

Effect of pregestational maternal, obstetric and perinatal factors on neonatal outcome in extreme prematurity

Yun Wang · Tom Tanbo · Liv Ellingsen ·
Thomas Åbyholm · Tore Henriksen

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Abstract

Purpose To investigate the effect of pregestational maternal, obstetric and perinatal factors on neonatal outcome in extreme preterm deliveries.

Methods Retrospective study of deliveries in a Norwegian tertiary teaching hospital. All women with live births at 24⁺⁰–27⁺⁶ weeks of gestation between 2004 and 2007 were included. Major morbidity is defined as intraventricular haemorrhage grade 3–4, periventricular leukomalacia, bronchopulmonary dysplasia or necrotizing enterocolitis. Pregestational maternal, obstetric and perinatal variables were initially compared for mortality and survival with major morbidity at 24-h, 7- or 28-day postpartum/discharge in univariate analysis. Then, a multivariate analysis was conducted in order to determine independent factors associated with mortality and survival with major morbidity.

Results A total of 109 babies were delivered alive in 92 women, representing 1.6% of total births. The survival rates were 93.6, 84.4 and 80.7%, with a prevalence of major morbidity among survivors of 40.4, 32.1 and 39.4% at 24-h, 7- and 30-day postpartum/discharge, respectively. After adjustment using multiple logistic regression, only a 5-min Apgar score ≤ 3 and babies with at least one major morbidity had significantly independent effects on neonatal survival. Multiple pregnancy and gestational age <26 weeks were the only two independent risk factors for survival with major morbidity.

Conclusions Neonatal survival was significantly predicted by a 5-min Apgar score and neonatal morbidity, independent of pregestational maternal disease, obstetric complications, method of delivery, gestational age and birth weight in extreme preterm deliveries. The excess morbidity rate was confined among multiples and babies who were delivered before 26 weeks of gestation.

Keywords Extreme prematurity · Survival · Morbidity

Introduction

Despite efforts directed towards prevention of preterm birth, the incidence of prematurity and infants born with very low birth weight (<1,500 g) in the USA has increased from 10.6 and 1.27% in 1990 to 12.8 and 1.48% in 2006, respectively [1]. In Norway, the incidence of prematurity has increased from 5.2% in 1980 to 6.5% in 2007; however, the percentage of extreme prematurity (between 22 and 27 weeks of gestation) has decreased from 0.5% in 1980 to 0.4% in 2007 (*The Medical Birth Registry of Norway*, available at <http://www.fhi.no>). Preterm delivery, especially extreme prematurity and its short- and long-term sequelae constitute a serious problem in terms of neonatal and infant mortality, disability, and cost to society [2]. Wise et al. [3] concluded that neonatal mortality patterns in the United States have become highly dependent on infants with gestational ages that approach the second trimester while very low birth weight infants (<1,500 g) account for 64.2% of all neonatal deaths. Advances in perinatal and neonatal care in recent years, along with an increased understanding of neonatal physiology, have greatly improved the chances of survival of extremely low gestational age and low birth weight infants [4]. However, with

Y. Wang (✉) · T. Tanbo · L. Ellingsen · T. Åbyholm ·
T. Henriksen

Department of Obstetrics, Oslo University Hospital,
Rikshospitalet, 0023 Oslo, Norway
e-mail: yun.wang@oslo-universitetssykehus.no

T. Tanbo · T. Åbyholm · T. Henriksen
Faculty of Medicine, University of Oslo, Oslo, Norway

extreme prematurity, most survivors experience significant morbidity and are at risk of long-term sequelae [5, 6] that may affect their quality of life as well as having major economic implications both for their families and for society [5]. Therefore, the survival outcome of extremely premature newborns is no longer the principle marker of success; long-term neurodevelopmental outcome has become the most important indicator of a successful outcome for infants born extremely premature.

There has been an effort in recent times to identify obstetric parameters as predictive factors of neonatal mortality and morbidity in extreme prematurity. However, few studies also include maternal and perinatal factors in their analyses [7, 8]. The aim of the present study was to investigate the effect of pregestational maternal, obstetric and perinatal factors on neonatal mortality and survival with major morbidity in infants born between 24⁺⁰ and 27⁺⁶ weeks of gestation.

