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Prevalence, Severity Patterns and Risk Factors of Bronchopulmonary Dysplasia in Preterm Infants less than 32 weeks of Gestation in a Tertiary Centre in Oman

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Abstract

Objectives: To determine the rate, severity patterns of bronchopulmonary dysplasia (BPD), and to identify antenatal and postnatal factors associated with BPD in preterm infants < 32 weeks of gestational age (GA). ***Methods:*** This study included preterm neonates < 32 weeks of gestation admitted into NICU between January 2010 and December 2017. A data set of antenatal and perinatal factors were collected. BPD was defined as need for oxygen and/or respiratory support at 36 weeks post-menstrual age (PMA). Infants with and without BPD were compared in their antenatal and perinatal factors. ***Results:*** A total of 589 preterm infants < 32 weeks were admitted, 505 (86%) survived to 36 weeks' PMA and 90 (17.8%) had BPD. The combined BPD and mortality rate was 28.4%. Grade I, II and III BPD constituted 77.8%, 7.8%, and 14.4%, respectively. BPD was associated with lower GA, lower birth weight, need for intubation at

resuscitation, lower Apgar scores, longer duration of ventilation, surfactant therapy, and higher rates of neonatal morbidities. On binary logistic regression analysis, predictors of BPD were longer duration of ventilation, IVH, and NEC. ***Conclusion:*** In an Omani center, 17.8% of preterm infants (<32 weeks GA) developed BPD. Various perinatal and neonatal factors were associated with BPD; however, longer duration of ventilation, IVH grades I and II, and NEC stages II and III were the significant predictors. Future multicenter research is necessary to provide the overall prevalence of BPD in Oman, to help in optimizing the resources for BPD prevention and management.

Keywords: Infant; Premature; Bronchopulmonary Dysplasia; Risk Factors.

Advances in Knowledge

- Bronchopulmonary dysplasia (BPD) (oxygen and or respiratory support at 36 weeks post-menstrual age) in preterm infants less than 32 weeks gestational age at a level III NICU at a single center in Oman is 17.8%.
- The development of BPD is associated with various perinatal and neonatal factors.
- Longer duration of invasive mechanical ventilation, interventricular hemorrhage, and necrotizing enterocolitis are the most significant predictors of bronchopulmonary dysplasia.

Application to Patient Care

- Contributes to the knowledge of identifying infants who are at risk for BPD.
- This enables healthcare providers to identify high-risk populations, and effectively tailor interventions and implement preventative measures.
- The findings help empower local medical professionals to optimize overall care strategies for such a high-risk group of infants.

Introduction

Bronchopulmonary dysplasia (BPD) continues to be one of the major comorbidities of prematurity, a chronic lung disease affecting preterm infants exposed to prolonged oxygen and mechanical ventilation.[1] Advancement in neonatal care over the years has led to improved survival rates of extreme and very preterm infants with BPD described as needing oxygen and/or respiratory support at PMA of 36 weeks.[2,3] The definition and classification of BPD have

undergone multiple revisions.[2,4–7] The most widely used definition is the National Institute of Child Health and Human Development (NICHD) Workshop definition, which was recently updated.[8]

Known postnatal risk factors for BPD development include low gestational age (GA), prolonged mechanical ventilation and oxygen exposure.[3] However, BPD has also been described in preterm infants who never received invasive mechanical ventilation.[9] Antenatal factors, including placental dysfunction, intrauterine growth restriction (IUGR), chorioamnionitis, preeclampsia, maternal hypertension, and smoking, have been described as factors associated with an increased risk of BPD.[10] The pathophysiology of how these factors contribute to BPD is complex and yet to be determined. The etiology of BPD is thought to be multifactorial, with both antenatal and postnatal factors playing a significant role in the abnormal alveolarization and pulmonary vascular remodeling seen in histology samples of preterm infants who died with BPD.[11]

BPD rates vary significantly between different centers and countries.[12-16] In a retrospective cohort study from all levels of neonatal intensive care units (NICU) within the California Perinatal Quality Care Collaborative, the overall combined BPD and death rate hugely varied from 17.7% to 73.4%.[13] In addition, the rate of BPD and death was highest in level II NICUs compared with level III and level IV NICUs.[17] The variations may be explained by altitude and different local practices.[14-15]

Approximately 10% of births in Oman occur before 37 weeks of gestation.[18] To our knowledge, there are no studies that have investigated the prevalence, patterns of severity, and risk factors for BPD in preterm infants in Oman. Therefore, this study was conducted with the primary objective of determining the rate of occurrence and severity patterns of BPD and, secondarily, to identify major antenatal and postnatal factors associated with BPD in preterm infants < 32 weeks of gestation admitted to a single level III NICU in Oman between 2010 and 2017.

