BRONCHOPULMONARY DYSPLASIA IN EXTREMELY PRETERM INFANTS: PREVALENCE AND RELATED FACTORS

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Infants born extremely preterm are defined as a birth under 28 weeks gestational age. Bronchopulmonary dysplasia (BPD) is the most common lung complication in this population and manyfactors can contribute to the development of BPD. The objective of this study was to identify the prevalence of BPD and to analyse the related factors of BPD in extremely preterm infants. Seventy two infants who met the inclusion criteria were included in the study. BPD was diagnosed according to Jobe and Bancalari definition. The prevalence of BPD was 79.2%. There was an inverse relationship between the percentage of BPD, the severity of BPD and the gestational age and birth weight. Invasive ventilation requirement of more than 7 days was the independent factor of BPD. Conclusion: The prevalence of BPD was high. Prolonged invasive ventilation was an independent factor of BPD.

Keywords: Bronchopulmonary dysplasia, extremely preterm infants, related factors.

I. INTRODUCTION

Infants born extremely preterm are defined as birth under 28 weeks gestational age.[1] This population may face many complications of prematurity where bronchopulmonary dysplasia (BPD) is the most common lung complication. Bronchopulmonary dysplasia is characterized by alveolar simplification, arrest in lung growth, impaired vascular development and abnormal pulmonary function.[2]

The reported global incidence range of BPD was from 10 to 89%, depending on region, gestational age and birth weight.[3] 38 publications from North America, two publications from Europe and North America, 19 publications from Asia, one publication from Asia and North America, six publications from Oceania, and zero publications from Africa or South America. The reported global incidence range of BPD

was 10–89% (10–73% in Europe, 18–89% in North America, 18–82% in Asia, and 30–62% in Oceania In Vietnam, the incidence of BPD differed from center to center, ranging from 9,3% to 50%.[4,5] In recent years, due to advance in neonatal care, the survival rate of extremely preterm infants increased but the incidence of BPD remained unchanged.

Multiple factors may contribute to the development of BPD, including prenatal, perinatal and postnatal factors. The results of the study of Chau et al showed that BPD was associated with gestational age under 28 weeks, birth weight under 1000 gram, infections and symptomatic patent ductus arteriosus (PDA).[6]

The National Hospital of Obstetrics and Gynecology (NOBGY) is one of the leading hospital in obstetrics, gynecology and neonatal care in the North of Vietnam. Its neonatal center treats all newborn at the hospital. The objective of this study was to identify the prevalence of BPD and to analyse the related factors of BPD in extremely preterm infants in the Neonatal center of the hospital.

II. METHODS

1. Study design

This cross–sectional study was conducted at the Neonatal center of The National Hospital of Obstetrics and Gynecology (NOBGY) from 8/2022 to 7/2023 and approved by the Hospital Ethics Committee number 1129/CN-PSTW. Written consent from parents or legal guardians was obtained before the study.

2. Participants

Inclusion criteria

All preterm infants who were live-born in NOBGY at the age of 28 weeks or below were included in the study. The diagnosis of BPD according to Jobe and Bancalari definition is preterm infants requiring oxygen at least 21% for at least 28 days.

Table 1. Definition of bronchopulmonary dysplasia: Diagnostic criteria[7]

Gestational age	< 32 week
Time point of assessment	36 week postmenstrual age (PMA) or discharge to home, which ever comes first
Oxygen requirement	Treatment with oxygen > 21% for at least 28 days
Mild BPD	Breathing room air at 36 weeks PMA or upon discharge, which ever comes first
Moderate BPD	Need for < 30% oxygen at 36 weeks PMA or upon discharge, which ever comes first
Severe BPD	Need for ≥ 30% oxygen and/or positive pressure at 36 weeks PMA or upon discharge, which ever comes first

Exclusion criteria

Infants were born by termination of pregnancy due to severe congenital birth defects, infants needed prolonged ventilation due to congenital heart disease or neurologic defects or infants who were tranferred to NOBGY were not included in the study.

