Original Article ISSN (O):2395-2822; ISSN (P):2395-2814

Mortality and Morbidity of Extreme Preterm Neonates

Abdul Tawab C N[1], Madhu George[2], Jino Joseph[3]

[1]Fellow in Neonatology, Department of Neonatology, Rajagiri Hospital, Aluva, Kochi, India.
[2]HOD and Consultant Neonatology, Department of Neonatology, Rajagiri Hospital, Aluva, Kochi, India.
[3]Consultant Neonatology, Department of Neonatology, Rajagiri Hospital, Aluva, Kochi, India.

Received: February 2019
Accepted: February 2019

Copyright: © the author(s), publisher. It is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Extremely preterm babies (22–27+6 weeks gestation) are at increased risk of death and morbidity. In recent years, more babies born between 22 and 25 weeks gestation are being resuscitated and requiring prolonged treatment instead of receiving comfort care only. Therefore, the present study was designed to evaluate the morbidity and mortality of extremely premature babies born between 22 weeks and 27weeks+6 days gestation during their hospital stay. **Methods:** The study was conducted at Rajagiri Hospital in Aluva, a tertiary care hospital in Kerala. This was a retrospective study that included all extremely preterm births between 22 weeks and 27weeks+6 days gestation over a period of 3 years. **Results:** Forty five extreme preterm neonates were born during the study period out of 2598 NICU admissions (1.7 %). Thirty of those forty five neonates (67 %) survived. The rate of survival of extreme preterms increases with gestational age. Moderate and severe bronchopulmonary dysplasia (BPD) were seen in 7 cases (16 %), grade 3 and 4 intraventricular hemorrhage (IVH) were seen in 6 cases (13 %), necrotizing enterocolitis (NEC) were seen in 8 cases (18%) and retinopathy of prematurity (ROP) requiring treatment were seen in 9 cases (20%). Higher incidence of mortality was seen in neonates who were small for gestational age (SGA) and whose mothers had chorioamnionitis. The average length of hospital stay was 76 days. The mean average duration of mechanical ventilation and non invasive ventilation were 19 days and 32 days respectively. **Conclusion:** Extremely preterm neonates remain at risk for mortality and major morbidity, with those between 22 to 25 weeks gestation having the highest risk. Survival is feasible in a tertiary care centre where adequate facilities are available. This data can be useful for patient counseling regarding preterm outcomes and NICU stay.

Keywords: Preterm neonates, low birth weight, mortality, outcome.

INTRODUCTION

Preterm birth has evolved as one of the major clinical problems in neonatology, as it has been found to be associated with perinatal morbidity and mortality.[1] Twenty times more mortality rate was recorded among preterm neonates.[2] Increased risk of various physical and mental abnormalities is always associated with survivor babies.[3] There are approximately more than 3.5 million preterm births in India per year. With advances in neonatal care, more neonates are surviving at earlier gestational ages. The incidence of mortality and severe neonatal morbidity increase with decrease in gestational age. Similarly, resuscitation practices for babies less than 26 weeks vary widely among neonatal units because there is no consensus on a "limit of viability" (defined as anywhere between 22 and 25 weeks).[4] In recent years, more babies born between 22 and 25 weeks gestation are being resuscitated instead of receiving comfort care only. Obstetricans and neonatologists are faced with ethical and technical problems regarding the care of these babies.[4]

Morbidity and mortality rate of preterm neonates have been influenced by various maternal, uteroplacental and fetal factors which induce premature delivery along with low birth weight neonates.[5] There are very few studies in India regarding extreme preterm neonates. Therefore, the objectives of this study are: -

1. To evaluate the morbidity and mortality of extremely premature neonates born between 22 weeks and 27weeks+ 6 days gestation during hospital stay
2. To prepare an institutional data that will help in counseling parents regarding the care of extreme preterm neonates

MATERIALS AND METHODS

This study was done at the neonatal intensive care unit at Rajagiri Hospital in Aluva in Kerala. The NICU is a level III neonatal intensive care unit which contains 16 beds and looks after babies born upwards of 22 weeks gestation. The study

