ORIGINAL ARTICLE

Prevalence and Risk Factors of Bronchopulmonary Dysplasia Among Very Premature Infants in a Tunisian Neonatal Intensive Care Unit

Prévalence et facteurs de risque de la dysplasie bronchopulmonaire chez les grands prématurés dans une unité de soins intensifs néonatals tunisienne

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Abstract

Introduction: Bronchopulmonary dysplasia (BPD) stands as the primary chronic respiratory complication in premature infants, posing a substantial public health concern due to its rising prevalence, potential mortality, and socioeconomic burden.
Aim: The aim of this study was to determine the prevalence of BPD in very preterm infants and identify its associated risk factors.
Methods: We conducted a retrospective, descriptive, and analytical study including all premature infants born between 26 and 31 weeks of gestation age (GA) who survived beyond the 28th day of life, over a five-year period (2017-2021). Patients were divided into two groups based on the presence or absence of BPD, which was defined by the need for oxygen supplementation for at least 28 days.
Results: we included 231 newborns. The prevalence of BPD was 37.7% among survivors on the 28th day of life and 36.7% among those reaching 36 weeks postmenstrual age. BPD was mild, moderate and severe in 25.2%, 4.9% and 6.6% of cases, respectively. Multivariate analysis identified maternal hypertensive disorders (RR=6.15, 95%CI=[2.27-16.67], p<0.001), chorioamnionitis (RR=4.23, 95%CI=[1.25 -14.27], p=0.02), intrauterine growth restriction (IUGR) (RR =20.4, 95%CI=[3.39 -122.66], p=0.001), GA less than 30 weeks (RR=26.97, 95%CI=[10.23 -71.14], p<0.001), and mechanical ventilation (MV) (RR=5.33, 95%CI=[1.95-14.54], p=0.001) as independent factors associated with BPD occurrence. The mortality rate was 10.3% among patients with BPD versus 0.7% in patients without BPD (p = 0.001).
Conclusion: Our study revealed a high prevalence of BPD in very preterm infants and identified several independent risk factors such as maternal hypertensive disorders, IUGR, chorioamnionitis, MV, and GA less than 30 weeks.

Key words: Bronchopulmonary dysplasia- Infant, Premature- Prevalence- Risk factors- Prognosis

Résumé

Introduction: La dysplasie bronchopulmonaire (DBP) est la principale complication respiratoire chronique du prématuré, constituant un problème majeur de santé publique en raison de sa prévalence croissante, de sa mortalité potentielle et de son cout socio-économique important.
Objectifs: déterminer la prévalence de la DBP chez les grands prématurés et identifier ses facteurs de risque.
Méthodes: il s'agissait d'une étude rétrospective, descriptive et analytique, incluant tous les prématurés entre 26 et 31 semaines d'âge gestationnel (AG) survivant au-delà du 28ème jour de vie, sur une période de cinq ans (2017-2021). Les patients ont été répartis en deux groupes selon la présence ou l'absence de DBP, définie par le besoin de supplémentation en oxygène pendant au moins 28 jours.
Résultats: Nous avons inclus 231 nouveau-nés. La prévalence de la DBP était de 37,7% parmi les survivants au 28ème jour de vie et de 36,7% parmi ceux atteignant 36 semaines d'âge corrigé. La DBP était légère, modérée et sévère dans 25,2%, 4,9% et 6,6% des cas, respectivement. La pathologie hypertensive maternelle (RR=6,15, IC95%=[2,27-16,67], p<0,001), la chorioamniotite (RR=4,23, IC95%=[1,25-14,27], p=0,02), le retard de croissance intra-utérin (RCIU) (RR=20,4, IC95%=[3,39-122,66], p=0,001), un AG inférieur à 30 semaines (RR=26,97, IC95%=[10,23-71,14], p<0,001) et la ventilation mécanique (VM) (RR=5,33, IC95%=[1,95-14,54], p=0,001) étaient des facteurs indépendants associés à la DBP.
Conclusion: Notre étude a révélé une prévalence élevée de la DBP chez les grands prématurés et a identifié plusieurs facteurs de risque tels que la pathologie hypertensive maternelle, le RCIU, la chorioamniotite, la VM et un AG inférieur à 30 semaines.