Materials and methods

This is a tertiary hospital-based retrospective analysis of all live births with a gestational age of 24⁺⁰ to 27⁺⁶ weeks. Birth registry records and neonatal records retrieved from local databases at Oslo University Hospital Rikshospitalet, Oslo, Norway between January 2004 and May 2007. Generally, women with a gestational age of 23⁺⁰ to 27⁺⁶ weeks with threatened preterm delivery are transferred to Oslo University Hospital Rikshospitalet from regional county hospitals in south-east Norway. After 27⁺⁶ weeks of gestation, the infants can be delivered at the regional county hospitals. All stillbirths were excluded. Infants delivered at other hospitals and then subsequently admitted to the Neonatal Intensive Care Unit (NICU) at Oslo University Hospital Rikshospitalet were also excluded. All women included in the present study were administered antenatal steroid (Betametason 12 mg i.m.) before labour with two doses spaced by 24 or 12 h. Antibiotics (Erythromycin 500 mg × 4 p.o. or Penicillin G 1.2 g × 4 i.v. for 3 days) were administered when indicated to women with signs of infection, or as a prophylaxis to women with preterm premature rupture of membranes (pPROM), or before acute caesarean section. Tocolytic therapy (atosiban three-step infusion) was given to women with uterine contractions.

Gestational age was defined as the number of completed weeks of gestation based on screening ultrasound examination which was performed between gestational weeks 18–20 as determined by the date of the last menstrual period. Neonatal major morbidity was defined as having at least one of the following diagnoses: intraventricular haemorrhage grade 3–4 [9], periventricular leukomalacia, bronchopulmonary dysplasia and necrotizing enterocolitis. Obstetric and

perinatal factors studied in relation to neonatal survival and survival with major morbidity were maternal age, multiple gestation, pre-eclampsia (blood pressure $\geq 140/90$ mmHg after 20 weeks gestation and a dipstick test for protein in urine $\geq +1$ or total protein/creatinine ratio in urine ≥ 30), antepartum haemorrhage (bleeding after 20 weeks gestation and before labour), pPROM (the amniotic sac ruptures more than an hour before the onset of labour before 37 weeks gestation), oligohydramnios (amniotic fluid index of less than 5 cm), chorioamnionitis (presence of uterine tenderness and/or purulent or malodorous amniotic fluid with any two of the following: antepartum temperature of more than 38°C, maternal tachycardia >120 beats/min, maternal leucocytosis $>18,000$ cells/mm³, or fetal tachycardia >160 beats/min). Cervical insufficiency (recurrent second- or early third-trimester fetal loss following painless cervical dilatation), intrauterine growth restriction (IUGR, a reduction in growth compared to the expected by a series of measurements with ultrasound, at least two measurements), delivery methods (vaginal birth vs. caesarean section), 5-min Apgar score, birth weight, neonatal major morbidity.

Pregestational maternal conditions (pulmonary stenosis, hypertension, diabetes mellitus, unilateral renal agenesis, hypothyreosis, asthma, Mb Chron disease, previous deep vein thrombosis and rheumatoid arthritis), obstetric and perinatal factors were initially compared for mortality and survival with major morbidity at 24-h, 7- or 30-day postpartum/discharge in univariate analysis using the Chi-square test. Multiple binary logistic regression (backward Wald model) was performed to determine independent risk factors associated with mortality and survival with major morbidity on outcome differences being significant in the univariate analysis. Survival or survival with major morbidity was used as dependent factor, gestational age <26 weeks, birth weight <800 g, Apgar score ≤ 3 at 5 min, survival with at least one major morbidity, multiple pregnancy and cervical insufficiency were used as covariate factors in the model for total survival. Gestational age <26 weeks, multiple pregnancy, birth weight <800 g and maternal age ≥ 35 years were used as covariate factors in the model for survival with major morbidity. Statistical analysis was performed using SPSS statistical program version 16 (SPSS, Chicago, IL, USA). The statistical significance threshold was set to $P \leq 0.05$ (2-tailed). Odds ratios (ORs) with 95% confidence intervals (95% CI) were calculated.

