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Original Research Article

Effect of gender and gestational age on short term morbidities and mortality in extremely low birth neonates

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ABSTRACT

Background: The Aim of this study was to see the effect of gender and gestational age on early morbidities and mortalities of extremely low birth weight neonates.
Methods: It was cross section retrospective. This retrospective study over a period of 5 years from June 2009 to May 2014 in a tertiary level teaching hospital. All the ELBW neonates admitted during the study period were recruited. Moving in a retrospective manner we collected previous case records relevant to our study from the institute and then categorized our data on the basis of gestational age and gender, then we compared and analysed our data on the basis of incidence of mortalities and morbidities and the effect of gender and gestational age on it.
Results: Out of 115 ELBW neonates 61(53%) were born at ≤ 28 weeks, 26 (22%) were born between 29 to 31 weeks and 28(24%) babies were born at 32 to 37 weeks. The most common maternal risk factors responsible for ELBW deliveries were Pregnancy induced hypertension 27 (23%) followed by premature rupture of membranes 20 (17%). Out of short term outcomes HMD (66%), Apnea (71%), hyperbilirubinemia (53%) and sepsis (54.7%) were most common comorbidities. There was no effect of gender on any short-term morbidity and mortality of ELBW newborns. There was a significant higher incidence of hyaline membrane disease, hypoglycemia and neonatal sepsis in ELBW neonates born before 28 weeks of gestational age as compared to born after 28 weeks. 50% of the neonates survived below 28 weeks of gestation.
Conclusions: Our study shows the high incidence of short-term neonatal morbidities. ELBW neonates born before 28 weeks of gestation had higher morbidity.

Keywords: Extremely low birth weight, Gestational age and gender

INTRODUCTION

Contemporary world is the world of science and technology. With the latest advances in technology the survival rate of extremely low birth weight newborns has increased. Extremely low birth weight newborns are defined as having birth weight less than 1000 grams. Apart from aggressive resuscitation and management of tiny infants, other factors that have contributed to the improved survival are widespread use of antenatal steroids and liberal surfactant replacement therapy, different types of ventilation, better control of nosocomial infections and early enteral feeding strategies.[1-3] Although extremely low birth weight infants (ELBW, birth-weight < 1000g) represent approximately 1% of live births, their length of stay in the neonatal unit can be protracted exacting a heavy burden on hospital resources.

Several studies have looked at the trends of mortality and morbidity of ELBW infants. In the last 20 years, survival of these ELBW infants has increased, but the incidence rates of the main neonatal complications remain unchanged. The survival rate of ELBW newborns worldwide is 10%. When the figures come to developing countries like India the neonatal mortality rate is 26% and

ELBW newborns contribute to 10%. In India, 501–750 g neonates have a 23% NICU survival and 751–1000 g neonates have a 61% survival.[4,5]

Surviving ELBW infants are at high risk for neurodevelopmental disabilities and generate substantial costs for their families and society.

Many ELBW infants experience major morbidities during their initial hospitalization, including bloodstream and central nervous system infections, Necrotizing enterocolitis (NEC), Chronic lung disease (CLD), Intraventricular hemorrhage (IVH), Periventricular leukomalacia (PVL), and Retinopathy of Prematurity (ROP).

Neurodevelopmental impairment (NDI) remains a major morbidity for infants born prematurely, particularly for extremely low birth weight (ELBW) infants (≤1000g).[1,2]

While many of these infants fare relatively well, data from the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD), Neonatal Research Network (NRN) and the Vermont Oxford Network indicate that approximately one-third of ELBW infants will die and approximately one-third of survivors will suffer NDI.[6-9]

Early variables known to correlate with the combined outcome of death in ELBW infants include gestational age, birth weight, race/ethnicity, antenatal steroids, multiple gestation, and 5-minute Apgar scores.[10-13]

To save the lives of ELBW infants, particularly those born at 22-23 gestational weeks, is thought to be at the frontier of current perinatal medicine. Gestational weeks 22 to 23 seem to be a limit of viability. Worldwide, ELBW survival may be evaluated with regard to birth weight, gestational age and gender due to their impact on survival.

