



# Factors Associated with Increased Risk of Death in Extremely Preterm Infants – Prospective Unicentric Study over Eleven Years

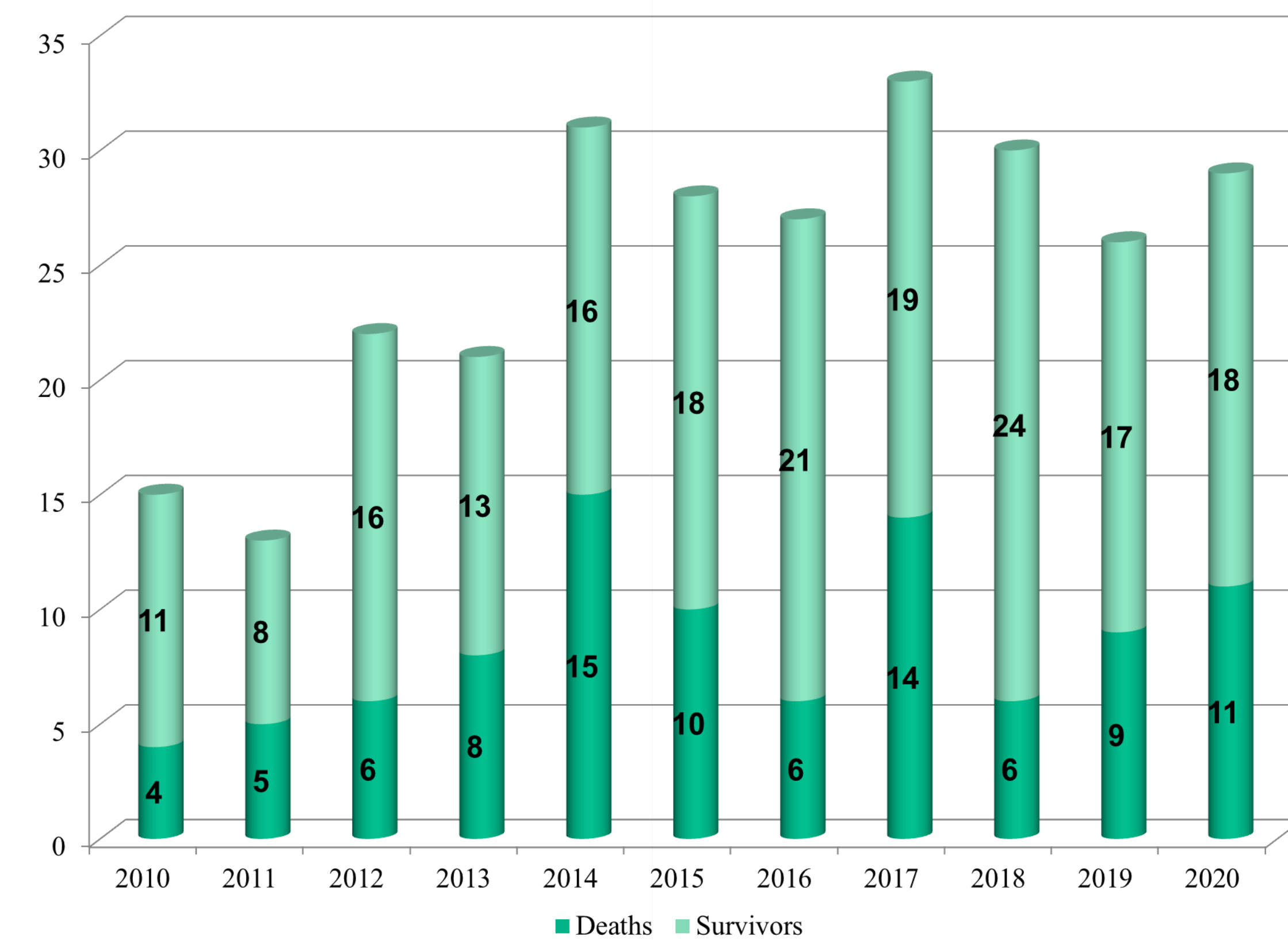
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**Background:** New diagnostic, treatment protocols and modern respiratory support have significantly improved survival rates of extremely preterm infants (EP)

**Objective:** To identify perinatal factors associated with increased risk of death among EP.



**Methods:** All EP (gestational age  $\leq 28$  weeks) cared for in our tertiary NICU between January 1, 2010 and December 31, 2020 were included (N=277). Perinatal maternal and neonatal data, data related to neonatal care, treatment, and complications were prospectively collected in the database of our unit. Data of surviving EP were compared to data of EP that died before discharge from the maternity hospital. Statistical analysis was performed using IBM SPSS Statistics 23.0,  $p < 0.05$  being considered statistically significant.