Results

A total of 132 infants were delivered in 109 women between 24⁺⁰ and 27⁺⁶ weeks' gestation during the study

Table 1 Maternal characteristic and obstetrical complication of gestation

	<i>n</i> = 92 (%)
Maternal age ≥ 35 years	31 (33.7)
Primipara	51 (55.4)
Pregestational disease	18 (19.6)
	(21 complications)
Pulmonary stenosis	1
Hypertention	6
Diabetes mellitus type I or type II	3
Unilateral renal agenesis	1
Hypothyreosis	3
Asthma	3
Mb Chron disease	2
Previous deep vein thrombosis	1
Remaroid arthritis	1
Pre-eclampsia	21 (22.8)
Gestational diabetes mellitus	1 (1.1)
Cervical insufficiency	8 (8.7)
Antepartum haemorrhage	17 (18.5)
Oligohydramnion	6 (6.5)
pPROM	24 (26.1)
Chorioamnionitis	20 (21.7)
Placental abruption	10 (10.9)

pPROM preterm premature rupture of membranes

period, representing 1.6% (109/6966) of total births. Extreme prematurity rates among singletons were 1.3% (89/6619) of the total births during the study period, while the corresponding rate among multiple gestations was 5.8% (20/347). 23 stillbirths were excluded, resulting in a total of 109 extremely premature newborns delivered by 92 women included in the present study. All 109 infants were transferred to the NICU at Oslo University Hospital Rikshospitalet. Maternal characteristics and obstetrical complications are presented in Table 1. In summary, 55.4% (51) were nulliparous and 19.6% (18) had different pregestational diseases. The three obstetric complications with highest frequency were pPROM, pre-eclampsia and chorioamnionitis. Neonatal survival at 28-day/discharge was 53.3% (8/15) for delivery at 24 weeks, 76.7% (23/30) for 25 weeks, 90% (27/30) for 26 weeks and 88.2% (30/34) for 27 weeks, respectively. Caesarean section was performed in 60.9% (56/92) of the cases, 26.7% (4/15) infants were delivered by caesarean section at 24 weeks, 60% (18/30) at 25 weeks, 70% (21/30) at 26 weeks and 70.6% (24/35) at 27 weeks of gestation, respectively. Major maternal and fetal indications for caesarean section were severe pre-eclampsia and preterm breech presentation among singletons.

Table 2 summarizes perinatal characteristics and neonatal survival and major morbidity. 32.1% (35/109) infants

Table 2 Perinatal characteristics and neonatal survival and major morbidity

	<i>n</i> = 109 (%)
Gender	
Male	58 (53.2)
Female	51 (46.8)
IUGR	19 (17.4)
Multiple pregnancy	45 (31.8)
Twins	25 (22.9)
Triplets	6 (5.5)
Quadruplets	4 (3.7)
Weeks of gestation	
24 ⁺⁰ –24 ⁺⁶	15 (13.8)
25 ⁺⁰ –25 ⁺⁶	30 (27.5)
26 ⁺⁰ –26 ⁺⁶	30 (27.5)
27 ⁺⁰ –27 ⁺⁶	34 (31.2)
Birth weight (g)	
<500	5 (4.6)
500–599	10 (9.2)
600–699	18 (16.5)
700–799	20 (18.3)
800–899	19 (17.4)
900–999	16 (14.7)
>1,000	21 (19.3)
Apgar score ≤ 3 at 5 min	11 (10.1)
Survival postpartum	
24-h	102 (93.6)
7-day	92 (84.4)
28-day/discharge	88 (80.7)
Survival with at least one major morbidity	
24-h	44 (40.4)
7-day	35 (32.1)
28-day/discharge	32 (29.4)
Major morbidity (with at least one)	51 (46.8)
Intraventricular haemorrhage grade 3–4	17 (15.6)
Periventricular leukomalacia	5 (4.6)
Bronchopulmonary dysplasia	29 (26.6)
Necrotizing enterocolitis	5 (4.6)

IUGR intrauterine growth restriction

were born of multiple pregnancies and bronchopulmonary dysplasia had the highest incident rates of 26.6% (29/109) among major morbidities.