Mots clés: Dysplasie bronchopulmonaire - Prématuré -Prévalence - Facteurs de risque - Pronostic

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LA TUNISIE MEDICALE-2024; Vol 102 (09): 551-557 DOI: 10.62438/tunismed.v102i9.5110

Introduction

Bronchopulmonary dysplasia (BPD) is recognized as the primary chronic respiratory complication among premature infants, defined by the need for supplemental oxygen for at least 28 days (1). The development of BPD involves multiple factors, with prematurity acting as the primary risk factor around which various insults converge. Prenatal factors such as intrauterine inflammation or maternal smoking, combined with postnatal exposures to mechanical ventilation (MV) and oxygen toxicity, significantly contribute to disruptions in bronchial, alveolar, and vascular development (2- 4).
Despite advances in neonatal care, the prevalence of BPD continues to increase, leading to concerns about its long-term consequences and socioeconomic impact (5,6). In Tunisia, there is limited clinical research on BPD, highlighting the importance of identifying key risk factors to guide targeted preventive strategies.
The aims of this study were to determine the prevalence of BPD among very premature infants in a Tunisian neonatal intensive care unit (NICU) and to identify its associated risk factors.

Methods

Study Design

This retrospective, descriptive, and analytical study was conducted at the neonatology department of Charles Nicolle Hospital in Tunis over a 5-year period, from January 1, 2017, to December 31, 2021.

Population

The study included premature infants with a gestation age (GA) ranging between 26 and 31 completed weeks of gestation, admitted to the NICU of Charles Nicolle Hospital in Tunis and surviving beyond the 28th day of life. Exclusion criteria were infants with severe congenital malformations or chromosomal aberrations, as well as those with incomplete or missing medical records.

Patients were divided into two groups according to the presence or absence of BPD on the 28th day of life. Group 1 included patients diagnosed with BPD, while Group 2 comprised patients without BPD.

BPD severity was assessed at a postmenstrual age (PMA) of 36 weeks for hospitalized newborns or at time of discharge home for those discharged earlier, according to Jobe and Bancalari classification (1). Severity categories were defined as mild (breathing room air),moderate (Fraction of Inspired Oxygen (FiO2) < 30% with respiratory support other than continuous positive airway pressure (CPAP) or MV), and severe (requiring CPAP or MV regardless of FiO2, or FiO2 ≥ 30% regardless of respiratory support) (1). Cases in which death occurred before 36 weeks PMA were classified as 'unclassifiable'.

Data Collection

Patient data were retrospectively extracted from medical records, including maternal demographics (age, parity, smoking history), pregnancy characteristics (maternal hypertensive disorders, gestational diabetes, intrauterine growth restriction (IUGR), antenatal corticosteroid therapy), delivery circumstances (fever, prolonged rupture of membranes, chorioamnionitis; non-reassuring fetal status, mode of delivery), neonatal characteristics at birth (sex, GA, birth weight (BW)), and neonatal outcomes during hospitalization.

Statistical Analysis

Data analysis was conducted using SPSS 22.0. Descriptive statistics were used for both qualitative and quantitative variables: student's t-test to compare means of quantitative variables and the Chi-square test or Fisher's exact test for comparing percentages of qualitative variables. Multivariate binary logistic regression analyses were conducted to identify independent factors associated with BPD occurrence. Relative risks (RR) and 95% confidence intervals (CIs) were calculated during the multivariate analysis. The significance level (p-value) was set at 5% for all tests.