The idea behind conducting this study was that current available data on the incidence of short-term morbidities and mortalities in ELBW infants from India are scarce. Almost all of the published studies from India have no focus on effect of Gender and Gestational age on ELBW infants mortalities and morbidities.

Therefore this study was planned to assess the effect of gender and gestational age on short-term outcomes in terms of morbidities and mortalities of infants with birth weights less than 1000 g born and treated at Neonatal ICU, Department of Pediatrics of a tertiary care center.

METHODS

This retrospective study was conducted from the case records of patients admitted in neonatal intensive care unit of a tertiary care center over a period of 5 years from June 01, 2009 to 31 May 2014.

Moving in a retrospective manner we collected previous case records relevant to our study from the neonatology unit department of pediatrics in our institute and then categorized our data on the basis of gestational age and gender, then we compared and analyzed our data on the basis of incidence of mortalities and morbidities and the effect of gender and gestational age on it.

From the case records of the neonates, details regarding maternal factor such as age of mother, parity, gestational age, maternal morbidities, mode of delivery etc. was noted in a predesigned proforma.

Neonatal factors such as birth weight, Apgar score, and associated morbidities such as neonatal sepsis, hyperbilirubinemia, necrotizing enterocolitis, hyaline membrane disease, duration of stay in NICU, death etc. were documented.

Stastical analysis

Data was entered in Microsoft excel for windows and analyzed in graph pad (demo version) software. Descriptive variables were presented as numbers and percentages.

Association of Neonatal outcomes with gender and different gestational age groups were analyzed using chi square test. Difference in quantitative data such as Apgar score, birth weight, duration of hospital stay in different groups were assessed using student t test and one way ANOVA whichever applicable. P <0.05 was considered as statistically significant.

RESULTS

During the study period of 5 year a total of 115 extremely low birth weight neonates were born or admitted in neonatal intensive care unit of a tertiary care Institute.

Out of 115 Neonates born, 69 (60%) neonates were male and 46 (40%) were female. Maximum no. of ELBW Neonates 61were born in less than 28 weeks of gestational age which accounted for 53% of the neonates in study. 64 (56%) of the neonates were small for gestational age and 51 (44%) of neonates were average for gestational age (Table 1).

Table 1: Characteristics of ELBW neonates studied.

Variables	Particulars
Gestational age groups	
≤28 weeks	61(53%)
29-31 weeks	26(23%)
32-37 weeks	28(24%)
Male: Female	69:46
SGA	64(56)
AGA	51(44)
LGA	0(0)

Table 2: Maternal cause of extreme low birth weight.

Maternal Morbidities	Number	Percent
Anatomical Septum Defect	1	0.9
APH	12	10.4
Asthma	1	0.9
Cervical incompetence	6	5.2
Eclampsia	5	4.3
Epilepsy	2	1.7
GDM	3	2.6
Hypothyroidism	4	3.4
Infertility treatment	7	6.1
K/C/O RHD (MS)	1	0.9
Oligohydroamnios	7	6.1
PIH	27	23.5
Polyhydroamnios	3	2.6
PROM	20	17.4
RTA	1	0.9
Triplets	2	1.7
Twins	4	3.4
UTI	1	0.9
No associated cause	13	11.3

No neonates were large for gestational age in present study. PIH, PROM and APH were common complications found in mothers of ELBW neonates. Other complications are shown in Table 2.

As shown in Table 3 the incidence of all comorbidities were statistically similar in males and females which shows there was no gender predilection in comorbidities. However despite of being insignificant association of gender with sepsis there was a high odds ratio of 1.85 showing males were more prone for sepsis as compared to females.

Hyaline membrane disease was found in 51 (83%) of cases born before 29 weeks of gestation. Its incidence was decreasing as gestation age was increasing. The distribution of HMD was found to be significant (p value<0.0001) (Table 4). The incidence of Hyperbilirubinemia increases as the gestational age increases. However the difference was not statistically significant. Sepsis was significantly higher in ELBW neonates who were born before gestational age of 29 weeks (p value =0.0008).

Table 3: Association of comorbidities and gender.

