

## Morbidity and Mortality Profile of Extremely Preterm Infants- A Multicenter Network Study from India

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### Abstract:

**Background:** This study was conducted to determine the morbidity profile and short-term outcomes of extremely preterm infants (gestational age <28 weeks) admitted in level III NICUs of India over a period of 5 years.

**Material and Methods:** This was a retrospective, observational study. 27 participating level III NICUs prospectively collected data of neonates meeting the pre-defined criteria, including gestational age and need of admission. Results were presented in form of mean with standard deviations and numbers with percentage. Trends of morbidities were noted over the years and among the different gestational age groups.

**Results:** The gestational age ranged from 22 to 27 weeks, the mean gestational age being 25.8 ( $\pm 1.44$ ) weeks. The mean birth weight was 846  $\pm$  264 grams. The major morbidities noted among infants of the study group were- RDS (84%), BPD, PDA (99%), NEC (7%), ROP (requiring treatment-2%), IVH (22%), PVL (2%) and sepsis (culture proven- 23%, probable 15%). The mortality rate was 42.39%, highest mortality seen among infants having NEC, followed by those having RDS and PDA.

**Conclusion:** This study showed the morbidity profile of extremely preterm infants in India. This is the first study of this kind and could help form a basis for other studies determining the long-term outcomes in this population.

**Keywords:** Extremely Preterm Infants, Morbidities, Mortality, India

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### Introduction

Preterm birth is a growing global health issue, and the number of preterm infants born worldwide was nearly 15 million annually.[1] Prematurity is a major cause of morbidity and mortality among neonates, with extremely premature infants, with gestational age <28 weeks having a greater risk. Due to prematurity, they have higher incidence of respiratory distress syndrome (RDS), necrotizing enterocolitis (NEC), intraventricular haemorrhage (IVH), bronchopulmonary dysplasia (BPD), retinopathy of prematurity (ROP), sepsis and so on.[2] According to a recent MDS (Million Death Study) report, prematurity accounts for 40% neonatal mortality rate in India.[3]

Survival continues to incrementally improve for extremely premature infants.[4-8] Understanding the outcome in this population is necessary for better counselling of families regarding antenatal and

postnatal care, as well as guide strategies to improve their survival without morbidity. Despite the improved survival worldwide, there have not been studies reporting their morbidity profile in India.

This study focuses on short-term outcomes of these infants as studied from the various level-III NICUs in the country, over a period of 5 years.

### Aim of the Study

This study was conducted with the aim to investigate the morbidity profile and short-term outcomes of extremely premature infants admitted in level III NICUs in India, and their trends over a period of 5 years.

### Material and Methods

A retrospective and observational study was conducted for infants of gestational age less than 28

weeks who were admitted in tertiary care neonatal intensive care units (NICUs) from January 2017 to March 2022. A total of 27 centres, both from government as well as private sector, all being level III NICUs had participated. Ethical approval was taken from the institutional ethical committee and written informed consent was taken from all the participants. Data was prospectively collected by the participating centres, of all neonates fulfilling the pre-defined criteria of gestational age and need of admission. For this study, the infants having gestational age less than 28 weeks were considered. Gestational age was calculated from the date of last menstrual period or was determined by foetal ultrasound assessment. Data of these infants was entered in form of electronic medical records through the website innc.in.

### Statistical Analysis

The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2007) and then exported to data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). For all tests, confidence level and level of significance were set at 95% and 5% respectively.

### Results

A total of 1439 infants were included in this study, who met the inclusion criteria for gestational age. Out of these, 828 (58%) were males and 611 (42%) were females. The gestational age ranged from 22 to 27 weeks, the mean gestational age being 25.8 ( $\pm 1.44$ ) weeks. The mean birth weight was 846  $\pm$  264 grams.

**Table 1: Distribution of infants as per gestational ages**

GA (in weeks)	Number of infants
<25	248
25	225
26	401
27	565

**Table 2: Incidence of various antenatal complications**

History of pregnancy problems	No.	%
Anaemia	39	2.71
PIH	226	15.71
Hypertensive disorders	226	15.71
Eclampsia	27	1.88
DM	149	10.35
APH	124	8.62
Absent or Reverse EDF	861	59.83

Maternal age of 35 years or more was considered as elderly pregnancy. 284 (19.74%) infants in the study population were born from elderly pregnancies. Out of the total, 994 infants (69.08%) were born from singleton pregnancies. The prevalence of maternal risk factors in pregnancy are tabulated below (Table 2). The most common antenatal complication noted was absence or reversal of end-diastolic flow. Antenatal steroids were received by 935 (64.98%) infants, out of which 421 (47.73%) received Dexamethasone and 461 (52.27%) received

Betamethasone. Data regarding type of steroids received was unavailable for 53 infants. Antenatal magnesium sulphate was received by 366 (25.43%) infants. Premature rupture of membrane was noted in 559 (38.85%) infants. 542 (37.67%) infants required resuscitation at time of birth. Respiratory distress syndrome was a common morbidity noted in the study population, seen in 1214 (84.36%) infants. Severity of RDS and subsequent BPD was noted in terms of requirement of surfactant therapy and need of respiratory support.

