Original Research Article

MAJOR MORBIDITY AND SURVIVAL OF EXTREMELY PRETERM INFANTS IN TERTIARY HOSPITAL

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Abstract: *The retrospective study was conducted in the Peadiatrics Department of Nishter Medical Hospital & CH & ICH Multan from January 2010 to January 2020 to evaluate major morbidity and survival rate in extremely preterm infants. A total of 9095 infants were included in the study. The study participants were divided into 2 groups. Group I included infants who survived for less than 1 day, and Group II included infants who survived for more than 1 day. Detailed information regarding infant and maternal characteristics, birth certificates, prenatal care, antenatal conditions, death records, and all maternal and infant record from a year before to a year after birth was derived from the database of the hospital. Results show that infants born at 22-24 weeks had neonatal morbidities, including retinopathy of prematurity, sepsis, bronchopulmonary dysplasia, necrotizing enterocolitis, periventricular leukomalacia or grade III or IV IVH (Table I). 9% (818 infants) of survivors had grade III or IV intraventricular hemorrhage, and 3% (273 infants) had PVL, infants born at 22nd to 23rd weeks were at higher risk of developing these complications. Almost 80% of infants born at 22-25 weeks gestation suffered from at least one major morbidity. The 1-year survival rate of infants born at 22, 23, and 24 weeks was 5.9%, 27%, and 59.9%, respectively. It is concluded that less than half of the infants born at the lowest gestational ages (22 and 23 weeks) survive after resuscitation, and two-thirds have more than 1 major morbidity.*

Keywords: Extremely preterm infants, neonatal morbidity, mortality, survival

Introduction

Advances in neonatal care are improving survival rates at early gestational age. However, decreased gestational age increases the rate of neonatal morbidity and mortality (Norman et al., 2019). Various studies approve of this trend; however, absolute morbidity and mortality rate at the earliest gestational age is variable (Lee et al., 2020; Rysavy et al., 2020). Extremely preterm infants are at increased risk of developing sepsis, necrotizing enterocolitis, also retinopathy of prematurity, intraventricular hemorrhage, bronchopulmonary dysplasia, and white matter damage (Kim et al., 2023). This poses a significant challenge for neonatologists. According to research, the premature birth rate in developed countries like UK, Greece, Turkey, and Germany was 73%, 75%, 69%, and 63%, respectively (Kim et al., 2023). Such infants' survival rate has significantly improved over the last twenty years. The survival rate in Germany increased from 42% to 54% during 1996-2018 (Kim et al., 2023). Russia has had a 3% increase in survival rate every year from 19096 to 2019 (Nørgaard et al., 2021).

Moreover, countries and hospitals have variable resuscitation practices before 26 weeks (Lee et al., 2020). The American College of Obstetricians and Gynecologists and the American Academy of Pediatrics acknowledged widely variable practices and treatment outcomes in infants born earlier than 26 weeks (Rossi et al., 2019). It was recommended that newborn cohort and population-based studies be conducted to analyze resuscitation practices and treatment outcomes in extremely preterm infants. Though, some countries have population based research, there is scarcity of local data on in this field. Thus, the aim of this study is to evaluate major morbidity and survival rate in extremely preterm infants born during 2010 to 2020 in Pakistan.

Methodology

The retrospective study was conducted in the Peadiatrics Department of Nishtar Medical Hospital & CH & ICU Multan from January 2010 to January 2020. The ethical board of the hospital approved the

study. The study population included live infants born between the 22nd and 28th weeks of gestation. Infants with congenital structural disabilities or chromosomal abnormalities were excluded. A total of 9095 infants were included in the study. Detailed information regarding infant and maternal characteristics, birth certificates, prenatal care, antenatal conditions, death records, and all maternal and infant record from the year before to a year after birth was derived from the database of the hospital. Ultrasound, or the last menstrual cycle, was used for estimating gestational age. NICU care was classified as short-term ventilatory support, long-term ventilator support, and full-range neonatal care services such as surgeries and NICUs. Death certificates and discharge information was used for deriving mortality measures. Maternal data, including maternal hypertension, chorioamnionitis, and gestational diabetes, was also recorded. Neonatal data including grade III or IV intraventricular hemorrhage (IVH), bronchopulmonary dysplasia (BPD), sepsis, periventricular leukomalacia (PVL), retinopathy of prematurity (RoP) and necrotizing enterocolitis (NEC) was recorded. Life-saving interventions were recorded, including noninvasive mechanical ventilation, cardiopulmonary resuscitation, insertion of endotracheal tube and continuous invasive mechanical ventilation. The study participants were divided into 2 groups. Group I included infants who survived for less than 1 day, and Group II included infants who survived for more than 1 day.