Co-morbidities	Female	Male	Total	P value	OR (95 % CI)
HMD	29(63)	47(68.1)	76(66)	0.574	1.252 (0.572-2.743)
Hyperbilirubinemia	24(52.2)	37(53.6)	61(53)	0.879	1.060 (0.502-2.238)
Sepsis	21(45.7)	42(60.9)	63(55)	0.108	1.852 (0.870-3.941)
NEC	7(15.2)	7(10.1)	14(12)	0.415	0.629 (0.205-1.931)
Apnea	32(69.6)	50(72.5)	82(71)	0.736	1.151 (0.507-2.616)
Hypoglycemia	3(6.5)	6(8.7)	9(8)	0.671	1.365 (0.324-5.756)
HIE	4(8.7)	3(4.3)	7(6)	0.339	0.477 (0.102-2.40)
Seizure	3(6.5)	6(8.7)	9(8)	0.671	1.365 (0.324-5.756)
Cardiac cause (PDA)	4(8.7)	7(10.1)	11(9)	0.796	1.185 (0.327-4.304)
BPD	3(6.5)	8(11.6)	11(9)	0.560	0.532 (0.1334-2.122)
PPHN	1(2.2)	1(1.5)	2(2)	0.7709	1.511 (0.921-24.799)
IVH	2(4.3)	2(2.9)	4(3)	0.678	0.657 (0.089-4.836)
ROP	12(26.1)	15(21.7)	27(23)	0.590	0.787 (0.329-1.882)
Hypocalcaemia	1(2.2)	2(2.9)	3(2)	0.811	1.343 (0.118-15.258)
Apgar score 0 min	5.89±2.23	6.26±2.20	6.12±2.21	0.383	-
Apgar score1 min	6.95±1.52	7.16±1.42	7.08±1.45	0.469	-
Apgar score 5 min	8.41±0.72	8.52±0.79	8.48±0.76	0.450	
Birth weight	865.89±127.69	867.93±114.55	867.11±119.54	0.925	-
Mortality	16 (34)	35 (50.7)	51 (44.3)	0.1351	1.930 (0.895-4.163)

Numbers in () represents percentages

Table 4: Association of gestational age with co-morbidities.

Co-morbidities	<29 weeks	29-31 weeks	32-37 weeks	P value
HMD	51(83.6)	14(53.8)	11(39.3)	<0.0001
Hyperbilirubinemia	29(47.5)	13(50.0)	19(67.9)	0.192
Sepsis	42(68.9)	12(46.1)	9(32.1)	0.0008
NEC	6(9.8)	4(15.4)	4(14.3)	0.712
Apnea	41(67.2)	21(80.8)	20(71.4)	0.441
Hypoglycemia	1(1.6)	2(7.7)	6(21.4)	0.005
HIE	6(9.8)	0(0.0)	1(3.6)	0.174
Seizure	5(8.2)	2(7.7)	2(7.1)	0.985
Cardiac cause	8(13.1)	1(3.8)	2(7.1)	0.357
BPD	6(9.8)	3(11.5)	2(7.1)	0.855
PPHN	1(1.6)	1(1.6)	0(0.0)	-
IVH	3(4.9)	0(0.0)	1(3.6)	0.518
ROP	11(18.0)	9(34.6)	7(25.0)	0.242
Hypocalcaemia	1(1.6)	2(7.7)	0(0.0)	0.164
Apgar score 0 min	5.73±2.31	7.08±1.71	6.04±2.2	0.033
Apgar score 3 min	6.9±1.40	7.69±1.01	6.89±1.64	0.049
Apgar score 5 min	8.32±0.86	8.77±0.514	8.54±0.693	0.041
Birth weight	817.5±130.17	924.5±61.83	921.79±85.59	<0.001
Mortality	31(50.8)	12(46.2)	8(28.6)	0.143

Numbers in () represents percentages

The incidence of NEC, HIE, IVH, ROP, Seizure and other comorbidities were similar in all gestational age group hence not statistically significant except hypoglycemia which was higher in 32-37 weeks (p value = 0.005).

51 (44.3%) of patients were died during the study period. High odds ratio of 1.9 suggest that males are at higher risk of mortality as compared to females however the frequency of mortality was Insignificant (p value 1.930). Looking at p value 0.143 we cannot correlate mortality to the gestational age.

DISCUSSION

This study was conducted with the aim to study effect of gender and gestational age on the short-term outcome of the extremely low birth weight (<1000 grams) neonates admitted in Neonatal Intensive care unit of a tertiary care center.