Ethical Considerations and Conflict of Interest

The study adhered to principles of medical confidentiality and patient anonymity. The authors declare no conflicts of interest.

Results

During the study period, 336 newborns with GA ranging from 26 to 31 completed weeks of gestation were admitted to the NICU at Charles Nicole Hospital. Among them, 231 newborns met the inclusion criteria (Figure 1). The prevalence of BPD among survivors at 28 days of life was 37.7% and 36.7% at 36 weeks of PMA. Among newborns who survived to 36 weeks PMA, BPD was categorized as mild in 25.2%, moderate in 4.9%, and severe in 6.6% of cases. Maternal hypertensive disorders were observed in 43.6% of patients in group 1 and 25% in group 2 (p=0.013). IUGR occurred in 13.8% of patients with BPD compared to 1.4% of patients without BPD (p<0.001) (Table 1).
The frequency of BPD was 71.9% in newborns with a GA less than 30 weeks compared to 15.4% in newborns with a GA of 30 weeks or more (p < 0.001). The mean BW was 1186g ± 312g in group 1 compared to 1542g ± 302g in group 2 (p < 0.001). BPD occurred in 78.3% of cases in patients having BW less than 1000g compared to 33.2% in patients having heavier BW (p < 0.001). Preterm infants classified as small for gestational age exhibited a higher incidence of BPD (59.1%) compared to those classified as appropriate or large for gestational age (35.4%, p = 0.032). MV was required in 88.5% of patients in group 1 compared to 54.9% in group 2 (p=0.001), with durations of 10±8 days and 4±3 days, respectively (Table 2).