Name & Address of Corresponding Author
Dr. Abdul Tawab C N
Fellow in Neonatology,
Department of Neonatology, Rajagiri Hospital,
Aluva, Kochi,
India.

population comprised of neonates admitted to the NICU with a gestational age between 22 weeks and 27 weeks over a period of three years from October 2015 to October 2018. Babies with congenital anomalies were excluded from the study. In this retrospective study, data was collected from hospital records in the labor ward, NICU and medical records of the admitted preterm babies. Data regarding gestational age, birth weight, causes of preterm birth, duration of hospital stay, various morbidity and mortality patterns and treatment provided in the NICU were reviewed. Maternal risk factors were also reviewed. Gestational age in weeks was obtained from the last menstrual period and first trimester antenatal ultrasound scans. Standard criteria were used for definition of common morbidities. All babies were regularly screened by ophthalmologists for retinopathy of prematurity (ROP) as per NNF guidelines. Portable ultrasound machine is present in the unit round the clock. Intraventricular hemorrhage was confirmed by the radiologist and patent ductus arteriosus by the cardiologist.

Statistical Analysis

Microsoft Office 2007 was used for the analysis. Descriptive statistics like mean and percentages were used for the analysis. Numerical variables were compared between the two groups by using the independent student's test. P values of less than 0.05 were considered as statistically significant.

RESULTS

The present study recorded delivery of forty five extreme preterm neonates (1.73 %) born during the study period out of 2598 NICU admissions and subsequent complications they faced after birth while admitted in NICU. Out of 45 premature babies, 27 (60%) were male and 18 (40%) were female babies. Sixteen babies (35.5%) had birth weight less 600 grams and further 29 babies (64.5%) had birth weight less 900grams.

Table 1: Maternal and perinatal characteristics among survivors and nonsurvivors

	22 to 24+6 weeks (n=16)			25 to 27+6 weeks (n=29)		
	Mortality (n=9)	Survivors (n=7)	P Valve	Mortality (n=6)	Survivors (n=23)	P valve
Mean birth weight	461 grams	580 grams	P < 0.0001	680 grams	874 grams	P < 0.0001
Maternal age	28 yrs	26 yrs	P = 0.3380	27 yrs	29 yrs	P = 0.0002
Primi Gravida	7 (77%)	5 (71%)	P = 0.7917	4 (66 %)	15 (65 %)	P = 0.9641
Male	6 (67%)	4 (57 %)	P = 0.6630	3(50 %)	14 (60 %)	P = 0.9641
LSCS	5 (55 %)	5 (71 %)	P = 0.5265	4 (66%)	6 (26 %)	P = 0.0708
Antenatal Steroids	7 (77%)	6 (86 %)	P = 0.6598	5 (83 %)	21 (91 %)	P = 0.0708
Antenatal MgSO4	6 (67%)	5 (71%)	P = 0.8683	5 (83 %)	20 (87 %)	P = 0.0708
Gestational Diabetes	5 (55%)	4 (57 %)	P = 0.9383	4 (66 %)	15 (65 %)	P = 0.9641
PIH	4 (44%)	3 (43 %)	P = 0.9691	3 (50 %)	7 (30 %)	P = 0.3659
Abnormal dopplers	3 (33%)	1 (14 %)	P = 0.3972	2 (33 %)	4 (17 %)	P = 0.3940
PPROM	5 (55%)	2 (28%)	P = 0.2950	3 (50 %)	10 (43 %)	P = 0.7627
SGA	5 (55%)	1(14 %)	P = 0.1029	3 (50 %)	2 (9 %)	P = 0.0207
Abruption	3 (33%)	2(28 %)	P = 0.8352	1 (16 %)	3 (13 %)	P = 0.8513
Multiple births	6 (67 %)	4 (57 %)	P = 0.6913	3 (50 %)	5 (21 %)	P = 0.1615
Chorioamnionitis	5 (55%)	3 (43 %)	P = 0.6913	3 (50 %)	5 (21 %)	P = 0.1615