Methods

Study design

This is a retrospective observational study conducted in a level III, 24-bed capacity NICU of a tertiary and academic hospital in Oman, servicing approximately 5,000 births per year. Ethical approval for the study was obtained through the institutional medical research ethics committee (MREC#1887). Consent was waived due to the retrospective nature of the study.

Participants

Eligible participants included preterm infants of less than 32 weeks of gestational age (GA), admitted into the NICU between January 1, 2010, and December 31, 2017. Infants were excluded if they were transferred to other health institutions before 36 weeks of PMA.

Data collection and outcomes

Pre-determined datasets were collected from the electronic charts of the patients, including antenatal factors (maternal age, maternal morbidities such as pre-eclampsia, sepsis chorioamnionitis), birth information (mode of delivery, gender, gestational age, birth growth parameters, Apgar scores, resuscitation at birth), type of ventilation received, intubation and extubation variables, duration of invasive mechanical ventilation, post-extubation support, respiratory status at 28 days of life and PMA of 36 weeks, other neonatal comorbidities(Intraventricular hemorrhage, necrotizing enterocolitis, bronchopulmonary dysplasia), discharge condition (PMA at discharge, weight and head circumference, oxygen therapy, and nutritional support).

The primary outcomes of this study were the rate, severity patterns of BPD and the combined mortality and BPD rate in preterm infants less than 32 weeks of gestation. Factors linked to BPD, as well as those that highly predicted BPD, were the secondary outcomes of this study.

Definition of BPD

The definition and severity of BPD were based on the most recent update of the NICHD workshop definition which was published in 2018.[8] In this updated scheme, BPD is defined as oxygen and/or respiratory support at a PMA of 36 weeks. The severity is graded into grades I, II,

and III based on the type of respiratory support and oxygen concertation as per the following: No BPD: at PMA of 36 weeks, the infant is already discharged home in room air or is still in-hospital but already in room air. Grade I BPD: if the infant at PMA of 36 weeks is on nasal continuous positive airway pressure (NCPAP)/nasal intermittent positive pressure ventilation (NIPPV)/cannula ≥ 3L/min with FiO_2 21%, or nasal cannula flow 1-2 L/min with FiO_2 22-29%, or nasal cannula <1L/min FiO2 22-70%. Grade II BPD: at PMA 36 weeks, the infant is on intermittent positive pressure ventilation (IPPV) with FiO_2 21%, or NCPAP/NIPPV/nasal cannula ≥ 3L/min with FiO_2 22-29%, or nasal cannula 1-2 L/min with FiO_2 ≥30, or nasal cannula <1L/min with FiO_2>70%. Grade III BPD: if at PMA of 36 weeks, the infant is on IPPV with FiO_2>21, or NCPAP/NIPPV/nasal cannula ≥3L/min FiO_2 ≥30.

Statistical analysis

IBM SPSS Statistics-23 software was used for the data analysis. The study population was divided into two groups: BPD and no BPD. Continuous variables have been expressed as mean ± standard deviation (SD) or median and interquartile range (IQR). Categorical variables are expressed as frequency and percentages. Chi-square and Fisher's exact tests were used to assess differences between the categorized variables and small frequencies. Independent sample t-tests or Mann-Whitney U tests were used to test parametric and non-parametric data, respectively. To estimate the risk of BPD for different factors, odds ratios and 95% confidence intervals were obtained. A binary logistic regression analysis was performed to identify the significant predictors for BPD. Additional analysis of primary outcomes based on stratification of infants into two gestational-age categories 22-28 weeks and 29-31 weeks. A p-value of less than 0.05 was considered statistically significant.