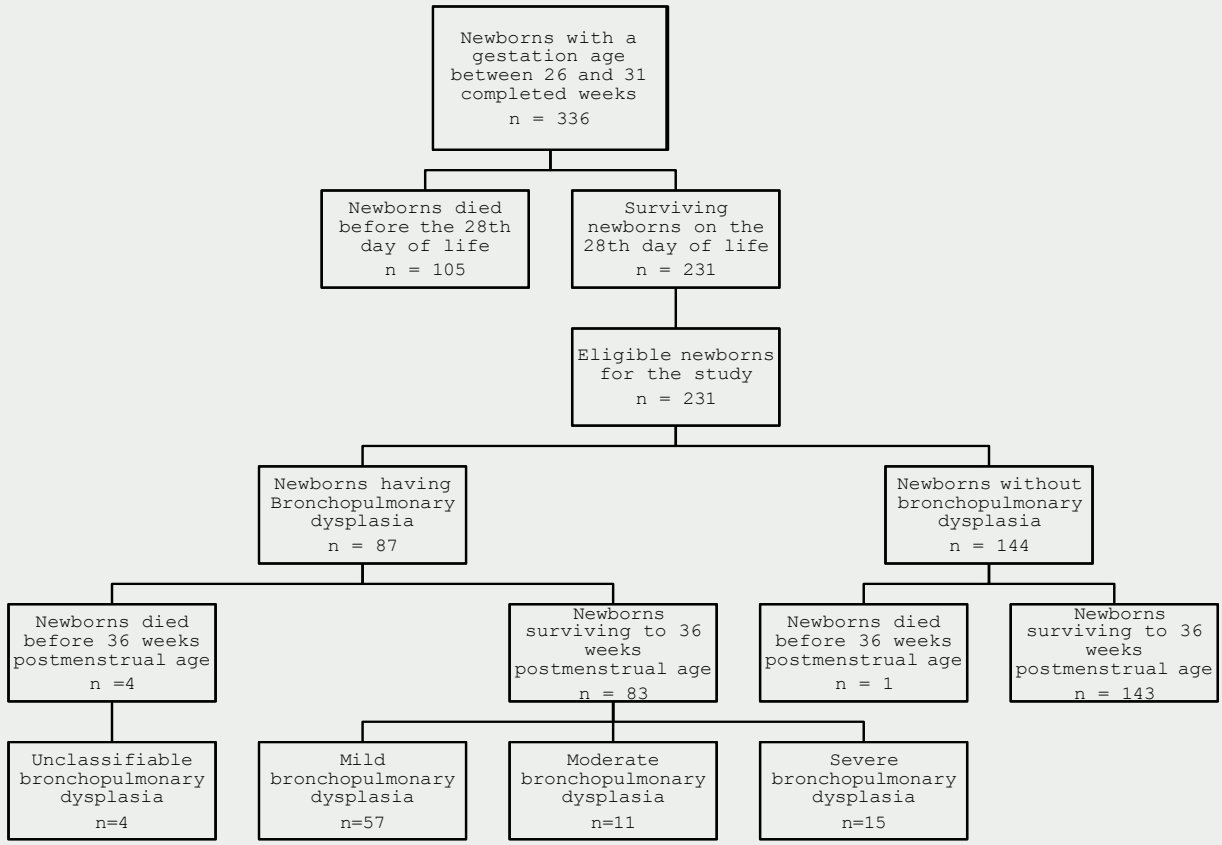

Figure 1. Study Flowchart: Classification of Newborns by Survival and Bronchopulmonary Dysplasia Status

Table 1. Comparison of Pregnancy and Delivery Characteristics Between Infants with and without Bronchopulmonary Dysplasia

	Bronchopulmonary Dysplasia		
	Yes (N=87)	**NO (N=144)**	**p**
	n (%)	**n (%)**	
Primiparity	25 (28.7%)	41 (28.5%)	NS*
Maternal smoking	4 (4.6%)	8 (5.6%)	NS
Single fetal pregnancy	74 (85.1%)	113 (78.5%)	NS
Maternal hypertensive disorder	38 (43.6%)	36 (25%)	**0.013**
Pre-existing or gestational diabetes	36 (41.4%)	51(35.4%)	NS
Confirmed infection with the SARS-CoV-2 virus during pregnancy	3 (3.4%)	8 (5.6%)	NS
Intrauterine growth restriction	12 (13.8%)	2 (1.4%)	**< 0.001**
Antenatal corticosteroid therapy	56 (64.4%)	101 (70.1%)	0.065
Incomplete	18 (20.7%)	17 (11.8%)	
Complete	38 (43.7%)	84 (58.3%)	
History of infection			
Maternal fever	12 (13.8%)	9 (6.3%)	0.053
Prolonged rupture of membranes	28 (32.2%)	31 (21.5%)	0.072
Chorioamnionitis	18 (20.7%)	9 (6.3%)	**0.001**
Spontaneous prematurity	54 (62.1%)	73 (50.7%)	**0.037**
Non-reassuring fetal condition	8 (9.2%)	16 (11.1%)	NS
Mode of delivery			
Vaginal delivery	15 (17.2%)	26 (18.1%)	NS
Caesarean section	72 (82.8%)	118 (81.9%)	

***NS** : non-significant (p≥0.05)

Nine patients with BPD (10.3%) died at a mean chronological age of 57.3 ± 25.4 days (range: 39 - 122 days) and a mean PMA of 36.1 ± 4.4 weeks (range: 31.6 - 46.4 weeks). Only one patient without BPD died on the 40th day of life, at a PMA of 32 weeks and 5 days. Statistical analysis revealed a significant association between mortality rate and BPD (p = 0.001). The mean hospital stay for survivors was 58.8 ± 17.1 days in newborns with BPD, compared to 35.4 ± 10.8 days in newborns without BPD (p < 0.001). Multivariate analysis revealed that maternal hypertensive disorders, chorioamnionitis, IUGR, GA less than 30 weeks, and MV were independently associated with the occurrence of BPD (Table 3).

Discussion

Our study aimed to determine the prevalence of BPD in very preterm infants and to identify its predictive factors. The prevalence of BPD was 37.7% among survivors at 28 days of life and 36.7% among survivors at 36 weeks PMA. These results are consistent with international studies that used similar inclusion criteria and the same definition of BPD (Table 4).