3. Study procedures

- All infants who met the criteria were recruited in the study. Information was collected from admission to 36 weeks corrected age or upon discharge whichever came first: gestational age, birth weight, temperature on admission, oxygen requirement at admission, infections, patent ductus arteriosus, blood transfusion, respiratory support at 36 weeks…

- Infants who survived until 36 weeks corrected age were included in the study. At 36 weeks corrected age, the infants who diagnosed with BPD were allocated in "BPD group", infants without BPD were allocated in "no BPD group".

- Comparing the characteristics of 2 groups for related factors of BPD

4. Variable definition

- Extremely low birth weight (ELBW): birth weight under 1000 gram.

- Very low birth weight (VLBW): birth weight from 1000 gram to 1499 gram.

- Hypothermia on admission: body temperature on admission under 36.5 Celcius degree.

- Invasive ventilation: ventilation via endotracheal tube.

- Symptomatic patent ductus arteriosus (PDA): was identified by echocardiogram which had one of these features:

+ Size of the duct ≥1,5 mm or ≥1,4 mm/kg

+ Dilated left atrium: left atrial/aortic root ratio ≥1.5

+ pulsatile transductal flow (Vmax) less than 1.8 m/second

- Late infection: having infection after 72 hours of birth.

5. Statistical analysis

Data were analyzed by using SPSS version 20.0. Descriptive statistics was used for frequency, percentage... Chi-square or Fisher's exact test was used for categorical variables. Univariate analysis and multivariate logistic regression analysis were used for analyzing related factors. The value of p less than 0.05 was considered significant.

III. RESULTS

1. General characteristics of the study population

From 8/2022 to 7/2023, 72 extremely preterm infants who met the criteria were included in the study. There were 35 males and 37 females, male to female ratio was 1/1.06. The mean birth weight was 948.61 ± 152.9 gram, the proportion of extremely low birth weight (<1000g) and very low birth weight (1000 – 1499g) was 48.6% and 51.4%, respectively. The mean gestational age was 27.11 ± 0.97 weeks. The percentage of 25 weeks, 26 weeks, 27 weeks and 28 weeks gestational age group were 8.3%, 16.7%, 30.6% and 44.4%, respectively.

2. Prevalence of BPD

In 72 infants, there were 57 infants diagnosed with BPD, accounting for 79.2%.
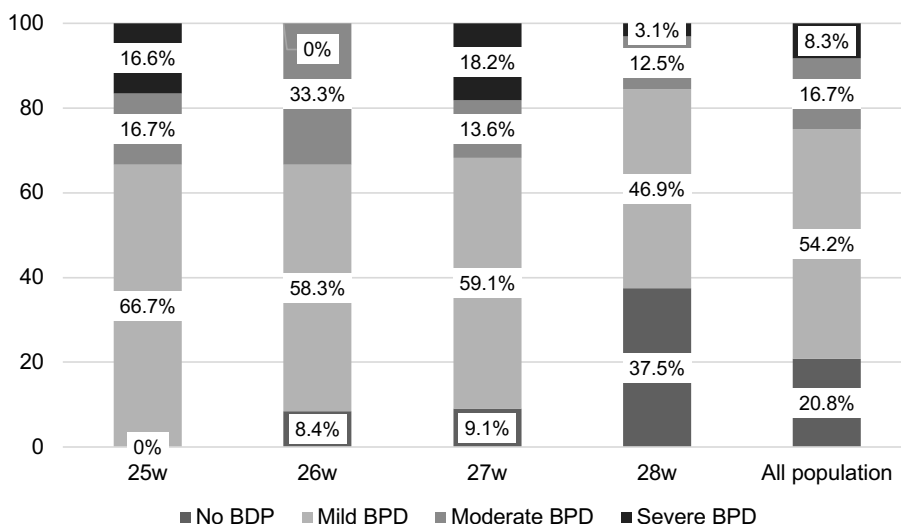
Figure 1. Distribution of severity of bronchopulmonary dysplasia by gestational age in percentage