	Survivors (N = 183)	Deaths (N = 94)	P value	OR (95% CI)
Gestational age (weeks)(mean $\pm$ SD)	26.8 $\pm$ 1.3	25.5 $\pm$ 1.6	<0.001	-
Birth weight (g) (mean $\pm$ SD)	954 $\pm$ 189	797 $\pm$ 206	<0.001	-
Male gender (N/%)	92/50.3	59/62.8	0.048	1.41(0.99-1.98)
SGA (N/%)	100/54.6	54/57.4	0.658	1.04(0.88-1.23)
Complicated pregnancy (N/%)	103/56.3	53/56.4	0.988	1.00(0.84-1.18)
C-section (N/%)	60/32.8	25/26.6	0.292	0.91(0.76-1.08)
PPROM >18 h (N/%)	44/24.0	20/21.3	0.606	0.95(0.78-1.15)
Prenatal corticosteroids (N/%)	121/66.1	49/52.1	0.024	0.81(0.67-0.98)
Outborn (N/%)	29/15.8	22/23.4	0.125	1.20(0.93-1.55)

Tabel 1. Neonatal and maternal characteristics

	Survivors (N = 183)	Deaths (N = 94)	P value
Apgar score at 1 minute (mean $\pm$ SD)	5.8 $\pm$ 1.9	4.4 $\pm$ 2.1	<0.001
Apgar score at 5 min. (mean $\pm$ SD)	7.0 $\pm$ 1.4	6.1 $\pm$ 1.7	<0.001
FiO2 at 1 hour (mean $\pm$ SD)	40.5 $\pm$ 20.4	53.1 $\pm$ 26.6	0.003
FiO2 at 12 hours (mean $\pm$ SD)	32.7 $\pm$ 16.1	39.9 $\pm$ 20.3	0.034
FiO2 at 18 hours (mean $\pm$ SD)	30.8 $\pm$ 14.8	41.9 $\pm$ 25.8	0.002
FiO2 at 24 hours (mean $\pm$ SD)	28.8 $\pm$ 12.6	38.3 $\pm$ 23.6	0.002
PEEP/CPAP at 1 hour in DR (cmH <sub>2</sub> O)(mean $\pm$ SD)	6.5 $\pm$ 0.3	6.7 $\pm$ 0.5	0.009
Mean blood pressure DOL1 (mmHg) (mean $\pm$ SD)	36.7 $\pm$ 7.0	35.0 $\pm$ 7.5	0.199
Temperature at NICU admission(°C)(mean $\pm$ SD)	36.2 $\pm$ 1.1	35.5 $\pm$ 1.7	0.009
Cord blood pH (mean $\pm$ SD)	7.25 $\pm$ 0.07	7.21 $\pm$ 0.14	0.032
Hemoglobin at birth (g/dL)(mean $\pm$ SD)	15.5 $\pm$ 1.9	15.2 $\pm$ 2.3	0.012
Creatinine, max. DOL1-3 (mg/dL)(mean $\pm$ SD)	1.04 $\pm$ 0.36	1.16 $\pm$ 0.40	0.028

Table 2. Baseline neonatal status

	Survivors (N = 183)	Deaths (N = 94)	P value	OR (95% CI)
Need for resuscitation (N/%)	145/79.2	84/89.4	0.035	1.25(1.05-1.49)
Intubation at birth (N/%)	23/12.6	33/35.1	<0.001	1.76(1.27-2.44)
Surfactant via INSURE (N/%)	82/44.8	32/34.0	0.085	0.86(0.73-1.02)
INSURE/LISA failure (N/%)	26/32.1	19/59.1	0.007	1.40(1.06-1.84)
Surfactant (N/%)	141/77.0	82/87.2	0.043	1.23(1.03-1.46)
Mechanical ventilation (N/%)	70/38.3	85/90.4	<0.001	2.05(1.71-2.46)
Barotrauma (N/%)	7/3.8	3/3.2	0.790	0.94(0.62-1.43)
NEC (N/%)	10/5.5	33/35.1	<0.001	3.18(1.84-5.50)
IVH (N/%)	86/47.3	47/54.0	0.301	1.09(0.92-1.29)
IVH grade 3 and 4 (N/%)	8/9.3	23/50.0	<0.001	-
PVL (N/%)	14/7.7	6/6.9	0.817	0.96(0.71-1.30)
PDA (N/%)	127/74.7	81/86.2	0.029	1.26(1.05-1.51)
EOS (N/%)	51/27.9	26/27.7	0.971	0.99(0.83-1.20)
LOS (N/%)	85/46.4	29/30.9	0.012	0.8(0.68-0.95)
Severe hydrocephalus (N/%)	8/7.6	23/32.9	<0.001	2.61(1.42-4.79)

Table 3. Interventions, complications, and outcomes

**Conclusions:** Comparative analysis showed that lower GA, BW, Apgar scores at 1 and 5 minutes, worse clinical status at birth – need for resuscitation and intubation in the delivery room - followed by higher oxygen needs in the first 24 hours of life, lower temperature and pH at NICU admission, higher levels of creatinine during the first 3 days of life were associated with significantly increased risk of death ( $p < 0.05$ ). INSURE failure, need of mechanical ventilation, PDA presence, NEC, severe IVH, and severe hydrocephalus were significantly more often found in EP that died. Prenatal corticosteroid administration emerged as a protective factor.

**Further improvement of perinatal and respiratory care is mandatory** as most of the factors identified in association with risk of death in EP in this univariate analysis are related to clinical status at birth, resuscitation, and stabilization in the first hours of life, indicating areas to target for further improvement of neonatal intensive care of EP.