Several factors could explain the wide variability in BPD prevalence in the literature. Firstly, published cohorts exhibit high heterogeneity, particularly regarding the GA and BW of included preterm infants, making result comparison challenging. Additionally, some study populations included all live-born preterm infants, while others were limited to those surviving until the 28th day of life or 36 weeks of PMA.

Table 2. Comparison of Neonatal outcomes between patients with and without Bronchopulmonary Dysplasia

	Bronchopulmonary Dysplasia		
	Yes (N=87) n (%)	NO (N=144) n (%)	p
Respiratory Distress Syndrome	49 (56.3%)	58 (40.3%)	**0.018**
Mechanical ventilation	77 (88.5%)	79 (54.9%)	**0.001**
Inspired oxygen fraction			
at 48 hours	26 ± 10	22±5	**0.001**
at Day 7	22 ± 4	21 ± 2	NS*
Duration of mechanical ventilation (days)	10 ± 8	4±3	**< 0.001**
Duration of non-invasive ventilation (days)	28 ± 12	10±6	**< 0.001**
Duration of oxygen supplementation (days)	45 ± 18	14±7	**< 0.001**
Vascular filling	(26.4%)	(29.9%)	**NS**
Use of vasoactive drugs	(28.7%)	(20.8%)	**NS**
Persistent patent ductus arteriosus	37 (44%)	29 (20.1%)	**< 0.001**
Confirmed early neonatal bacterial infection	**7 (8%)**	**4 (2.8%)**	**0.06**
Confirmed healthcare-associated bacterial infection	25 (28.7%)	18 (12.5%)	**0.002**
Intraventricular hemorrhage	43 (49.4%)	23 (15.9%)	**< 0.001**
Grade 1	12 (13.8%)	13 (9%)	
Grade 2	5 (5.7%)	3 (2.1%)	
Grade 3	22 (25.3%)	7 (4.9%)	
Grade 4	4 (4.6%)	0	
Retinopathy of prematurity	15/38 (39.5%)	2/82 (2.4%)	**< 0.001**
Duration of parenteral nutrition (days)	23 ± 12,9	12,3 ± 5,5	**< 0.001**
Necrotizing enterocolitis (n, %)	14 (16.1%)	9 (6.3%)	**0.015**
Cholestasis (n, %)	19 (21.8%)	16 (11.1%)	**0.035**
Hemoglobin level at birth (g/dl)	14.3 ± 1.9	15.2 ± 2.1	0.001
Minimum hemoglobin level (g/dl)	7.9 ± 1.4	9.5 ± 2.3	< 0.001
Minimum platelet count (per mm3)	127256 ± 74865	159339 ± 73151	0.006
Disseminated intravascular coagulation	14 (16.1%)	6 (4.2%)	0.002
Transfusion			
Packed red blood cells	80 (92%)	82 (56.9%)	< 0.001
Platelet-packed red blood cells	19 (21.8%)	9 (6.3%)	< 0.001
Fresh frozen plasma	23 (26.4%)	18 (12.5%)	0.006

***NS** : non-significant (p≥0.05)

Table 3. Multivariate Analysis of Factors Associated with Bronchopulmonary Dysplasia

	P	Relative Risk	95% Confidence Interval	
			Lower	Upper
Maternal hypertensive disorder	<0.001	6.15	2.27	16.67
Intrauterine growth restriction	0.001	20.4	3.39	122.66
Chorioamnionitis	0.02	4.23	1.25	14.27
Gestation age less than 30 weeks	<0.001	26.97	10.23	71.14
Mechanical ventilation	0.001	5.33	1.95	14.54