Table 2: Mortality and morbidity in extreme preterms

Gestational age in weeks	Total number of babies (n)	Mortality (n)	Survival Percentage (%)	ROP requiring treatment (n)	IVH (3&4) (n)	NEC (n)	BPD (Mod/severe) (n)
22	3	1	66.6	2	1	0	2
23	8	6	25	1	3	4	1
24	5	2	60	3	1	1	1
25	5	2	60	0	0	0	1
26	10	2	80	1	1	1	2
27	14	2	85.7	2	0	2	0
Total	45	15	66.6	9	6	8	7

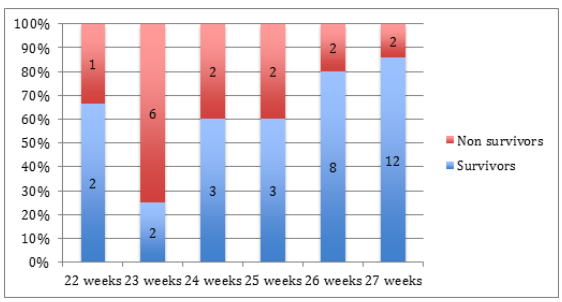

Figure 1: Mortality among extreme preterm babies.

[Table 1] shows that out of 45 premature babies 16 babies were in the gestational age category of 22 to 24+6 weeks. In this group, 9 babies died with a mean birth weight of 461 grams. Whereas 7 babies who survived had a mean birth weight of 580 grams were recorded. Among 9 causality of this group 6 babies were males and 3 babies were female. While among the survivors 4 were males and 3 were females. Further, out of 45 premature babies 29 babies were in the gestational age category of 25 to 27+6 weeks. In this group, 6 babies who died had a

mean birth weight of 680 grams. While the 23 babies who survived, their mean birth weight was 874 grams. Among the 6 deaths in the group, 3 babies were males and 3 babies were female. Whereas, among the survivors, 14 babies were males and 9 babies were females. There was no statistically significant difference between the incidence of LSCS, gestational diabetes mellitus, use of antenatal steroids and coverage of antenatal magnesium sulphate among all survivor and non-survivor preterm babies. Mortality was found to be more in babies with lower birth weight ($P < 0.0001$) in both gestational groups (less than 25 weeks and more than 25 weeks). Though not statistically significant, there higher incidence of mortality was seen in neonates who were small for gestational age (SGA) and whose mothers had chorioamnionitis. Mortality was found to be more in SGA babies in both gestational groups.

[Table 2] shows that thirty out of the forty five babies (67%) survived. Maximum survival rate were recorded among 27 weeks gestational age (85.7%) followed by 26 weeks (80%). On the other hand, maximum mortality rate was recorded in the gestational age 23 weeks (75%). Moderate and severe bronchopulmonary dysplasia (BPD) were seen in 7 cases (16 %), grade 3 and 4 intraventricular hemorrhage (IVH) were seen in 6 cases (13 %), necrotizing enterocolitis (NEC) were seen in 8 cases (18%) and retinopathy of prematurity (ROP) requiring treatment were seen in 9 cases (20%). Neonates whos were small for gestational age (SGA) and whose mother had chorioamnionitis had increased risk of mortality.

Table 3: Interventions in survivors (n=30)

Weeks	Mechanical ventilation in days (Mean)	Non invasive ventilation in days (Mean)	Postnatal steroids (n)	Diuretics	NEC needing surgery	ROP requiring treatment (n)		PDA treatment (n)		Average length of stay of survivors (in days)
						Laser	Bevacizumab	Ibuprofen	Paracetamol	
22 (n=2)	46 ±8	68±14	0	2	0	1	1	2	0	148±0
23 (n=2)	43±6	46±12	0	2	0	1	0	1	1	119±20
24 (n=3)	38±8	34±9	1	2	0	1	2	1	2	82±14
25 (n=3)	16±4	35±10	1	1	0	0	0	1	1	75±12
26 (n=8)	13±4	30±6	0	0	0	0	1	2	2	69±10
27 (n=12)	10±3	24±4	0	1	0	1	1	2	3	60±9
Total (n=30)	19 (Mean)	32 (mean)	2	8	0	4	5	9	9	76 (mean)