Results

Primary Outcomes:

A summary of the study's population flowchart is shown in (Figure 1). A total of 589 preterm infants with gestational ages less than 32 weeks were admitted to the NICU during the study period, including 83 deaths (a mortality rate of 14.1%). BPD was diagnosed in 90 out of 505 infants who survived up to PMA of 36 weeks (17.8%). The combined mortality and BPD rate in this study was 28.4% (Table 1). The severity patterns of BPD are presented in Table 2. Grade I,

grade II, and grade III BPD constituted 77.8%, 7.8%, and 14.4%, respectively. When infants were stratified into two gestational age categories 22-28 and 29-31 weeks, the BPD rate was found to be 36% and 6.2%, respectively, ($p<0.0001$). Similarly, the mortality rate was significantly higher in the 22-28 weeks category [24.3% vs. 5.8%, $p <0.0001$]. The combined mortality and/or BPD rate was also significantly higher in the 22-28 weeks GA category [50.9% vs. 11.1%, $p<0.000$]. However, no significant differences in the severity grades of BPD between the two GA categories, (Table 3). Further analysis of the rate of BPD in each year was performed (Figure 2). The yearly BP rate ranged between 9.3-25.4% of infants who survived to PMA of 36 weeks.

Secondary outcomes

Table 4 shows the differences in antenatal, perinatal, and postnatal characteristics of the BPD and no BPD groups. No significant differences were observed in maternal age, maternal complications, antenatal steroid use, or method of birth. Significantly more infants in the BPD group needed intubation as part of the resuscitation at birth (83.3% vs. 45.3%, p=<0.01). Infants with BPD had significantly lower gestational age (median 26 vs. 29 weeks, $p =0.001$), birth weight (median 830g vs. 1150 g, $p < 0.001$), head circumference (median 23.5 cm vs. 26 cm, $p < 0.001$), and Apgar score at 1 minute and 5 minutes [(5 vs. 6, $p <0.001$) and (8 and 8, $p<0.001$) respectively. Invasive mechanical ventilation was received by 98.9% of infants with BPD as compared to only 58.3% of those without BPD, ($p < 0.001$). Infants with BPD were extubated at a median of 29 days of life (as compared to a median of two days of life in those without BPD, ($p < 0.001$). Infants with BPD had a significantly longer median duration of mechanical ventilation (median of 28 days vs. 2 days, $p < 0.001$). A total of 36 (40.2%) infants with BPD received ≥ 2 episodes of mechanical ventilation as compared to 42 (17.5%) of infants without BPD, $p < 0.001$. At day 28 of life, all infants with BPD were still on respiratory support, as compared to only 30.6% of those without BPD ($p < 0.001$).

The need for surfactant replacement therapy at two or more doses was higher in infants with BPD (96% vs. 53%, $p<0.001$). Similarly, the rates of other prematurity complications, including pulmonary hemorrhage, intraventricular hemorrhage (IVH), patent ductus arteriosus (PDA), necrotizing enterocolitis (NEC), and sepsis, were significantly higher in infants with BPD (Table

5). The need for dexamethasone for extubation was similarly significantly higher in infants with BPD (33.3% vs. 1.1%, $p < 0.001$).

The mortality rate after a PMA of 36 weeks was noted to be 5.6% in infants with BPD, which is significantly higher than that of infants without BPD (0.2%). Infants with BPD had a longer duration of NICU stay, as they were discharged at a median PMA of 40 weeks, as compared to 35 weeks in those without BPD ($p < 0.001$). At discharge, infants with BPD had significantly higher weight and head circumference (Table 4). Approximately 75% of infants without BPD were already discharged at the PMA of 36 weeks. This is compared to 100% of those with BPD who were still inpatients (Table 4).

Binary logistic regression analysis for the variables which were associated with BPD (Table 6) showed that factors that significantly predicted BPD were duration of mechanical ventilation [OR 1.097, CI (1.097-1.173), $p = 0.007$], IVH Grade 1 and 2 [OR 4.19, CI (1.218-14.461), $p = 0.023$], and NEC stages II and III [OR 5.272, CI 1.042-26.6750, $p = 0.044$]. Other factors that were associated with BPD, such as gestational age, birth weight, resuscitation at birth, Apgar scores, number of episodes of mechanical ventilation, surfactant use, pulmonary hemorrhage, PDA, sepsis, and age at intubation and extubation, did not significantly predict BPD.