**Table 3: Comparison of respiratory support required among different gestational ages**

GA (Weeks)	OXYGEN DAYS		CPAP DAYS		Invasive Ventilation (Days)	
	Mean	SD	Mean	SD	Mean	SD
<25	10.69	11.22	35.82	34.21	14.21	17.77
25	10.56	14.15	29.74	26.74	9.66	11.03
26	15.77	17.16	26.36	27.83	8.56	11.50
27	10.90	17.16	23.65	64.25	5.79	7.23

The requirement of respiratory support was graded in terms of need of oxygen, non-invasive or invasive ventilation, which was compared among the different gestational ages, as shown in Table 3.

Patent ductus arteriosus was seen in 1432 (99.51%) infants. However, surgical ligation was needed in only 10 (0.7%) infants. ROP screening was documented in 478 (33.21%) infants. 29 infants (2.01%) had aggressive posterior ROP. 136 infants (28.45% out of those screened) required treatment for ROP. 121 babies were given laser treatment, and 56

given Anti-VEGF treatment. 41 babies required treatment with both modalities. Necrotising enterocolitis was noted in 106 (7.36%) infants. Bell's staging criteria were used and these were divided on the basis of stages of NEC as follows (Figure 4), maximum number of infants being diagnosed in stage 2B. (Graph 1)

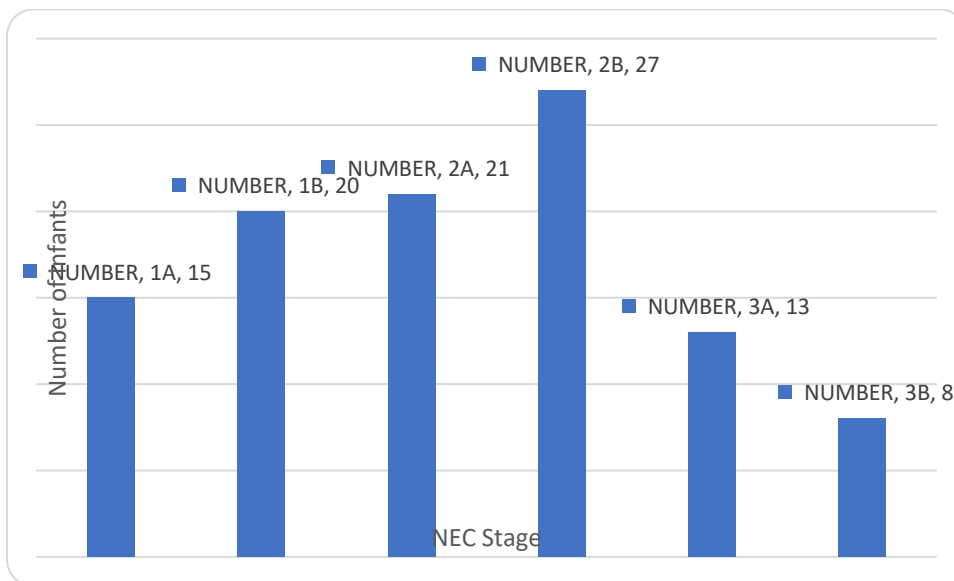


Figure 1: Incidence of different stages of NEC

Spontaneous intestinal perforation was seen in 21 (1.45%) infants. Overall, surgical management for perforation was required in 52 infants.

Intraventricular haemorrhage was seen in 315 (21.89%) infants, and cystic periventricular leukomalacia was notes in 28 (1.94%) infants. IVH was noted in 31.04% infants of gestational age <25 weeks, in 27.56% infants of 25 weeks gestational age, 18.95% infants with gestational age 26 weeks, and 17.88% infants with gestational age 27 weeks. (Graph 2)

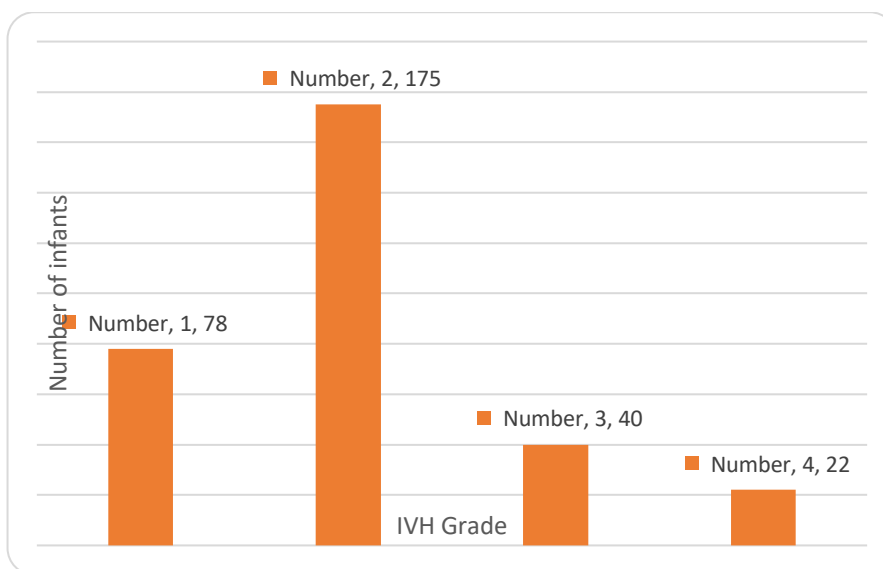


Figure 2: Incidence of different grades of IVH

Among the study group, 331 infants (23%) were found to have culture positive sepsis and 218 (15.14%) had probable sepsis.

