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Original Research Article

Mortality and major morbidity profile of extremely preterm newborns at a tertiary level neonatal intensive care unit in Western India

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ABSTRACT

Background: Extremely premature newborns are at highest risk of mortality and long-term morbidities. A few studies were conducted on the outcomes of extreme preterm newborns in developing countries like India.
Methods: This retro prospective observational study was done at neonatal intensive care unit of Deenanath Mangeshkar hospital, Pune, a tertiary care hospital in Maharashtra. Study included all extremely preterm newborns over a period of 32 months.
Results: Among 64 eligible newborns, overall mortality rate was 35.9%. Overall survival to discharge among study population was 53.1%. Survival to discharge increased with advancing gestational age:20 % at 23 weeks, 12.5% at 24 weeks, 37.5% at 25 weeks, 46.7% at 26 weeks, 81.5% at 27 weeks of gestational age. 90.6% newborns had any 1 major morbidity and 17.4% newborns survived without any major morbidity. The major morbidities in this study were 60.9% moderate -severe BPD, 9.4% PVL,4.7% severe IVH ,1.6% definite NEC, 45.3 % sepsis, 1.6 % severe ROP. Other morbidities such as RDS (95%), Apnoea of prematurity (83%), Anaemia of prematurity (69%), HsPDA (56%) and SIP (11%) were also observed. The survival rate was observed more among intramural newborns as compared to extramural newborns.
Conclusions: The mortality and morbidities of extreme preterm newborn are still higher. Survival increases with advancing gestational age. Knowing the outcome of extremely preterm newborns guides in clinical decision making, framing resuscitation guidelines, standard protocols as well as in parent counselling.

Keywords: Extreme preterm newborns, Mortality, Major morbidity, Outcome

INTRODUCTION

An estimated 13.4 million newborns were preterm or "born too soon" in 2020, 9.9% of births worldwide. Preterm birth complications remained the top cause of under-5 child mortality globally in 2022, accounting for about 1 million neonatal deaths.[1]

Although just 5.2% of all preterm births globally are extremely preterm (i.e., delivered with a gestational age of fewer than 28 weeks), these babies are at a higher risk of death and morbidity.[2] Numerous problems that are linked to poor long-term outcomes, including retinopathy of prematurity, necrotizing enterocolitis, sepsis, intraventricular hemorrhage, bronchopulmonary dysplasia, and white matter damage, are more likely to occur in these most immature newborns.[3] Recent in hospital statistics of mortality and morbidity profile of extremely preterm newborns is crucial for family counselling and the development of innovative therapies aimed at improving outcomes.

There are a very few studies in India regarding extreme preterm newborns. The study's aim is to evaluate the mortality and major morbidity among extremely preterm newborn prior to discharge from a tertiary level neonatal intensive care unit in Western India.

METHODS

This hospital based retro prospective observational study was done from 1st April 2022 to 31st December 2024 at the neonatal intensive care unit of Deenanath Mangeshkar hospital at Pune, a Level IIIB NICU in Maharashtra. The study population comprise of all extremely preterm neonates (i.e. gestational age less than 28 week) admitted to NICU over the study period. All live intramural as well as extramural newborns were included. Babies with congenital anomalies were excluded from the study. Neonatal and maternal data was obtained by analyzing the hospital records. Relevant antepartum, intrapartum details, including age, parity, mode of conception, maternity risk factors were recorded. Neonatal details including gender, birth weight, gestational age, resuscitation details and APGAR scores were recorded. Gestational age in weeks was obtained from the last menstrual period and first trimester antenatal ultrasound scans. Birth weight was also expressed in percentile based on Intergrowth 21 chart. All neonates were managed as per Neonatal Intensive Care Protocols (NICU) of the institution. Comorbidities observed during NICU stay was defined as per the standard criteria and recorded. All babies were regularly screened for retinopathy of prematurity as per NNF guidelines. Diagnosis of IVH, PVL were done by cranial sonography by radiologists. Study main outcomes were mortality and major morbidities of extreme preterm newborns which was defined as presence of at least one of the following issues: severe IVH (Grade III-IV), NEC (stage II-III), PVL, severe ROP (stage 3-5), moderate - severe BPD and sepsis during the NICU stay.