Table 3 shows the relation between total survival and maternal, obstetric and perinatal characteristics in univariate analysis. 24-h, 7- and 28-day/discharge survival was significantly lower in the group with birth weight <800 g compared with birth weight ≥ 800 g, as well as in the group with gestational age <26 weeks compared with gestational age ≥ 26 weeks, with a 5-min Apgar score ≤ 3 compared

Table 3 Relation between neonatal survival and maternal, obstetric and neonatal characteristics in univariate analysis

	24-h			7-day			28-day/discharge		
	Alive	Dead	<i>P</i>	Alive	Dead	<i>P</i>	Alive	Dead	<i>P</i>
Maternal age ≥ 35 years	29.4 (30)	57.1 (4)	0.126	30.4 (28)	35.3 (6)	0.691	28.4 (25)	42.9 (9)	0.199
Nulliparous	56.9 (58)	42.9 (3)	0.47	58.7 (54)	41.2 (7)	0.18	60.2 (53)	38.1 (8)	0.066
Pregestational disease	19.6 (20)	14.3 (1)	0.73	18.5 (17)	23.5 (4)	0.628	19.3 (17)	19 (4)	0.977
Pre-eclampsia	18.6 (19)	28.6 (2)	0.519	19.6 (18)	17.3 (3)	0.854	20.5 (18)	14.3 (3)	0.52
Antepartum haemorrhage	16.7 (17)	28.6 (2)	0.422	16.3 (15)	23.5 (4)	0.471	17 (15)	19 (4)	0.828
pPROM	23.5 (24)	42.9 (3)	0.252	25 (23)	23.5 (4)	0.897	26.1 (23)	19 (4)	0.499
Cervical insufficiency	15.7 (16)	0 (0)	0.257	12 (11)	29.4 (5)	0.062	11.4 (10)	28.6 (6)	0.045
Oligohydramnion	4.9 (5)	14.4 (1)	0.292	5.4 (5)	5.9 (1)	0.941	5.7 (5)	4.8 (1)	0.868
Chorioamnionitis	21.6 (22)	28.6 (2)	0.665	20.7 (19)	29.4 (5)	0.423	20.5 (18)	28.6 (6)	0.42
Placental abruption	9.8 (10)	14.3 (1)	0.703	8.7 (8)	17.6 (3)	0.26	9.1 (8)	14.3 (3)	0.478
IUGR	18.6 (19)	0 (0)	0.209	18.5 (17)	11.8 (2)	0.503	17 (15)	19 (4)	0.828
Gestational age < 26 weeks	38.2 (39)	85.7 (6)	0.014	34.8 (32)	76.5 (13)	0.001	35.2 (31)	66.7 (14)	0.009
Multiple pregnancy	67.7 (69)	71.4 (5)	0.836	72.8 (67)	41.2 (7)	0.01	73.9 (65)	42.9 (9)	0.006
Caesarean section	62.7 (64)	42.9 (3)	0.536	60.9 (56)	64.7 (11)	0.883	60.2 (53)	66.7 (14)	0.787
Male infants	51 (52)	85.7 (6)	0.075	50 (46)	70.6 (12)	0.118	48.9 (43)	71.4 (15)	0.063
Birth weight < 800 g	46.1 (47)	85.7 (6)	0.042	43.5 (40)	76.5 (13)	0.012	42 (37)	76.2 (16)	0.005
Apgar score ≤ 3 at 5 min	4.9 (5)	85.7 (6)	< 0.005	4.3 (4)	41.2 (7)	< 0.005	4.5 (4)	33.3 (7)	< 0.005
At least one major morbidity	43.1 (44)	100 (7)	0.004	38 (35)	94.1 (16)	< 0.005	36.4 (32)	90.5 (19)	< 0.005

Values are expressed in % (no.)

pPROM preterm premature rupture of membranes, IUGR intrauterine growth restriction

with 5-min Apgar score > 3 and in the group with at least one major morbidity compared the babies without any morbidity. Besides, 7- and 28-day/discharge survival were significantly lower in multiple pregnancies compared with singletons.

Table 4 shows the relation between neonatal survival with at least one major morbidity and maternal, obstetric and perinatal characteristics in univariate analysis. 24-hour, 7- and 28-day/discharge survival with at least one major morbidity were significantly lower in the group with birth weight < 800 g compared with birth weight ≥ 800 g, in the group with gestational age < 26 weeks compared with gestational age ≥ 26 weeks, and in multiple pregnancies compared with singletons. Neonatal survival with at least one major morbidity was not significantly associated with pregestational maternal disease, obstetric factors and method of delivery, except that 7-day survival was significantly lower in the group with maternal age ≥ 35 years compared with < 35 years.