Discussion

To our knowledge, this is the first study investigating BPD rate, severity, and risk factors among at-risk preterm infants (< 32 weeks' GA) in Oman. The study found that the BPD rate; defined as oxygen and/or respiratory support at PMA of 36 weeks, is 17.8% and the combined death and BPD rate is 28.4%. Most of the BPD cases were grade I. This study did not identify any significant antenatal risk factors related to BPD; however, multiple perinatal and postnatal factors were associated with BPD such as lower birth weight, lower GA at birth, lower Apgar scores, resuscitation at birth, mechanical ventilation, and longer duration of mechanical ventilation. Other prematurity comorbidities were also associated with BPD.

The BPD rate in our NICU is comparable to other centers across the world, falling within the broad global incidence range of 17-75%, using the same definition of oxygen and/or respiratory

support at 36 PMA.[19] However, worldwide, the reported rates of BPD vary widely depending on the range of gestational age and birth weight of the population of preterm infants included in the studies.[20-22] For example, in a single-center US study by Sharma et al. (2019) which reported on BPD in 263 extremely preterm infants (23–27 weeks), 58.9% of infants were on oxygen and/or respiratory support at a PMA of 36 weeks.[23] In comparison, a single-center Korean study that included 629 preterm infants less than 30 weeks GA, admitted between 2009 and 2018, 13.8% of infants were on oxygen or respiratory support at 36 weeks PMA.[24]

The prevalence of BPD also varies across centers in multi-center studies.[17, 24] In a multicenter US study that included 15779 infants born between 22 and 29 weeks across 116 NICUs within the California Perinatal Quality Care Collaborative, approximately 33% of survivors to PMA of 36 weeks were either still in the hospital on oxygen or discharged home on oxygen.[17] NICU level of care may affect the prevalence of BPD, as level II NICUs seem to have higher rates of BPD compared to level III.[17]. This variation may be related to the level of experience and variation in practices in the management of preterm infants at risk of BPD.[25,26]

This study did not identify any antenatal factors significantly related to BPD, as no significant differences were observed in maternal age, and maternal morbidities such as pregnancy-induced hypertension, pre-eclampsia, and chorioamnionitis. These findings correlate with Morrow et al. 2017, who also showed similar findings except for maternal smoking status and pre-existing hypertension, which significantly correlated with BPD.[27] Maternal smoking was not investigated in this study considering that female smoking is generally rare in the Omani population.[28] Likely, risks for BPD are related to neonatal factors, as demonstrated in this study. This study has identified various perinatal and postnatal factors associated with BPD including lower GA, lower birth weight, need for resuscitation at birth, lower Apgar scores at 1 and 5 minutes, need for mechanical ventilation, longer duration of mechanical ventilation, need for respiratory support at 28 days, surfactant therapy, pulmonary hemorrhage, IVH, PDA, NEC, and need for dexamethasone for extubation. Previous studies have also shown similar associations.[29-32] This is possibly explained by the prematurity of the anatomy and physiology of these neonates.

In this study, NEC stages II and III significantly predicted BPD. This is likely related to the fact that the two conditions shared a common physiological factor which is inflammation. The relationship between NEC and BPD and the hypothesis of the gut-lung axis has been extensively reviewed recently.[33] The hypothesis postulates that there is crosstalk between the gastrointestinal tract and respiratory tract at various levels such as the microbiome, immunity and metabolites. Intestinal dysbiosis coupled with a dysregulated immune system can mediate lung inflammation and injury through inflammatory cytokines and cellular immune signaling pathways. Ultimately, the lung inflammation occurring concurrently with NEC contributes to the development of BPD.[33]

The association between IVH and BPD has also been described in the literature. For instance, in the study by Jassem-Bobowic et al. 2021, IVH was significantly associated with BPD in their univariate analysis.[34] However, to our knowledge, no study reported that IVH is predictive of BPD. Interestingly, although both IVH grades I &II and grades III&VI were associated with BPD in univariate analysis of this study, only grades I/II predicted BPD according to our binary regression analysis. We believe this could be related to the survival effect because infants with more severe IVH tend to have higher mortality.[35] Further future prospective studies are recommended to validate the value of IVH as a factor in predicting the risk of developing BPD.