Data entry and analysis

Data collection was done using a pre-designed semi-structured questionnaire. All collected data were coded and entered into Microsoft Office Excel sheet and all entered data were checked twice. Data cleaning was done for any errors. Analysis was done by using Statistical Package for Social Sciences (SPSS) version 27. Data analysis for quantitative process included the sample general characteristics, univariate and bivariate analysis. All qualitative (categorical) variables were expressed as frequency and percentage and quantitative variables using mean and standard deviation. Chi-square test and Fisher's exact test were done to find the association between qualitative variables. A p value less than 0.05 are considered to be statistically significant.

Ethical consideration

The study was conducted after obtaining the approval of the Institutional Ethics Committee confidentiality of the attained information were maintained by not revealing personal identification details and all collected data were stored in a password protected system which is accessible to the principal investigator alone. Observed complications were dealt accordingly.

Statistical analysis

All collected data were coded and entered into Microsoft Office Excel sheet Analysis was done by using Statistical Package for Social Sciences (SPSS) version 27. Data analysis for quantitative process included sample general characteristics, univariate and bivariate analysis. All qualitative (categorical) variables were expressed as frequency and percentage and quantitative variables using mean and standard deviation. Chi-square test and Fisher's exact test were done to find the association between qualitative variables.

RESULTS

Table 1 shows that out of 64 eligible newborns, 54.7% were male, 20.3% were small for gestational age (SGA). 43.8% were IVF conception, 64.1 % were singletons and 64.1% born via caesarean deliveries, The rate of complete antenatal corticosteroid was 40.6%. and MgS04 use was 31.3% in the present study. Among study population, 40.6% had low APGAR score at 5 min of birth, 53.1% were intubated at birth, 73.4% required invasive ventilatory support, 89.1% received at least 1 dose of surfactant during the NICU stay. The mean length of stay for survivors were 45.26±36.56 days.

Table 1: Association between maternal and neonatal baseline characteristics with gestational age.

Baseline characteristics	<22 (n=1)	23 (n=5)	24 (n=8)	25 (n=8)	26 (n=15)	27 (n=27)	Total	P Value
Maternal characteristics								
Maternal age >35 years	1 (100)	0 (0.0)	1 (12.5)	1 (12.5)	1 (6.7)	6 (22.2)	10 (15.6)	0.26
Primigravida	0 (0.0)	2 (40.0)	5 (62.5)	4 (50.0)	7 (46.7)	16 (59.3)	34 (53.1)	0.02
BMI (kg/m^2)								
18.5-22.9	1	0 (0.0)	0 (0.0)	0 (0.0)	1 (6.7)	2 (7.4)	4 (6.3)	
23-24.9	(100)	0 (0.0)	2 (25.0)	0 (0.0)	3 (20.0)	1 (3.7)	6 (9.4)	0.13
>25	0 (0.0)	5 (100)	6 (75.0)	8 (100)	11 (73.3)	24 (88.9)	54 (84.4)	
IVF	0 (0.0)	3 (60.0)	4 (50.0)	3 (37.5)	6 (40.0)	12 (44.4)	28 (43.8)	0.97
Multiple	0 (0.0)	2 (40.0)	7 (87.5)	2 (25.0)	3 (20.0)	9 (33.3)	23 (35.9)	0.03

Continued.

Baseline characteristics	<22 (n=1)	23 (n=5)	24 (n=8)	25 (n=8)	26 (n=15)	27 (n=27)	Total	P Value
pregnancies								
Complete antenatal								0.21
Steroid use	0 (0.0)	2 (40.0)	1 (12.5)	2 (25.0)	6 (40.0)	15 (55.6)	26 (40.6)	
MGSO4 use	1 (100)	0 (0.0)	0 (0.0)	1 (12.5)	7 (46.7)	11 (40.7)	20 (31.3)	0.02
Caesarean delivery	1 (100)	0 (0.0)	5 (62.5)	4 (50.0)	12 (80.0)	19 (70.4)	41 (64.1)	0.02
GDM	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (6.7)	2 (7.4)	3 (4.7)	1.00
PPROM	1 (100)	3 (60.0)	4 (50.0)	0 (0.0)	6 (40.0)	7 (25.9)	21 (32.81)	0.05
Placenta praevia/ Placental abruption	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (3.7)	1 (1.6)	1.00
Neonatal characteristics								
Birth weight(g)								
<500	1(100)	1(20.0)	0 (0.0)	1 (12.5)	1 (6.7)	0 (0.0)	4 (6.3)	
500-749	0 (0.0)	4(80.0)	6 (75.0)	5 (62.5)	5 (33.3)	7 (25.9)	27(42.2)	0.01
750-999	0 (0.0)	0 (0.0)	1 (12.5)	2 (25.0)	7 (46.7)	15(55.6)	25(39.1)	
>1000	0 (0.0)	0 (0.0)	1 (12.5)	0 (0.0)	2 (13.3)	5 (18.5)	8 (12.5)	
SGA	-	-	2 (12.5)	3 (25.0)	1 (6.7)	7 (22.2)	13 (20.3)	0.14
Male	1(100)	2(40.0)	5 (62.5)	3 (37.5)	11(73.3)	13 (48.1)	35(54.7)	0.43
Low APGAR score (APGAR score at 5 min <7)	1(100)	4(80.0)	4 (50.0)	5 (62.5)	7 (46.7)	5 (18.5)	26(40.6)	0.02
Intubated at birth	1(100)	5(100)	7 (100)	4 (80.0)	7 (87.5)	10 (83.3)	34(53.1)	0.86