There was slightly high preponderance of male in our study, which is similar to study by Lin et al and Mukopadhyay et al.[14,15] However Kalimba et al and Narayan et al showed the female preponderance.[4,16] Ogawa et al reported almost similar incidence of male and female in ELBW neonates.[17]

The most common gestational age in our study is less than 28 weeks. In Narayan et al study out of 137 ELBW neonates 89 neonates were born before the 29 weeks of gestation.[4] Mukopadhyay et al and Lin et al reported the average gestational age of 29.[14,15] 1 weeks and 28.1 weeks respectively. Ogawa et al in a large case control study from Japan reported 82% of ELBW neonates were born before 29 weeks of gestation and only 3.3% of them were born at or after 32 weeks of gestation.[17]

Similar to our study Ogawa et al and Mukopadhyayet al also reported vaginal mode of delivery as a common mode of delivery.[15,17] This may be due to the fact that most of the neonates were born due to premature rupture of membranes. Secondly LSCS was mostly avoided due to poor outcome of these neonates.

The incidence of Hyaline membrane disease in our study was 76 out of 115 (66%). Narayan et al and Sehgal et al reported incidence of Hyaline membrane disease to be 65% in their individual studies.[4,18] Lin et al reported a slightly higher incidence 73.2% of HMD in ELBW neonates.[14] Kalimbaet al reported that the cause of death was HMD in 25.9% of ELBW neonates.[16] HMD was found to be significantly higher in neonates who were born less than 28 weeks. This was attributed to the intrauterine production of surfactant at around 34 weeks of gestation.

Hyperbilirubinemia was found in 61 (53%) ELBW neonates in our study. Narayan et al4 and Sehgal et al reported the incidence of hyperbilirubinemia in neonates as 65% and 78% respectively, which was higher than our study.[18] There was no significant association of hyperbilirubinemia with gestational age and gender in our study.

Narayan et al and mukhopadhyay et al reported 52% and 46% incidence of neonatal sepsis in their study which is similar to our study that is 63 (54.7%).[4,15] Lin et al and Ogawa et al reported the lower incidence of neonatal sepsis to be 21.8% and 13% respectively.[14,17] This was found to be statistically significant with gestational age as lesser the gestational age more the duration of stay and more the probability of sepsis.

NEC was found in 14 (12.2%) of cases in present study which was very higher from the studies reported by Sehgal et al, Lin HJ et al, Narayan et al reported 13% incidence which is similar to our study.[4,14,18] No significant association of NEC was found with gender and gestational age.

Hypoglycemia incidence was found lower in present study as compared to Sehgalet al study.[18] Significant higher incidence of hypoglycemia was observed in ELBW neonates born at or before gestational age of 28 weeks as compared to ELBW neonates born after 28 weeks. This may be due to the fact that glycogen and fat storage increases with increasing gestational age. There is a lack of storage and high insulin activity in ELBW neonates who are born at or before 28 weeks of gestation which promptsthem to at high risk of hypoglycemia.

The higher incidence of IVH was reported by Narayan et al (29%) and Sehgal et al (17.1%) than the present study 4 (4.3%).[4,18] There was no significant association of IVH with gender and gestational age.

The incidence of ROP in present study was 27 (23.4%) which is quite lower than the study done by Lin HJ et al.[14] Sehgal et al and Narayan et al reported the incidence of ROP as 25% and 14% in ELBW neonates.[4,18]

Seizure incidence was found in 9 (7.8%) in our study, which was slightly lower than Narayan et al.[4] There was no effect of gender and gestational age on it.

Limitation

The limitation of the study is that we have not compared the other obstetric complication with the incidence of mortality and neonatal comorbidities. We have not compared the morbidities and mortalities with normal birth weight neonate group.

CONCLUSION

Our study shows the high incidence of short-term neonatal morbidities. 50% of the neonates survived below 28 weeks of gestation. There was a significant higher incidence of hyaline membrane disease, hypoglycemia and neonatal sepsis in ELBW neonates born before 28 weeks of gestational age as compared to born after 28 weeks. There was no effect of gender on any short-term morbidity and mortality of ELBW newborns.

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