Differences in BPD prevalence rates also arise from varying diagnostic criteria (14). While some authors still use the traditional definition of BPD, which is oxygen dependency for at least 28 days or at 36 weeks of PMA, others adopt the definition of Jobe and Bancalari, published in 2001, which is the most widely used definition worldwide (1). Walsh et al. proposed another physiological definition of BPD, classifying patients into two groups: those with or without BPD. They consider preterm infants weaned from oxygen at 36 weeks of PMA as not having BPD, even if oxygen-dependent for 28 days. Thus, preterm infants classified as having mild BPD according to Jobe and Bancalari are considered as not having BPD according to Walsh's criteria. The implementation of this new physiologic definition of BPD decreased the BPD rates from 35% based on clinical definition to 25% according to "physiologic" definition across 17 centers of the neonatal research network (1).

It is also important to emphasize that FiO2, the main determinant parameter in BPD diagnosis and severity, is adjusted based on the oxygen saturation targets adopted by the care team. Variability in saturation targets among different teams contribute to the wide variability in BPD prevalence observed in published studies. Another crucial factor affecting BPD prevalence is the level of neonatal intensive care provided. Consequently, the prevalence is higher in services with a more developed level of neonatal intensive care and, therefore, a lower mortality rate.

Multivariate analysis identified maternal hypertensive disorders, chorioamnionitis, IUGR, GA less than 30 weeks, and the use of MV as independent risk factors associated with BPD.

In our study, maternal hypertensive disorders were independently associated with an increased risk of BPD (RR = 6.15, 95% CI = [2.27 - 16.67], p < 0.001). This finding is consistent with previous research demonstrating a significant association between MHD and BPD (8,13,15). The causal relationship can be attributed to a disturbance in the balance between circulating pro- and anti-angiogenic mediators, leading to impaired angiogenesis and subsequent pulmonary growth impairment (3). However, two meta-analysis (16,17) revealed that while maternal hypertensive disorders were not directly associated with BPD, they were significantly correlated with severe BPD.

It is essential to consider IUGR as a major confounding factor when interpreting the relationship between BPD and maternal hypertensive disorders. We raise the question of whether these disorders directly increase the risk of BPD or if they act indirectly through IUGR, which is often of vascular origin.

Indeed, studies have demonstrated that IUGR substantially elevates the risk of BPD, especially in infants born between 22 and 24 weeks of GA (8,18). This is attributed to biological mechanisms such as placental dysfunction and deficiencies in growth factors like insulin-like growth factor, vascular endothelial growth factor, which can restrict fetal pulmonary, vascular, and alveolar growth. Additionally, epigenetic alterations induced by an unfavorable intrauterine environment may contribute to BPD pathogenesis (3,19). A systematic review and metanalysis published par Pierro and al revealed that placental vascular dysfunction accompanied by IUGR was associated with an increased risk of developing

moderate or severe BPD and BPD- associated pulmonary hypertension.

Both our study and the European MOSAIC study demonstrated that maternal hypertensive disorders and IUGR were independently associated with BPD (8). However, Torchin et al. found that maternal hypertensive disorders were implicated in BPD pathogenesis only when associated with IUGR (7).

Therefore, to minimize the frequency of BPD, obstetric care for pregnant women should prioritize the management of maternal hypertensive disorders and their associated complications, particularly IUGR.

Table 4. Comparison of Bronchopulmonary Dysplasia Prevalence Among Published International Studies

Location	Years	Inclusion	N	Mortality	BPD[e]	Moderate to severe BPD
Our study	2017 - 2021	GA[c] < 32 weeks	231	31.3%	**37.7%**	11.5%
France [7] [a]	2011	GA< 32 weeks	2638	14.7%	-	11.1%
Europe (10 countries) [8] [b]	2003	GA< 32 weeks	4185	10.3%- 29%	-	16.2% (10.2%- 24.8%)
Spain [9] [a]	2013 - 2022	GA< 33 weeks	202	9.5%	**28.7%**	10.4%
		BW[d] < 1500 g				
China [10] [a]	2016-2020	GA<32 weeks	409	-	**61,1%**	51,6%
Korea [11] [a]	2009-2018	GA < 30 weeks	521	20,7%	**48,4**	13,9
Saudi Arabia [12] [a]	2009 - 2019	GA< 32 weeks	637	2.8%	**30.5%**	16.5%
		BW< 1500 g				
India [13] [a]	2017 - 2018	GA< 33 weeks	80	22%	**31%**	24%