**Table 4: Mortality in infants with major morbidities**

Disposition	Number of deaths	%	Likelihood ratio	95% CI
RDS	516	42.50	1.237	1.127 to 1.357
BPD	30	13.57	0.263	0.180 to 0.384
PDA	607	42.39	1.231	1.135 to 1.336
ROP	0	0.00	0	0.000 to 0.0988
NEC	60	56.60	2.182	1.495 to 3.186
IVH	102	32.28	0.797	0.636 to 1.000
PVL	3	10.34	0.193	0.0585 to 0.637
Sepsis	98	29.61	0.704	0.561 to 0.883

As depicted above, the highest mortality in our study was seen among infants having NEC, followed by those having RDS and PDA.

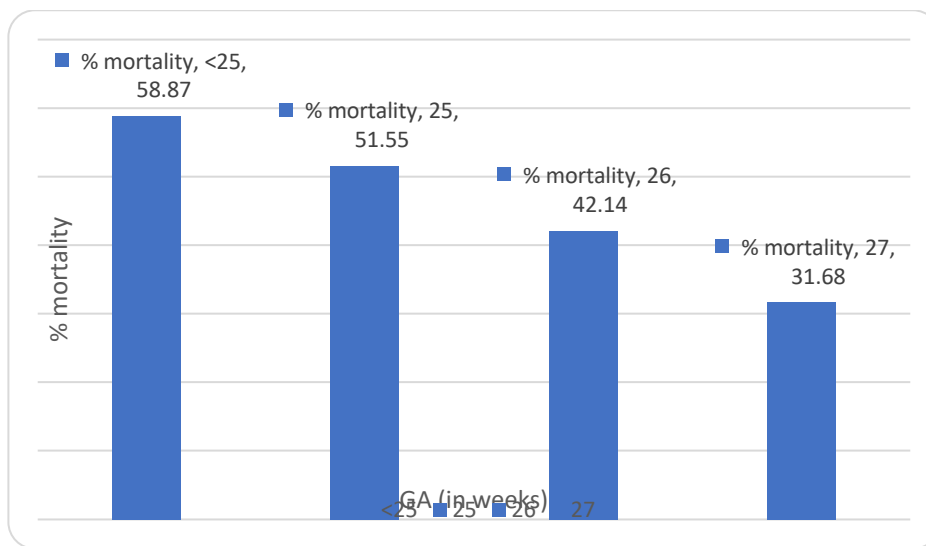
In our study, 46.35% infants were found to be successfully discharged home. The total mortality in the study was 42.39%. The overall disposition of all these infants taken in this study is tabulated as follows (Table 5)

**Table 5: Overall dispositions in the study population**

Disposition	No.	%
Discharged home	667	46.35
Transferred to other hospital	96	6.67
LAMA	66	4.59
Death	610	42.39
Total	1439	100

The mortality rate was further compared among the gestational ages. Infants with gestational age <25 weeks had mortality of 58%. It was 51% in infants of 25 weeks gestational age, 42% among 26 weeks and 31% among 27 weeks.

The mortality rates in different gestational ages are depicted below (Graph 3)



**Figure 3: Comparison of mortality rate among different gestational ages**

**Discussion**

This is the first study showing the morbidity and mortality profile of extremely preterm infants in India

over 5 years. Most studies demonstrating survival of the extreme preterm infants are from developed countries.

A similar study from China<sup>2</sup>, conducted from 2008-2017 showed the short term outcomes of extreme preterm infants. This study also noted that RDS was the most common morbidity among this group, and other major complications during hospitalisation included BPD, ROP, NEC, IVH, PVL and blood culture positive nosocomial sepsis.

The mortality rate noted in our study was 42.39%. This was comparable to the study from China<sup>2</sup> where the mortality was 47.5%. A recent study was conducted in southern India<sup>3</sup> to demonstrate the mortality of extreme and very preterm infants. In this study, the mortality was 74.2% for extreme preterm and 42.7% for very preterm infants, and RDS and IVH attributed to 75% of deaths among prematurity-related complication. The most significant predictor of death was gestational age, regardless of the cause of death, as shown in other similar studies also.<sup>[3,9,10]</sup>

This study compiled the data from multiple centres and over a long time frame. However, it does not include the outcome of infants born without NICU facilities. Also, further studies are needed to determine the long-term outcomes in this population.

### Conclusion

This study showed the morbidity profile of extremely preterm infants in India. This is the first study of this kind and could help form a basis for other studies determining the long-term outcomes in this population.

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