Test used: Fischer's exact test, p value <0.05: Statistically significant.

Table 2: Association between survival and major morbidity with gestational age among study subjects.

Variables	<22 (n=1)	23 (n=5)	24 (n=8)	25 (n=8)	26 (n=15)	27 (n=27)	Total	P Value
Survival								
Primary outcome survived	0 (0.0)	1 (20.0)	1 (12.5)	3 (37.5)	7 (46.7)	22(81.5)	34(53.1)	<0.001
Death	1 (100)	4 (80.0)	6 (75.0)	5 (62.5)	6 (40.0)	1 (3.7)	23(35.9)	
Lama	0 (0.0)	0 (0.0)	1 (12.5)	0 (0.0)	2 (13.3)	4 (14.8)	7 (10.9)	
Postnatal time until death								
<7 days	1 (100)	2 (50.0)	3 (50.0)	4 (80.0)	1 (16.7)	0 (0.0)	11 (47.8)	0.28
>7 days	0 (0.0)	2 (50.0)	3 (50.0)	1 (20.0)	5 (83.3)	1 (100)	12 (52.2)	
Length of stay for Infants who survived mean (SD), days	66	8.0 (7.16)	43.67 (53.19)	73.20 (14.58)	49.33 (26.71)	19.00	45.26 (36.56)	0.14*
Major morbidity								
BPD	0 (0.0)	1 (20.0)	3 (37.5)	4 (50.0)	8 (53.3)	23 (85.2)	39 (60.9)	0.005
IVH grade III-IV	0 (0.0)	0 (0.0	0 (0.0)	0 (0.0)	3(20.0)	0 (0.0)	3(4.7)	0.02
PVL	0 (0.0)	0 (0.0)	2 (25.0)	0 (0.0)	2 (13.3)	2 (7.4)	6 (9.4)	0.49

Continued.

Variables	<22 (n=1)	23 (n=5)	24 (n=8)	25 (n=8)	26 (n=15)	27 (n=27)	Total	P Value
Sepsis	1 (100)	2 (40.0)	3 (37.5)	2 (25.0)	7 (46.7)	14 (51.9)	29 (45.3)	0.72
Severe ROP stage 3-5	(0.0)	1 (20.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.6)	0.26
Any major morbidity	1(100)	4 (80.0)	8 (100)	5 (62.5)	15 (100)	25 (92.5)	58 (90.6)	0.066
Survival without major morbidity	0 (0.0)	1 (25.0)	0 (0.0)	3 (60.0)	0 (0.0)	0 (0.0)	4 (17.4)	0.08

Test used: Fischer's exact test, One-way ANOVA* p value <0.05: Statistically significant.

Figure 2 and 3 shows that the proportion of mortality in this study was 35.9%. Among all the major morbidities assessed, majority (60.9%) of the study subjects had BPD followed by neonatal sepsis (45.3%)., whereas as ROP stage 3-5, NEC stage II-III had least incidence (1.6%).

Table 3: Association between mortality with place of delivery.

Mortality	Place of delivery		X^2	P value
	intramural (n=50) N (%)	Extramural (n=14) N (%)		
Survived	28 (56.0)	6 (42.9)		
Expired	16 (32.0)	7 (50.0)	1.47	0.55
Lama	6 (12.0)	1 (7.1)		

Test used: Fischer's exact test, p value <0.05: Statistically significant.