This study serves as a grounding stone for assessing the magnitude of BPD in preterm infants in Oman. To ensure optimal outcomes and efficient allocation of necessary resources and interventions, a comprehensive multi-central collaborative study on BPD in Oman is of paramount importance. Such studies not only aid in understanding the risk factors, pathogenesis, and long-term implications of the condition but also provide valuable insights into tailored treatment strategies and preventative measures. By identifying high-risk groups and prognostic indicators, healthcare providers can prioritize resources for early detection, intervention, and ongoing support, ultimately improving the quality of life for affected infants and their families. In addition, research on BPD facilitates the development of innovative therapies and advances in neonatal care, enhancing the overall healthcare landscape for preterm infants. The continuous effort to study and comprehend BPD underscores the significance of evidence-based approaches in guiding clinical decisions and optimizing resource allocation for the best possible outcome.

The strength of this study is related to its relatively large population size of <32 weeks GA infants and the use of the updated NICHD's BPD definition and classification system to define BPD. However, there are a few limitations worth discussing. This study is a single-center, retrospective and observational study with an unbalanced number of infants in the non-BPD and BPD groups, limiting the generalizability of the findings to other cohorts.

Conclusion

The rate of BPD in a level III NICU in Oman was 17.8%; mostly classified as grade 1. BPD is significantly associated with lower birth weight, lower gestational age, lower Apgar scores, the need for intubation and invasive mechanical ventilation, pulmonary hemorrhage, PDA, sepsis, and receiving dexamethasone. However, only longer duration of mechanical ventilation, grades I and II IVH, and stages II and III NEC are predictors for BPD in this study. Accordingly, strategies to avoid invasive mechanical ventilation and limiting its duration may help in decreasing BPD rates. A multi-center study including various level III and II NICUs in the country will provide valuable data on the overall prevalence of BPD in Oman. It will help in shedding further insights into the predictive values of IVH and NEC and provide valuable data for the optimal allocation of necessary resources and interventions for the prevention and management of BPD in the country.

Authors' Contribution

The initial idea and the proposal of the study started by HM, AK, AS, and MA. Data collection was completed by AK, AS, MA, and SA. Analysis of data was performed by HM, SR, SM, AK and SQ. All authors contributed equally to the write-up and revision of the final state of the manuscript.

Conflict of Interest

The authors declare no conflicts of interest.