The percentage of infants who survived without BPD increased from 0% in 25 weeks gestational age group to 37.5% in 28 weeks gestational age group, accounting for 20.8% in the whole population. The percentage of moderate and severe BPD were the highest in 26 weeks gestational age group and 27 weeks gestational age group, respectively.
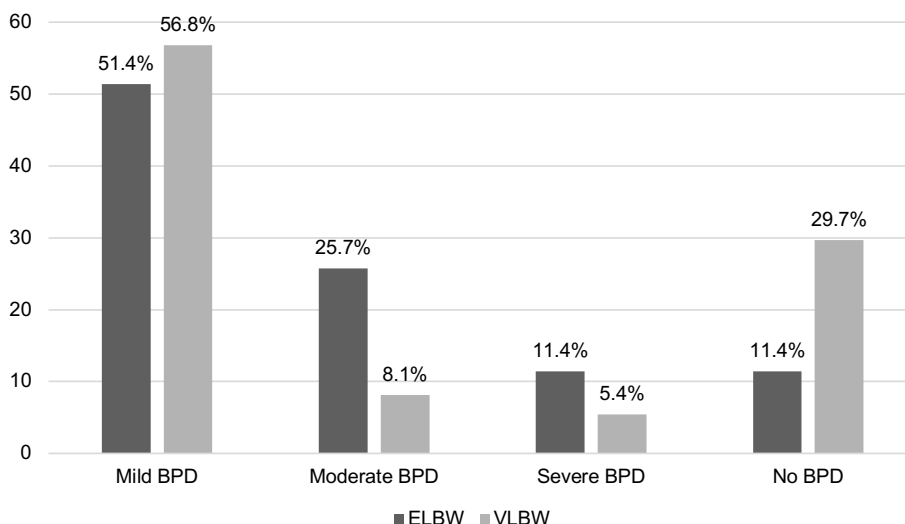
Figure 2. Distribution of severity of bronchopulmonary dysplasia by birth weight in percentage

The percentage of BPD and severity of BPD in extremely low birth weight (ELBW) infants were higher than in the very low birth weight (VLBW) infants, except for mild BPD.

The differences were significant with $p < 0.05$ (Fisher's exact test).

3. Related factors of BPD

Table 2. Related factors of BPD

Factors		BPD				Univariate analysis		Multivariate analysis	
		Yes		No		OR (95%CI)	p	OR (95%CI)	p
		n	%	n	%				
Less than 28w	Yes	37	92.5	3	7.5	7.40 (1.87 – 29.33)	0.002	4.65 (0.64 – 33.89)	0.13
	No	20	62.5	12	37.5				
ELBW	Yes	31	88.6	4	11.4	3.28 (0.93 – 11.53)	0.06	2.09 (0.34 – 12.78)	0.42
	No	26	7.03	11	29.7				
Hypothermia at admission	Yes	19	86.4	3	13.6	0.50 (0.13 – 1.99)	0.32	0.69 (0.10 – 4.62)	0.69
	No	38	76.0	12	24.0				
FiO_2 >30% at admission	Yes	37	86.0	6	14.0	0.36 (0.11 – 1.16)	0.08	0.60 (0.11 – 3.28)	0.55
	No	20	69.0	9	31.0				
Needing invasive ventilation > 7 days	Yes	43	95.6	2	4.4	19.96 (4.01 – 99.50)	0.00	14.07 (1.62 – 122.10)	0.01
	No	14	51.9	13	48.1				

Factors		BPD				Univariate analysis		Multivariate analysis	
		Yes		No		OR (95%CI)	p	OR (95%CI)	p
		n	%	n	%				
Symptomatic PDA	Yes	23	88.5	3	11.5	2.71 (0.69 – 10.66)	0.14	0.74 (0.08 – 6.80)	0.78
	No	34	73.9	12	26.1				
Having late infection	Yes	34	89.5	4	10.5	4.07 (1.15 – 14.34)	0.02	2.42 (0.36 – 16.41)	0.36
	No	23	67.6	11	32.4				
Needing blood transfusion	Yes	49	90.7	5	9.3	12.25 (3.31 – 45.31)	0.00	4.39 (0.84 – 23.06)	0.08
	No	8	44.4	10	55.6				

In univariate analysis, related factors included gestational age less than 28 weeks, need invasive ventilation more than 7 days, had late infection and need blood transfusion. In multivariate logistic regression analysis, the only related factor was needing invasive ventilation more than 7 days.