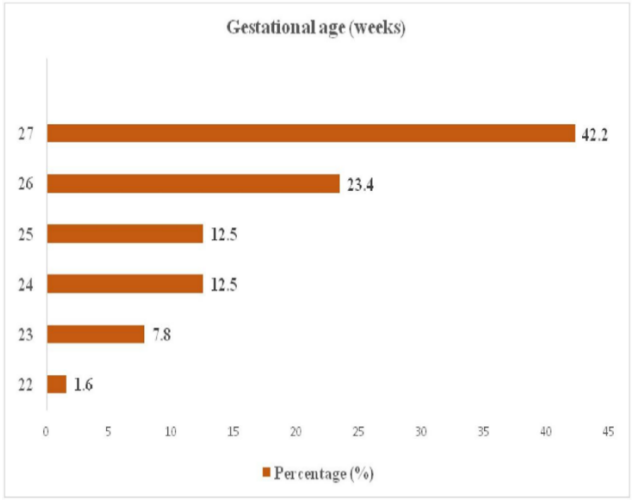

Figure 1: Distribution of study subjects based on gestational age.

Figure 4 shows incidence of other morbidities such as RDS (95%), apnoea of prematurity (83%), anemia of prematurity (69%), HsPDA (56%) and SIP (11%) among extremely low gestational age newborns. It is evident from (Table 2) that overall survival to discharge among study population was 53.1%. Survival to discharge increased with advancing gestational age: 20% at 23 weeks, 12.5% at 24 weeks, 37.5% at 25 weeks, 46.7% at 26 weeks, 81.5% at 27 weeks of gestational age. The incidence of BPD and IVH increases with advancing gestational age (p value <0.05). 90.6 % newborns had any 1 major morbidity and 17.4% newborns survived without any major morbidity.

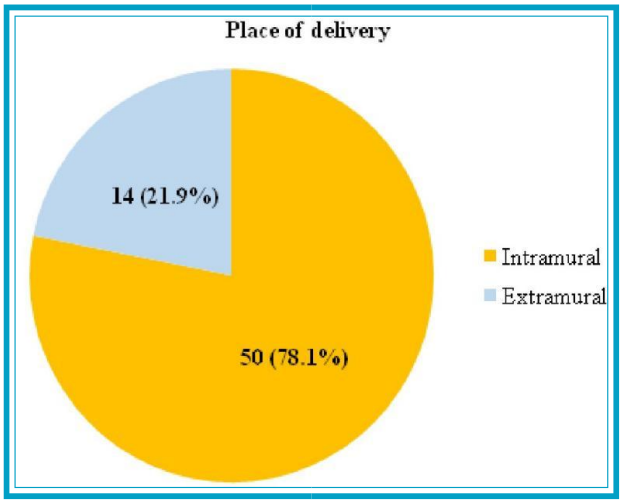

Figure 2: Distribution of study subjects based on place of delivery.

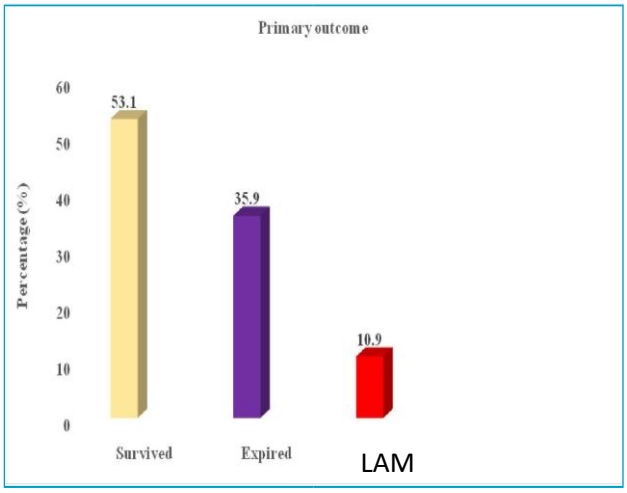

Figure 3: Distribution of study subjects based on primary outcome.

Table 3 shows that the survival rate was more among intramural newborns as compared to extramural newborns emphasing the importance of in utero transfer to a tertiary care setting.