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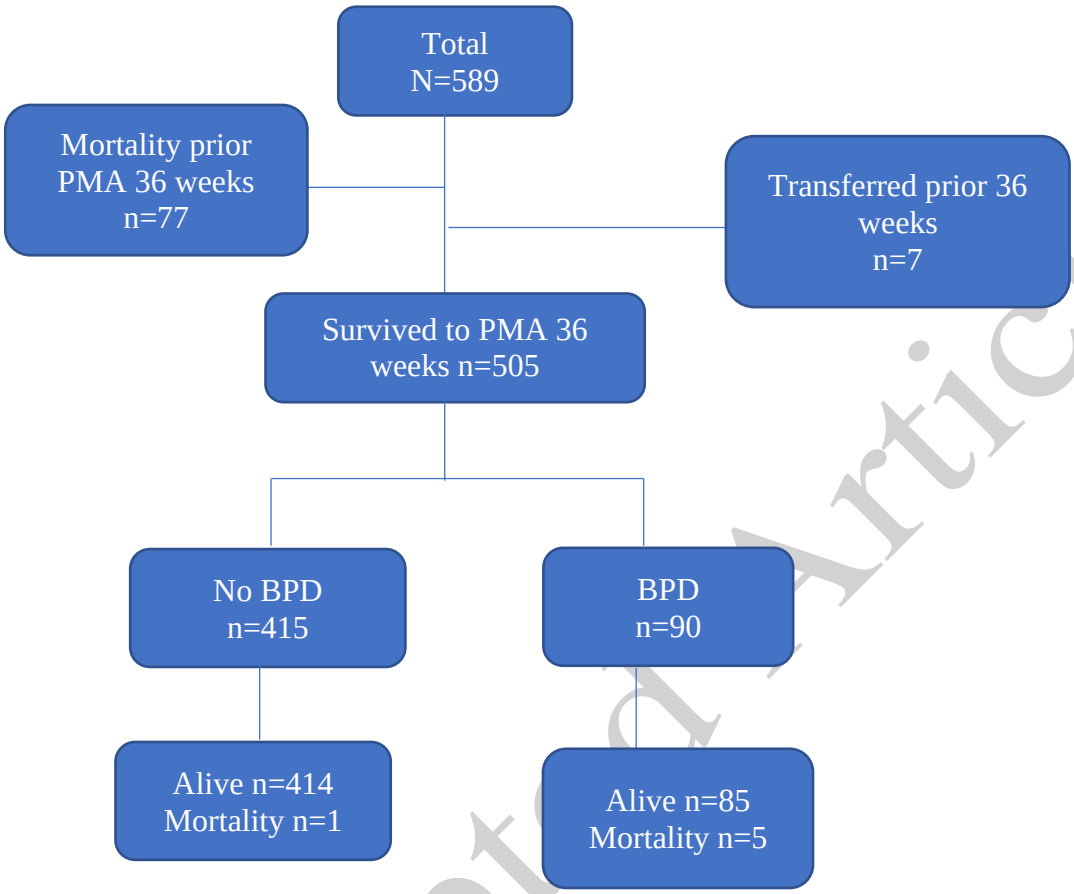
Figure 1: Study population Flowchart



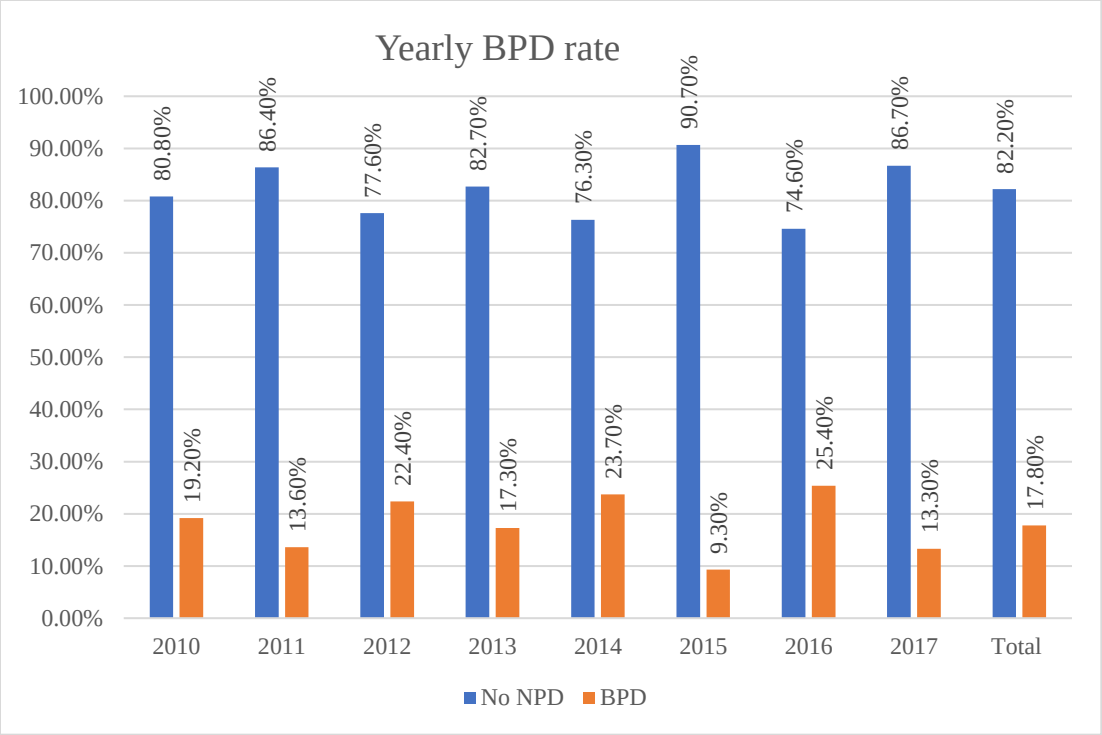


Figure 2: Yearly BPD rate in infants surviving to PMA 36 weeks during the study period