It is evident from [Table 3] that the mean duration of hospital stay among survivor babies was 76 days. The mean average duration of mechanical ventilation and non invasive ventilation among survivor babies were 19 days and 32 days respectively. Among the survivor babies, babies born at 22 weeks gestation needed the most number of days of both invasive ventilation days (46 days) and non-invasive ventilation days. (68 days). It was noted to have a steady decrease in ventilation days with increase in gestation. Among survivor babies, 9 babies needed treatment for ROP. 5 babies were treated with Bevacizumab and the rest were treated with laser therapy. 18 babies among the survivor babies needed treatment for PDA (9 each with oral ibuprofen and intravenous paracetamol). None of the babies required any surgical ligation for PDA. Among the survivor babies, 7 babies had moderate and severe BPD, while only 2 babies were treated with postnatal steroids. None of the survivor babies required any surgeries for NEC.

DISCUSSION

Various studies show that incidence of mortality and preterm delivery has been found to be linked with socio-economical status, quality of perinatal care and availability of standard medical facilities. Although the mortality among extreme preterm babies has decreased, the morbidities and adverse long term outcome in survivors continues to be high.[6,7]

Such babies requires prolonged NICU stay and other interventions. They require prolonged ventilation days, central lines, total parenteral nutrition and multiple intravenous antibiotics. They may also have significant morbidities like NEC, BPD, IVH, PVL etc. They have an increased incidence of neurodevelopmental impairment and required frequent followup visits to hospitals. This leads to psychological and financial burden to the families. The aim of our study was to to evaluate the morbidity and mortality of extremely premature neonates and during hospital stay ando prepare an

institutional data that will help in counselling parents regarding the care of extreme preterm neonates .

The present study observed a 1.73 % incidence of extreme preterm deliveries. These findings are very similar to the findings of the previous studies of Xiang et al,[8] as they recorded an incidence of 1.1%.

Results of the current study showed that there was 33.33% incidence of mortality among extreme premature babies. These results were better than the results obtained by earlier studies of Li J et al,[9] as they observed 60 % mortality rate among extreme preterm babies. Similarly, Xiang et al,[8] showed mortality of 57 % in extreme premature babies. Further the present study recorded that survival rate of the preterm babies was increased with increase in the gestational age of babies. These results are very similar to the results of the previous study of Chen C 10 et al as they recorded significant decrease in mortality of babies with increase in gestational age of babies. Similarly, Shah PS,[11] and Isayama T et al,[12] showed in their studies that there was an increase in survival rate of babies with increase in their gestational age.

Various earlier studies have reported mortality rate of babies according to the birth weight. However, outcomes based on gestational age are also considered as important and valuable for prenatal counseling and physician/family decision-making.[13]

The present study showed that there was a significantly high rate of mortality among the extreme preterm babies with birth weight less than 500 grams. These, findings are consistent with the findings of the earlier study of Stephen J. Bacek et al,[14] as they recorded in their study that the lower the birth weight higher is the mortality rate. In addition, Sangamam R,[15] recorded that the mortality of babies was maximum in lower birth weight groups.

The current study showed the mean average days of mechanical ventilation and non invasive ventilation among survivor babies were 19 days and 32 days respectively. The ventilation hours were the longest for babies born at 22 weeks gestation and the shortest for babies born at 27 weeks gestation. The duration of invasive and non invasive ventilation hours were found to be inversely proportional to gestational age of babies.

These findings are very similar to the findings of a previous study of Goldenberg RL et al,[17] in which they observed significantly high incidence of longer duration of mechanical ventilation and non invasive ventilation in survivor neonates of lesser gestational age babies. In a similar study, Khan MR et al,[18] recorded an increased incidence as well as longer duration of both type of ventilation in younger gestational age neonates.

In our study, higher level of intensive care was more frequently needed for the lesser gestational age babies. Various studies suggested that the mortality rate was found to decrease with an increase in the gestational age of babies. Higher the gestational age, lesser would be the complications and duration of hospital stay of neonates.[16-18]

The small sample size of the study and the study being done in a single-center were the major limitations.

CONCLUSION

Extremely preterm neonates remain at risk for mortality and major morbidity, with 22 to 25 week gestation neonates carrying the highest risk. Survival is feasible in a tertiary care center where adequate facilities are available. This data can be useful for patient counseling regarding preterm outcomes and NICU stay.