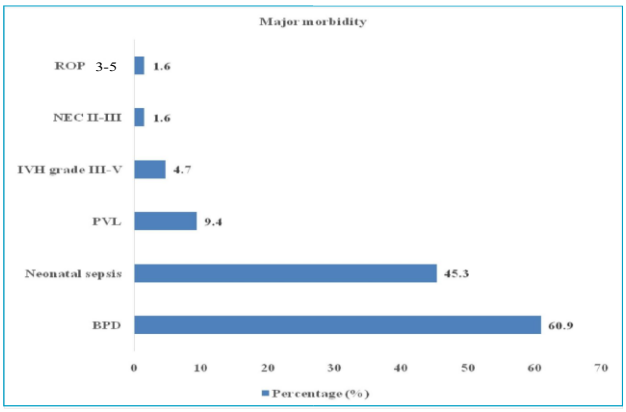

Figure 4: Distribution of study subjects based on major morbidity.

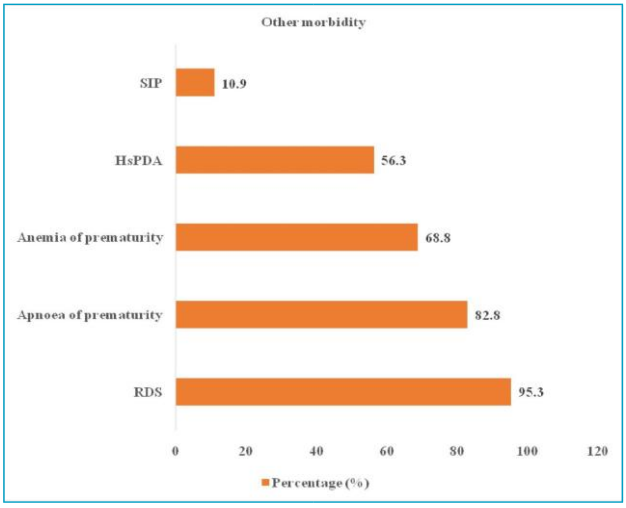

Figure 5: Distribution of study subjects based on other morbidity.

DISCUSSION

The present retro prospective observational study was done in Neonatal intensive care unit at our tertiary care center for a duration of 32 months. During this study period, 64 eligible extremely low gestational age newborns were identified. The aim of the study was to determine the outcome of extremely low gestational age newborns in terms of mortality and major morbidity prior to discharge from neonatal intensive care unit. The proportion of mortality in this study was 35.9%. This result was better than mortality observed in earlier studies done by Maheta et al and Shanmugam RS et al where mortality was 42.39% and 74.2% respectively.[4,5] Overall survival in this study, was 53.1% whereas survival rate in the studies done by Zhu Z et al, Kong Xetal, Davide et al was 62.3%, 91.2% and 74% respectively.[6-8] Survival to discharge increased with advancing gestational age: 20% at 23 weeks, 12.5% at 24 weeks, 37.5% at 25 weeks, 46.7% at 26 weeks, 81.5% at 27 weeks. Similar findings were observed in the study done by Zhu Z et al, Kong X et al, Davide et al and Maheta et al.[4-8] In this study, any 1 major morbidity present in 90.6% and 17.4% survived without any major morbidity. Out of the major morbidities studied, majority had moderate-severe BPD (60.9%) and least common are definite NEC and severe ROP, 1.6% each. Results were comparable to study done by Zhu Z et al where any 1 major morbidity was present in 72.4%, and 9.4% survived without any major morbidity.[6] Moderate -severe BPD was the most common major morbidity and least common was NEC (10.1%) and severe ROP (18.8%). The study also shows that the mortality among extramural newborns is higher than that of intramural one. similar findings were observed in the study done by Sasaki et al emphasing the importance of in utero transfer to tertiary care settings.[9]

The results obtained in this study guide the clinician in antenatal and postnatal counselling of the parents. To generalize these findings, multicenter cohort study design involving larger sample size is recommended. certain limitations are there in this study. Firstly, all the data were collected from only one neonatal intensive care unit over a shorter period of time, hence outcome may not be generalizable. Further multicenter prospective cohort studies with larger sample size are required to increase accuracy of results. Also, this is a hospital based retro prospective observational study, not population based. Further, study only presented short term outcomes. long term neurodevelopmental outcome analysis with a cohort-based study design is needed.

CONCLUSION

This study found that infants born extremely preterm are at increased risk of mortality and major morbidity. The prevalence of major morbidities that have adverse long-term neurodevelopmental consequences are still higher at extreme low gestational age newborn.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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