Table 1: Primary outcomes

	Frequency (n)	%
BPD	90	17.8*
No BPD	415	82*
Total Mortality alone	83	14.1#
Combined BPD and mortality	167	28.4#

BPD: bronchopulmonary dysplasia,

** % out of the total number of infants who were alive at PMA 36 weeks (N=505)*

 # % out of the total number of infants (N=589)

Table 2: BPD severity classification patterns (N=90)

Severity	Grade I	Grade II	Grade III
Frequency (n)	70	7	13
Percentage %	77.8	7.8	14.4

BPD: Bronchopulmonary dysplasia

Table 3: Primary outcomes based on stratification of gestational age

Outcome	GA22-28 weeks n (%)	GA 29-31 weeks n (%)	P value
BPD	71 (36) *	19 (6.2) #	<0.0001
Total Mortality	64 (24.3) ^	19 (5.8) $	<0.0001
Combined BPD and/or Mortality	132 (50.9) ^	35 (11.1) $	<0.0001
BPD Grade I	54 (76.1)	16 (84.2)	0.362
BPD Grade II	7 (9.8)	0 (0)	
BPD Grade III	10 (14.1)	3 (15.8)	

GA: gestational age, BPD: bronchopulmonary dysplasia.
**% out of the total number of neonates GA 22-28 weeks who survived to PMA 36 weeks N=197*
#% out of the total number of neonates GA 29-32 weeks who survived to PMA 36 weeks, N=308
^% out of the total number of neonates GA 22-28, N=259
$% out of the total number of neonates GA 29-32 weeks, N=330
p-value < 0.05 is significant

Table 4: Difference in Patients' antenatal, perinatal and post-natal characteristics

	No BPD (n=415)	BPD (n=90)	P value
Maternal age (years)*	28 (9)	29(8)	0.909
Maternal complications#			0.602
No Complication	169 (40.7)	43 (47.8)	
PIH/Pre-eclampsia	75 (18.1)	14 (15.6)	
Sepsis/Chorioamnionitis	22 (5.3)	3 (3.3)	
Others	149 (35.9)	30 (33.3)	
Antenatal steroids#	258 (62.2)	55 (61.1)	0.946
Mode of delivery#			0.579
SVD	144 (34.7)	37 (41.1)	
Instrumental	4 (1.0)	1 (1.1)	
El LSCS	2 (0.5)	1 (1.1)	
Em LSCS	265 (63.9)	51 (56.7)	
Resuscitation#			<0.001
Routine	89 (21.4)	1 (1.1)	
PPV	135 (32.5)	9 (10)	
Intubation	188 (45.3)	75 (83.3)	
CPR (Med)	3 (0.7)	5 (5.6)	
Gestational Age (weeks) *	29 (3)	26 (3)	<0.001
Gender#			0.589
Male	224(54)	52 (57.8)	
Female	119 (46)	38 (47.2)	
Birth weight (gm) *	1150 (425)	830 (265)	<0.001
Birth HC (cm) *	26 (4)	23.5 (3)	<0.001
Apgar@1 min*	6 (3)	5 (4)	<0.001
Apgar@5 min*	8 (1)	8 (3)	<0.001
Required Invasive ventilation*	242 (58.3)	89 (98.9)	<0.001
DOL at intubation#	1 (0)	1 (0)	0.556

DOL at extubation*	2 (6)	29 (33)	<0.001
Duration of MV (days) *	2 (6)	28 (30)	<0.001
Episodes of MV#			<0.001
1 episode	198 (82.5)	53 (59.6)	
≥ 2 episodes	42 (17.5)	36 (40.4)	
Respiratory status @ D28#			<0.001
Discharged	19 (4.6)	0 (0)	
Respiratory support	127 (30.6)	90 (100)	
Room air	269 (64.8)	0	
Respiratory status @ 36 weeks#			<0.001
Discharged	310 (74.7)	0	
MV	0	10 (11.1)	
CPAP	0	22 (24.4)	
HFNC	0	10 (11.1)	
LFNC	0	48 (53.3)	
Room air	105 (25.3)	0	