SPSS version 23.0 was used for data analysis. Bivariate analysis was done to compare perinatal and maternal characteristics between both groups using Student's t-test and χ^2 test for continuous and categorical variables, respectively. P value < 0.05 was considered statistically significant.

Results

The mean birth weight at 22 weeks was 489g, and at 28 weeks was 1116g. There were 54% male infants and 78% singleton births. The frequency of cesarean delivery at 22 weeks was 15%, and at 28 weeks was 74%. 2546(27.9%) infants died within the first year. The 1-year survival rate of infants born at 22, 23, and 24 weeks was 5.9%, 27%, and 59.9%, respectively. The survival rate increased from 77% on the 25th to 93% on the 28th week. 71% of total deaths occurred in infants born at 22-24 weeks, 82% in the first week and 95% in the first month of life. After 6 days, the survival rate at all gestational ages remained higher than 90%. The survival rate at all gestational ages was higher than 95% during the postneonatal period. Only 1.1% (109 infants) deaths occurred after NICU discharge.

The frequency of morbidity at different gestational ages is summarized in Table I. Infants born at 22-24 weeks had neonatal morbidities, including RoP surgery, sepsis, BPD, NEC PVL, or grade III or IV IVH. 9% (818 infants) of survivors had grade III or IV IVH, and 3% (273 infants) had PVL, infants born at 22nd to 23rd weeks were at higher risk of these complications. About 8% (727 infants) had NEC; however, infants born at 22nd -23rd weeks were at increased risk. The BPD rate at 22 weeks gestation was 65% and decreased to 21% at 28 weeks. The sepsis rate decreased from 68% at 22 weeks gestation to 42% at 28 weeks. Infants born at 22nd – 24th weeks had the highest risk of developing RoP. Almost 80% of infants born at 22-25 weeks gestation suffered from at least one major morbidity. Infants born at 22-23 weeks had more than one major morbidity.

Resuscitation was done in 22%, 65%, and 94% of infants born at the 22nd, 23rd, and 24th weeks respectively. 1-year survival rate was 32%, 43%, and 65% at 22, 23, and 24 weeks respectively (Table II). The largest increase in survival after resuscitation was seen in infants born at 23-24 weeks. Resuscitation attempt at increased gestational age was also associated with decreased risk of major morbidity.

Bivariate analysis showed that the female sex and higher birth weight were significantly associated with the increased survival rate of the infants (P<.001). Cesarean section was associated with an increase in the survival rate of the infants born at 22-24 weeks (P=.003). Resuscitation attempt was associated with an increased survival rate in infants born to mothers >34 years old (P=.001) and who have more than 12 years of education (P=.013). Resuscitation at NICU that conferred survival benefits was also associated with an increase in survival rate (P=.001)

Table I Major Morbidity in Survivors

Variables	Gestational age (weeks)							
	22 n=176	23 n=314	24 n=582	25 n=700	26 n=950	27 n=1500	28 n=1841	22-24 n=6063
Any major morbidity n (%)	153 (87%)	278 (88.5%)	494 (85%)	560 (80%0	678 (71.4%)	915 (61%)	994 (54%)	4072 (67.1%)

More than 1 morbidity n (%)	115 (68.4%)	207 (65.9%)	331 (56.8%)	315 (45%)	314 (33%)	367 (24.6%)	304 (16.5%)	1953 (32.2%)
None n (%)	25 (14%)	31 (9.8%)	84 (14.4%)	140 (20%)	271 (28.5%)	555 (37%)	856 (46.5%)	1962 (32.3%)