Acknowledgements

The authors thank the Medical Director and the hospital management for permission to carry out this study.

REFERENCES

1. Ellen Girerd-Barclay, Miriam Krantz, Subodha Shakya-Shrestha, Kalpana Tiwari. Reduction of low birth weight: a south Asia priority. In: Ellen Girerd-Barclay, Miriam Krantz, Subodha Shakya-Shrestha, Kalpana Tiwari, eds. United Nations Children's Fund. UN: Regional Office for South Asia; 2002.
2. World Health Organization. Low birth weight: a tabulation of available information. In: WHO, eds. WHO/MCH/92.2. Geneva, and New York: World Health Organization, and UNICEF; 1992.
3. Joame Bregman. Developmental outcome in very low birth weight infants - current status and future trends. Pediatr Clin N Am. 1998 Jun;45(3):48-5
4. Anderson JG, Baer RJ, Partridge JC, et al. Survivaland Major Morbidity of Extremely Preterm Infants: A population-Based Study. Pediatrics. 2016;138(1):e20154434
5. Lt Col PK Bhatnagar. Study of low birth weight neonates. MJAFI. 2000;56:293-5.
6. Blencowe H, Cousens S, Oestergaard MZ, Chou D, Moller AB, Narwal R, et al. National, regional, and worldwide estimates of preterm birth rates in the year 2010 with time trends since 1990 for selected countries: a systematic analysis and implications. Lancet. 2012;379(9832):2162–72.
7. Blencowe H, Cousens S, Chou D, Oestergaard M, Say L, Moller AB, et al. Born too soon: the global epidemiology of 15 million preterm births. Reprod Health. 2013;10 Suppl 1:S2.
8. XiangYong Kong1, FengDan Xu, Rong Wumet al. BMC Pediatrics (2016) 16:174
9. Li J, Wang QH, Wei KL, Wei KL, Yang YJ, DU LZ, et al. A survey of neonatal birth in maternal department in urban China in 2005. Chin J Contemp Pediatr. 2012;14(1):7–10.
10. Chen C, Zhang QS. Advances in medical care for extremely low birth weight infants worldwide. Chin J Contemp Pediatr. 2013;15(8):703–7.
11. Shah PS, Sankaran K, Aziz K, Allen AC, Seshia M, Ohlsson A, et al. Outcomes of preterm infants <29 weeks gestation over 10-year period in Canada: a cause for concern? J Perinatol. 2012;32(2):132–8.
12. Isayama T, Lee SK, Mori R, Kusuda S, Fujimura M, Ye XY, et al. Comparison of mortality and morbidity of very low birth weight infants between Canada and Japan. Pediatrics. 2012;130(4):e957–65.

13. Bolisetty S, Legge N, Bajuk B, Lui K. Preterm infant outcomes in New South Wales and the Australian Capital Territory. J Paediatr Child Health. 2015;51(7):713–21.
14. Bacak SJ, Baptiste-Roberts K, Amon E, Ireland B, Leet T. Risk factors for neonatal mortality among extremely low birth weight infants. Am J Obstet Gynecol. 2005;192:862-7.
15. Riza Sangamam. Perinatal mortality and morbidity among low birth weight babies. Int J Community Med Public Health. 2015 Feb;2(1):51-58
16. Stoll BJ, Hansen IN, Bell FE, Shankaran S, Laptook RA, Walsh MC, et al. Neonatal outcomes of extremely preterm infants from the NICHD Neonatal Research Network Pediatrics. 2010;126(3):443.
17. Goldenberg RL, Culhane JF, Iams JD, Romero R.Epidemiology and causes of preterm birth. Lancet 2008; 371.
18. Khan MR, Maheshwari PK, Shamim H, Ahmed S, Ali R. Morbidity pattern of sick hospitalized preterm infants in Karachi, Pakistan. J Pak Med Assoc 2012;62(4):386-8.

How to cite this article: Tawab CNA, George M, Joseph J, Shafi M. Mortality and Morbidity of Extreme Preterm Neonates. Ann. Int. Med. Den. Res. 2019; 5(3):PE04-PE08.

Source of Support: Nil, **Conflict of Interest:** None declared