BPD: Bronchopulmonary dysplasia, CPAP: continuous positive airway pressure, CPR: cardiopulmonary resuscitation, El LSCS: elective lower segment cesarian section, EmLSCS: emergency lower segment cesarian section, DOL: day of life, HFNC: high flow nasal cannula, LFNC: low flow nasal cannula, MV: mechanical ventilation, PPV: positive pressure ventilation, SVD: spontaneous vaginal delivery,

**Variable expressed as median (IQR)*

#Variable expressed as n (%)

p-value < 0.05 is significant

Table 5: Prematurity comorbidities and discharge variables

	No BPD (n=415)	BPD (n=90)	
Surfactant given[#]	220 (53)	86 (95.6)	<0.001
Pulmonary Hemorrhage[#]	12 (2.9)	13 (14.4)	<0.001
Intraventricular Hemorrhage[#]			
Grades 1&2	18 (4.3)	16 (17.8)	<0.001
Grades 3 &4	11 (2.7)	14 (15.6)	
PDA[#]	45 (10.8)	46 (51.1)	<0.001
Sepsis[#]	80 (19.3)	54 (60.0)	<0.001
NEC[#]			<0.001
NEC I	22 (5.3)	12 (13.3)	
NEC II, III	5 (1.2)	17 (18.9)	
Dexamethasone [#]	5 (1.2)	30 (33.3%)	<0.001
Outcome[#]			<0.001
Alive	414 (99.8)	85 (94.4)	
Expired	1 (0.2)	5 (5.6)	
PMA at Discharge (Weeks) [*]	35 (2)	40 (5)	<0.001
Discharge weight (gm) [*]	1825 (360)	2565 (908)	<0.001
Discharge HC (cm) [*]	30 (2)	32 (3.35)	<0.001
Readmission[#]	87 (21.1)	39 (34.4)	<0.001

BPD: bronchopulmonary dysplasia, HC: head circumference, NEC: necrotizing enterocolitis,
PMA: post-menstrual age, PDA: patent ductus arteriosus,
[*]Variable expressed as median (IQR)
[#]Variable expressed as n (%)
p-value < 0.05 is significant

Table 6: Binary Logistic Regression analysis

Variables	B	Sig.	Odds ratio	95% C.I.	
Resuscitation					
Routine					
PPV	1.224	0.425	3.401	0.168	68.788
Intubation	1.163	0.452	3.200	0.154	66.530
CPR	2.403	0.195	11.059	0.293	417.802
Gestational age (weeks)	0.214	0.138	1.239	0.933	1.645
Birth weight (gm)	-0.001	0.128	0.999	0.997	1.000
Apgar at 1 minute	-0.146	0.256	0.864	0.672	1.111
Apgar at 5 minutes	0.074	0.647	1.077	0.784	1.480
Episodes of Mechanical ventilation					
1 episode					
≥2 episodes	-0.362	0.433	0.697	0.282	1.721
Surfactant given	0.235	0.847	1.265	0.117	13.716
Pulmonary hemorrhage	-0.311	0.619	0.733	0.215	2.498
Intraventricular hemorrhage					

No IVH					
Grade1&2	1.434	0.023	4.197	1.218	14.461
Grade3 &4	0.361	0.593	1.435	0.381	5.400
PDA	0.234	0.587	1.263	0.543	2.937
Blood culture sepsis	0.315	0.444	1.370	0.612	3.070
NEC					
No NEC					
NEC I	0.363	0.569	1.438	0.413	5.011
NEC II, III	1.662	0.044	5.272	1.042	26.675
Dexamethasone	0.111	0.900	1.117	0.199	6.282
Day of life at intubation	-0.039	0.706	0.962	0.785	1.178
Day of life of extubation	0.021	0.340	1.021	0.978	1.067
Mechanical ventilation duration (days)	0.093	0.007	1.097	1.026	1.173

CPR: cardiopulmonary resuscitation, IVH: intraventricular hemorrhage, NEC: necrotizing enterocolitis, PDA; patent ductus arteriosus,
p-value < 0.05 is significant