Multiple binary logistic regression was performed to determine independent risk factors associated with mortality and survival with major morbidity. A 5-min Apgar score ≤ 3 was the only independent risk factor for 24-h survival (OR 136.7, 95% CI 11.6–1618.6). Because of a quasi-complete separation (all 7 babies who died within 24 h postpartum had at least one major complication), the

maximum likelihood estimates do not exist for 24-h survival for babies with at least one major morbidity in multiple logistic regression analysis. Both the 5-min Apgar score ≤ 3 and babies with at least one major morbidity had significantly independent effects on 7-day (OR 13, 95% CI 2.6–66; OR 11.9, 95% CI 1.3–106.7) and 28-day/discharge survival (OR 10.2, 95% CI 2.1–50.8; OR 8.1, 95% CI 1.4–45.7). However, multiple pregnancy and gestational age < 26 weeks were the only two independent risk factors for survival with at least one major morbidity on 24-h (OR 5.9, 95% CI 2.1–16.4; OR 7.9, 95% CI 3.0–21.2), 7-day (OR 3.9, 95% CI 1.3–11.6; OR 7.7, 95% CI 2.8–21.4) and 28-day/discharge survival (OR 5.2, 95% CI 1.6–17.0; OR 9.5, 95% CI 3.2–28.6).

Discussion

Estimates of survival and morbidity of extreme prematurity ranged widely, partially because of differences in criteria for selection and in measures of outcomes, in organization of care, in attitude towards resuscitation and life support. In addition, most of the studies were based on a small number of extremely premature newborns. Synnes et al. [10] studied infants born at 23–28 weeks of gestation from 1983 to 1989 in 1,024 births and showed that gestational age

Table 4 Relation between neonatal survival with at least one major morbidity and maternal, obstetric and neonatal characteristics in univariate analysis

	24-h			7-day			28-day/discharge		
	Yes	No	<i>P</i>	Yes	No	<i>P</i>	Yes	No	<i>P</i>
Maternal age ≥ 35 years	36.2 (16)	24.1 (14)	0.18	42.9 (15)	22.8 (13)	0.042	37.5 (12)	23.2 (13)	0.153
Nulliparous	50 (22)	62.1 (36)	0.223	54.3 (19)	61.4 (35)	0.501	59.4 (19)	40.6 (13)	0.902
Pregestational disease	20.5 (9)	19 (11)	0.851	17.1 (6)	19.3 (11)	0.796	18.8 (6)	19.6 (11)	0.919
Pre-eclampsia	15.9 (7)	20.7 (12)	0.539	20 (7)	19.3 (11)	0.934	21.9 (7)	19.6 (11)	0.803
Antepartum haemorrhage	11.4 (5)	20.7 (12)	0.211	8.6 (3)	21.1 (12)	0.116	9.4 (3)	21.4 (12)	0.148
pPROM	15.9 (7)	29.3 (17)	0.114	20 (7)	28.1 (16)	0.385	21.9 (7)	28.6 (16)	0.492
Cervical insufficiency	22.7 (10)	10.3 (6)	0.89	14.3 (5)	10.5 (6)	0.589	12.5 (4)	10.7 (6)	0.8
Oligohydramnion	4.5 (2)	5.2 (3)	0.885	5.7 (2)	5.3 (3)	0.926	6.2 (2)	5.4 (3)	0.862
Chorioamnionitis	15.9 (7)	25.9 (15)	0.226	11.4 (4)	26.3 (15)	0.087	9.4 (3)	26.8 (15)	0.051
Placental abruption	9.1 (4)	10.3 (6)	0.833	5.7 (2)	10.5 (6)	0.426	6.3 (2)	10.7 (6)	0.483
IUGR	15.9 (7)	20.7 (12)	0.539	17.1 (6)	19.3 (11)	0.796	15.6 (5)	17.9 (10)	0.789
Gestational age <26 weeks	61.4 (27)	20.7 (12)	<0.005	20 (21)	19.3 (11)	<0.005	62.5 (20)	19.6 (11)	<0.005
Multiple pregnancy	50 (22)	19 (11)	0.001	40 (14)	19.3 (11)	0.03	40.6 (13)	17.9 (10)	0.019
Caesarean section	63.6 (28)	62.1 (36)	0.681	60 (21)	61.4 (35)	0.713	59.4 (19)	60.7 (34)	0.73
Male infants	54.5 (24)	48.3 (28)	0.53	54.3 (19)	47.3 (27)	0.519	53.1 (17)	46.4 (26)	0.545
Birth weight <800 g	61.4 (27)	34.5 (20)	0.007	60 (21)	33.3 (19)	0.012	59.4 (19)	32.1 (18)	0.013
Apgar score ≤ 3 at 5 min	6.8 (3)	3.4 (2)	0.435	5.7 (2)	3.5 (2)	0.615	6.2 (2)	3.6 (2)	0.562