Table II Attempted Resuscitation and Survival

	Gestational age (weeks)							
Variables	22 n=570	23 n=602	24 n=769	25 n=890	26 n=1554	27 n=2150	28 n=2560	22-28 n=9095
Total survival (n,%)	37 (6.5%)	112 (17%)	239 (31%)	394 (44.2%)	1119 (72%)	1705 (70.3%)	2457 (95.9%)	6063 (66.6%)
Survived ≤ 1 day (n)	478	299	135	67	38	38	24	1079
CPR or ventilation/intubation (n,%)	27 (5.7%)	79 (26.4%)	77 (57%)	41 (61.1%)	32 (84.2%)	28 (73.6%)	16 (66.6%)	300 (28%)
Survived ≥1 day (n)	73	406	651	833	1300	1967	2447	7677
CPR or ventilation/intubation (n,%)	49 (67%)	373 (92%)	631 (97%)	816 (97.9%)	1244 (95.7%)	1809 (91.9%)	2177 (89)	7099 (92.4%)
Resuscitation attempted (n,%)*	125 (22%)	391 (65%)	723 (94%)	872 (98%)	1487 (95.7%)	1971 (91.6%)	2288 (89.3%)	7857 (86.3%)
Survival after resuscitation (n, %)	20 (16%)	88 (22.5%)	370 (51%)	699 (67%)	1106 (74.3%)	1697 (86%)	2083 (91%)	6063 (77.1%)
Survival without any major morbidity (n,%)	6 (4.6%)	17 (4.3%)	92 (66.5%)	138 (15.8%)	381 (25.6%)	686% (34.8%)	997 (43.6%)	2317 (29.4%)

*Survived ≤1 day and CPR attempted or survived ≥1 day.

Discussion

In the current study, 1-year survival of extremely preterm infants born at 22-28 weeks was significantly associated with gestational age. Our study's survival and resuscitation rates are similar to the previous study (Crilly et al., 2021). In this study, almost 80% of infants born at 22-25 weeks gestation suffered from at least one major morbidity. Infants born at 22-23 weeks had more than one major morbidity. RoP, sepsis, NEC, BPD, PVL, and IVH cause neurodevelopmental impairment (Aubert et al., 2023). Previous studies show that extremely preterm infants are at risk of major morbidities, including cognitive and behavioral impairment and cerebral palsy, significantly hindering normal life activities later (O'Reilly et al., 2020). In our study, the 1-year survival rate after resuscitation was 32%, 43%, and 65% at 22, 23, and 24 weeks respectively. A previous study showed that the survival rate after resuscitation at 22 weeks was 28%-31%, and at 23 weeks, it was 41%-43%. At 24 weeks was 64%, and at 25 weeks was 81%-80 %(Bell et al., 2022). Another study showed that survival rates at 22, 23, 24, and 25 weeks were 7%, 24%, 44%, and 65%, respectively (Hashmi et al., 2021). This difference may be due to variations in active treatment or resuscitation techniques in different settings. A study conducted by Ramachandran et al. showed that hospital survival depends on treatment initiation in hospitals (Ramachandran et al., 2022). Previous studies were conducted on macro variation in resuscitation practice and practitioners' decision-making (Myrhaug et al., 2019). Population-based studies are required to understand how variation in regional practices affects the mortality rate.

In the current study, maternal and perinatal characteristics like female sex and higher birth weight were associated with increased survival, as reported in a previous study (Kono and Japan, 2021). However, there was no association between singleton birth and survival. In our study, extremely preterm infants born at well-maintained NICU had an increased survival rate, which is in line with the finding of a previous study (Janevic et al., 2021). Moreover, maternal age and socio-demographic education factors were also associated with survival after resuscitation. A previous study by Mehra et al. also reported the association between survival rate and maternal race, age, income, and education (Mehra et al., 2019). However, more research is required to understand how such factors impact survival.

The strength of our study is that it was conducted on a large sample, and morbidity and mortality up to a year of life were studied. The limitation of our study is that we were unable to retrieve record bout antenatal steroid exposure; studies have shown its

association with increased survival rate (Crilly et al., 2021). Another limitation is that many preterm infants born at 22-28 weeks did not have complete hospital records and discharge certificates, so they could not be included in the study. Moreover, neurodevelopmental outcomes were not followed up in the long term. More detailed studies are needed to understand outcomes in the longer term.

Conclusion

Less than half of the infants born at the lowest gestational ages (22 and 23 weeks) survive after resuscitation, and two-thirds have more than 1 major morbidity.

Conflict of interest

The authors declared absence of conflict of interest.

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