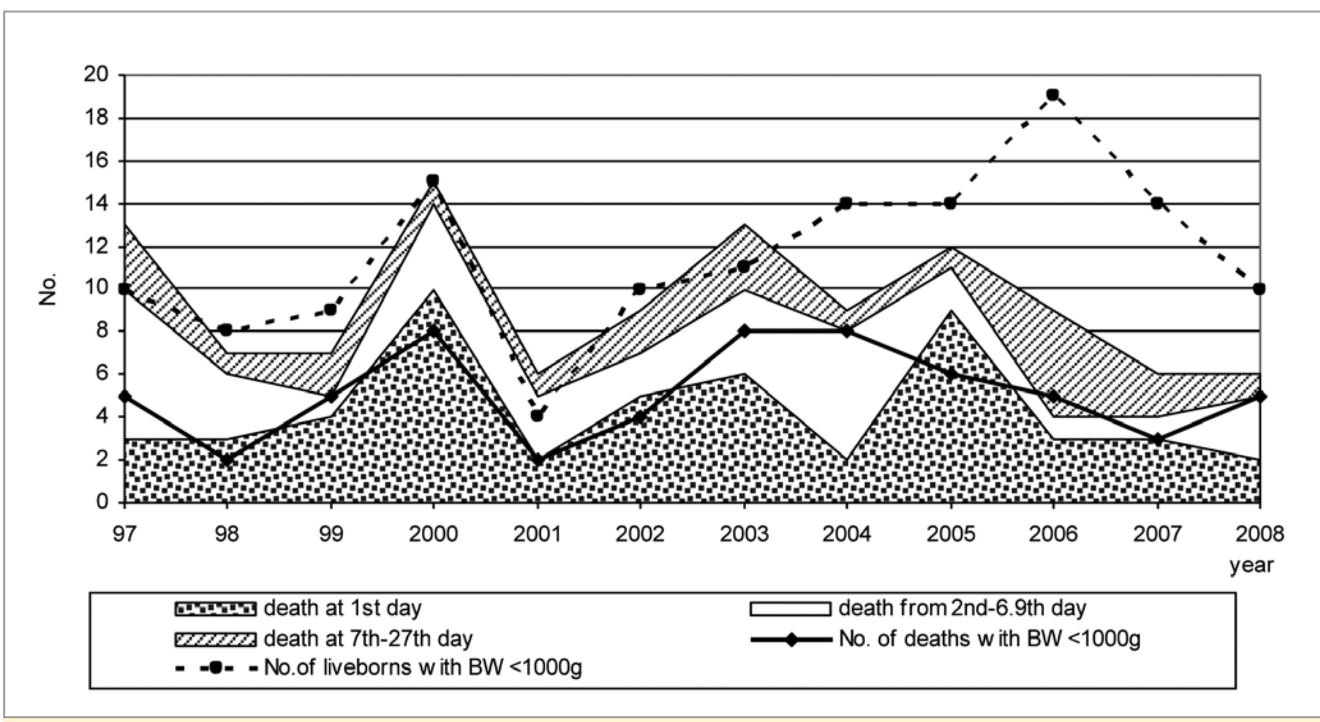

Figure 4. Demonstration of oscillations in mortality rates with the yearly number of extremely premature newborns with BWs < 1000 g.

place; a higher number of premature and live births with BWs of 1000-1500 g has persisted and the NMR was lower (Table 1 and Fig. 4).

The survival rate in this BW group (< 1000 g) was 50–60%, in the 1000-2500 g BW group the survival rate was approximately 80% and in the > 2500 g BW group the survival rate was 90–100%. An extremely LBW rate was shown to be an excellent predictor of NMR and is very similar to other reports from Europe and the USA (10, 15, 16, 17). As reported in the USA, approximately 4% of newborn babies have a BW < 2500 g (15); however, this small group accounts for > 50% of perinatal deaths. Newborns weighing < 1500 g comprised < 2.5% of all births, but accounted for approximately 50% of neonatal deaths (15). In the group investigated in Maribor, approximately 8% of newborns had a BW < 2500 g and accounted for > 80% of neonatal deaths. Newborns weighing < 1500 g comprised approximately 1.5% of all births in Maribor and accounted for approximately 70% of neonatal deaths, but the smallest group with a BW < 1000 g comprised 0.8% of all births and accounted for approximately 50% of all neonatal deaths. As reported by a Center of Disease Control analysis of NMR, the proportion of neonatal deaths occurring in the LBW and extremely low birth weight (ELBW) groups was 65% and 51%, respectively (9).

The largest percentage of neonatal deaths was due to immaturity (GS < 28 weeks and BW<1000 g), representing 54% of all reported deaths in the investigated period, followed by deaths due to prematurity (GS ≥ 28 weeks and BW 1000-2499 g; intracranial haemorrhage and sepsis) representing 19% and deaths classified as congenital malformations (19%) and deaths from different perinatal causes (perinatal asphyxia and meconium aspiration syndrome, 8%; Fig. 4). In most European countries, approximately one-quarter of early neonatal deaths are attributed to congenital anomalies and complications to very preterm births (17). The causes of neonatal deaths in the United States are related to congenital malformations (20%) and short gestation or LBW not attributed to other specific causes (17%), pregnancy complications (6.1%), placental complications (3.4%), bacterial sepsis (2.7%), diseases of the circulation (2.4%), intrauterine hypoxia and birth asphyxia (2.1%), and all other causes amounting to 46.3% of deaths (9).

In many recent reports on causes of preterm birth, 15–25% of preterm infants are delivered because of maternal or fetal complications of pregnancy (11). The principle causes are hypertensive disorders of pregnancy and severe intrauterine growth retardation. The decision to deliver these infants is formed by balancing the risk of preterm birth for the infant against the consequence of continued pregnancy for the mother and fetus. Over the past two decades, improved antenatal and perinatal care have increased the iatrogenic preterm delivery rate in the Maribor region also.

Differences in quality indicators in the Maribor region during the observed 12-year period are mainly related to differences in extremely preterm birth rates (GA < 28 weeks) and higher rates of newborns with LBWs. In the last 4 years of the 12-year observation period, we observed a new and better quality indicator (a lower NMR in spite of an increased preterm delivery rate). Spontaneous, extremely preterm birth is a major category of neonatal mortality. The preterm rate has not decreased over the last 10 years; in the past 4 years we have observed an increasing number of live births with BWs <1000 g (Fig. 4), live births with BWs of 1000-1499 g, and live births with BWs of 1500-1999 g. The characteristics of the population of childbearing women are changing in Slovenia as in the rest of the world, in particular as a result of older women giving birth and an increasing proportion of pregnancies resulting from assisted reproductive technology, with the associated increased risk of preterm birth.

CONCLUSION

The NMR is a key measure of health and care during pregnancy and delivery. As perinatal medicine lowers the limit of viability in the group of preterm infants with ELBW, only the fetal loss rate decreases while the mortality rate of extremely immature infants and the perinatal mortality rate both increase. In view of our incapacity to solve the problem of extremely premature birth, this shifting of responsibility for the results of management of extremely immature infants (< 24 weeks) into the hands of neonatologists seems pointless. Also, in this new millennium the decrease in the NMR, and particularly the concern for the quality of survival, both remain the basic tasks of perinatologists and pediatricians.

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