Values are expressed in % (no.)

pPROM preterm premature rupture of membranes, IUGR intrauterine growth restriction

(GA)-specific mortality rates decreased with increasing GA. The mortality rate was 84% at 23 weeks, 57% at 24 weeks, 45% at 25 weeks, 37% at 26 weeks, 23% at 27 weeks and 13% at 28 weeks GA. In a large Norwegian cohort study [5] including 903,402 infants without congenital anomalies born alive between 1967 and 1983 and followed through 2003, survival rates were only 17.8% at 23–27 weeks of gestation. In a recent review of data available in 2007 [11], survival figures for live births from a number of large, population-based cohort studies on premature births between 1990 and 1997 were summarized. At 24 weeks gestation, mean survival ranged from 16 to 44%, corresponding figures were 33–64% at 25 weeks, 54–68% at 26 weeks and 68–85% at 27 weeks, respectively. A Norwegian nationally based cohort study [12] investigated all infants with a gestational age 22–27 completed weeks or a birth weight 500–999 g who were born in Norway in 1999 and 2000. It reported the survival rates for all infants admitted to NICU of 60% for 24 weeks, 80% for 25 weeks, 84% for 26 weeks and 93% for 27 weeks, respectively. In our study, the neonatal survival rate was higher compared with previous studies [5, 10] and those survival data reviewed in 2007 [11], but was consistent with the Norwegian population-based study [12]. Perinatal care has changed dramatically over the past 20 years. New treatment strategies including antenatal steroid therapy and

surfactant administration have contributed in preventing mortality and morbidity of extremely preterm infants [13, 14]. The two previous studies mentioned before [5, 10] included premature births before 1990, where antenatal steroid therapy and surfactant administration were not available. However, administration of antenatal steroid was a standard treatment in our study population. This may partially explain why neonatal survival in our study is higher than the two previous studies.

None of the pregestational maternal diseases, obstetric complications and mode of delivery proved to be a significant risk factor of neonatal mortality of extreme prematurity in the present study, which was inconsistent with some previous studies [15, 16], but in accordance with others [8, 17]. A 5-min Apgar score ≤ 3 and infants with at least one major morbidity were the only two independent predictors of neonatal mortality at 7 and 28 days postpartum/discharge in the present study. A Low 5-min Apgar score has previously been reported as a predictor of neonatal mortality. Locatelli et al. [18] showed that small for gestational age and birth weight, female gender, low 5-min Apgar score and failure of steroid administration were independent predictors of survival in infants weighing 750 g or less. Cumulatively, these five predictors explained 69% of neonatal survival. A recent study from India [16] showed common antenatal and perinatal predictors of mortality in

VLBW infants (500–1,500 g and >26 weeks' gestations), including maternal bleeding, failure to administer antenatal steroids, low Apgar score, apnoea, extreme prematurity, neonatal septicaemia and shock. Previous studies showed that chorioamnionitis was not only significantly associated with higher short-term but also higher long-term major morbidity of immature neonates, such as intraventricular haemorrhage, bronchopulmonary dysplasia and necrotizing enterocolitis, cerebral palsy and early childhood asthma [15, 19, 20]. In the present study, clinical chorioamnionitis only showed an increased trend towards neonatal morbidity in the univariate analysis, a factor which could have been influenced by the small number of subjects. A large sampling would improve the precision of estimates of chorioamnionitis on the outcome of extremely premature infants.