IV. DISCUSSION

From 8/2022 to 7/2023, 72 extremely preterm infants who met the criteria were included in the study. The mean birth weight was 948.61 ± 152.9 gram and the mean gestational age was 27.11 ± 0.97 weeks. Our results were higher than the results of Geetha et al.[8] This difference may be due to the difference in study population.

Among 72 infants, there were 57 infants diagnosed with BPD, accounting for 79.2%. The majority of infants had mild BPD. The prevalence of BPD in our study was higher than found in the study of Chau et al and Geetha et al.[6,8] However, the percentage of severe BPD in our study was lower than in the study of Navarro et al.[9] These differences indicated that the prevalence of BPD and severity of BPD differed from country to country and in the same country, it differed from center to center. The differences in the rate of BPD may reflect the socioeconomic status and health system of the country. The incidence of BPD tent to be higher in low income country compared to high income country.[3] 38 publications from North America, two publications from Europe and North America, 19 publications from Asia, one publication from Asia and North America, six publications from Oceania, and zero publications from Africa or South America. The reported global incidence range of BPD was 10–89% (10–73% in Europe, 18–89% in North America, 18–82% in Asia, and 30–62% in Oceania

Multiple previous studies showed gestational age was the strongest predictor of BPD, with incidence and severity inversely proportional to both. The smaller the age group, the higher the rate of BPD and vice versa. In our study, the rate of BPD decreased when gestational age increased (Figure 1). Our results were similar to the results of Navarro et al.[9] However, the severity of BPD in our study did not show the same feature. The percentage of severe BPD was the highest in 27 weeks age group, compared to 25 and 26 week age group. This result showed the survival rate of 27 weeks infants was higher than the 25 weeks and 26 weeks infants. Therefore, the rate of severe BPD in this age group was the highest.

Distribution of severity of BPD by birth weight was showed in Figure 2. There was an inverse relationship between severity of BPD and birth weight. Our results were similar to the results of Klinger et al.[10] According to the results of Chau et al, infants with birth weight less than 1000 gram had an increased risk of BPD to 5.17 times compared to infants with birth weight more than 1000 gram.[6]

Multiple factors may contribute to the development of BPD. Results from Table 2 showed that for univariate analysis, gestational age less than 28 weeks, needing invasive ventilation for more than 7 days, having late onset infection and needing blood transfusion during treatment were found to have a relation with BPD with the risk increased 7.40 times, 19.96 times, 4.07 times and 12,25 times, respectively. However, in multivariate logistic regression analysis, needing invasive ventilation more than 7 days was the only independent factor of BPD. Results in the study of Navarro et al found that the length of exposure to mechanical ventilation was the most important postnatal risk factor associated to the severity of bronchopulmonary dysplasia.[9] Invasive ventilation may be necessary in management of respiratory distress syndrome in preterm infants. However, ventilation can cause barotrauma, volutrauma, atelectrauma and biotrauma to the lung, resulting in uninhibited inflammation and interrupted lung development which contributed to the development of BPD.[11]

V. CONCLUSION

The prevalence of BPD in our study was quite high. Many factors may contribute to the development of BPD but in our study, prolonged invasive ventilation was the only independent factor of BPD. Therefore, shortening the duration of invasive ventilation may play a pivotal role in reducing the prevalence of BPD.

LIMITATIONS

There are limitations to our study, including performance in a single center and a small sample size. This is a cross-sectional study therefore the results cannot be inferred to a cause-effect relationship.

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