Results of studies on survival of preterm twins, by comparison with preterm singletons matched for gestational age, are conflicting. Some studies showed that extremely premature twins do not suffer more deaths than singletons [21, 22], while others have shown an increased mortality compared with singletons [10, 23]. A recent population-based study on mortality of twin and singleton live births under 30 weeks' gestation [24] showed that the increased mortality among twins of less than 30 weeks' gestation between 1998 and 2001 was confined to 25 weeks or less than singletons. However, there appeared to be no excess mortality in twin neonates less than 30 weeks' gestation when compared with singletons delivered between 2002 and 2005. This is consistent with our findings based on the data 2004–2007 that extremely prematurity multiple infants appeared to have no excess neonatal mortality than singletons.

There was a trend in the obstetric management of preterm labour in the direction of more active policies with caesarean section to avoid traumatic and asphyxial damage to the baby. Solum [25] suggested that caesarean section might be used liberally due to the fragility of the immature fetus and any kind of birth trauma should be minimized. When complicated by breech presentation, delivery seems to be best performed by the abdominal route. The guidelines of our institution state that premature fetuses between 25 and 34 weeks' gestation complicated by breech presentation should be delivered by caesarean section. There are conflicting data regarding the outcome of caesarean section in delivering extremely premature infants before 26 weeks' gestation. Some studies showed that caesarean section was associated with improved neonatal survival and morbidity [4, 26], while others failed to show any survival benefit [17, 27]. Mukhopadhyay et al. [27] showed that the survival rates for newborns delivered by caesarean section for fetal reasons before 26 weeks is very poor and suggested that caesarean section before 26 weeks should therefore be performed predominantly for maternal reasons only. In the

present study, caesarean section showed neither survival nor morbidity benefit for these extremely premature infants. Among the four infants at 24 weeks' gestation who were delivered by caesarean section, there was one triplet pregnancy where all infants died before 7-day postpartum. The one survivor was a singleton with 5-min Apgar score of 9 which still suffered from both periventricular leukomalacia and bronchopulmonary dysplasia. Indeed, preterm caesarean section is technically difficult and does sometimes require vertical lower segment incision with possible adverse consequences on future pregnancy. Maternal co-morbid and life-threatening conditions further complicate the issue. Excess morbidity was observed among survivors of extremely premature multiple infants and babies that were delivered before 26 weeks of gestation in the present study. Therefore, offering caesarean section deliveries to infants before 26 weeks of gestation, especially to multiple infants, should be carefully judged against the short- and long-term neonatal outcome.

Conflicts of interest between parents facing the risk of a handicapped child and/or between parents and society are likely to be encountered in cases of extreme prematurity, thus making it essential for the medical staff to give preference to the patient's best interests. In a New South Wales and Australian Capital Territory multidisciplinary workshop with consumers' and parents' participation and extended consultations [28], there was consensus that there was an increasing obligation to treat cases involving between 23⁺⁰ and 25⁺⁶ weeks of gestation, while it was acceptable not to initiate intensive care following appropriate counselling with the parents. In Norway, the gestational age limit for offering resuscitation should be 23–25 completed weeks and within this range an individual approach is appropriate (Norwegian Research Council 1999). Although the present study showed that gestational age was not a significant predictor of neonatal mortality of extremely premature newborns, an excess morbidity rate among infants who were delivered before 26 weeks of gestation and among multiple infants was observed. The present study highlights that decisions about obstetric management and resuscitation of extremely preterm infants should be a collaborative process combining multidisciplinary team management and the wishes of parents before/during labour and after delivery, especially for multiple infants and babies who were delivered before 26 weeks of gestation.

The strength of our study is that high-quality medical care is readily accessible to all extremely premature live births, which assures a degree of uniformity of management. However, a retrospective study such as our study also has several limitations. First, as suggested above, it has the attendant limitations of a hospital-based study with a possible risk of selection bias. Second, it failed to adjust for all

confounding/intermediate variables, which may affect perinatal outcomes of extremely premature infants but are not commonly collected in the administrative database, such as rates, smoking practices and alcohol exposure. Another weakness was the small number of subjects included in the study; a large sampling would improve the precision of estimates of outcome. Hence some of our results require a rather cautious interpretation.

Conclusions

Neonatal survival was significantly predicted by a 5-min Apgar score and neonatal morbidity, independent of pregestational maternal disease, obstetric complications, method of delivery, gestational age and birth weight in extreme preterm deliveries. The excess morbidity rate was confined among multiples and babies who were delivered before 26 weeks of gestation.

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Conflict of interest The authors report no conflicts of interest.

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