[a] BPD was defined as the requirement for oxygen supplementation for at least 28 days.
[b] Europe: BPD was defined as the requirement for oxygen supplementation or mechanical ventilation at 36 weeks of postmenstrual age.
[c] GA: Gestation age; d: BW: Birth Weight ; e: BPD: Bronchopulmonary Dysplasia

Pulmonary inflammation plays a pivotal role in the intricate pathogenesis of BPD. Both prenatal and postnatal factors such as chorioamnionitis, oxygen toxicity, MV, neonatal resuscitation, and postnatal pulmonary or systemic infections, can trigger a harmful inflammatory cascade within the respiratory pathways and lung tissues of premature infants (4,20). In our study, we observed a significant and independent association between chorioamnionitis and BPD (RR=4.23, 95% CI=1.25-14.27, p = 0.02). Systematic reviews and meta-analyses (21) consistently demonstrated a significant correlation between chorioamnionitis and BPD, even after adjusting for confounding factors such as GA and BW. It is important to recognize that the timing, magnitude, and impact of the pro-inflammatory response on alveolar and vascular growth can be influenced by preventive and therapeutic measures targeting prenatal and postnatal infections, antenatal, and possibly postnatal corticosteroid therapy (22).

In our study, we found that MV emerged as an independent risk factor for BPD. These findings align with previously published data demonstrating a significant association between BPD and MV (8,12,18). BPD was significantly more prevalent and severe when MV was initiated within the first 24 hours of life (9,23), or when higher inspiratory pressures or FiO2 levels were applied (12). Furthermore, the duration of MV showed a statistically significant correlation with the development of BPD in preterm infants (12,18,24).

MV and associated injuries are crucial risk factors in the development of BPD. The pathogenesis of ventilator-induced lung injury (VILI) is multifactorial and results from complex interactions between the ventilator and patient-related factors. Ventilator-related factors, including barotrauma (injury caused by excessive airway pressure), volutrauma (injury caused by excessive tidal volume), atelectrauma (injury caused by repetitive opening and closing of alveoli), and biotrauma (injury caused by inflammatory mediators released in response to MV), play significant roles in VILI (4). These injuries may manifest as structural damage to the alveoli, pulmonary edema, inflammation, and fibrosis. it appears that volutrauma is a more critical factor in determining lung injury compared to barotrauma (4).

Premature infants are especially susceptible to MV-induced lung injuries which can occur even with short-duration MV and appropriate ventilation strategies. To mitigate MV-induced lung injuries and potentially reduce the risk of BPD, it is essential to adopt appropriate ventilation strategies. These may include permissive hypercapnia, permissive hypoxemia, volume-guaranteed ventilation, MV with low inspiratory pressure, rapid frequency, short inspiratory time, early extubation, and especially early CPAP initiation in the delivery room (25). Early in the disease course, respiratory support should focus on limiting additional lung injury by utilizing non-invasive ventilation or “gentle” invasive MV with a low tidal volume, short inspiratory time, and high respiratory rate strategy. Non-invasive ventilation used as both initial support for infants with respiratory distress syndrome and/or as post-extubation support can limit lung injury, minimize exposure to MV, and theoretically can reduce the risk of severe BPD.

The primary factor identified as a determinant of risk for BPD, and arguably the most significant, is immaturity (2). Numerous studies in the literature have highlighted the inverse correlation between the incidence and severity of BPD and GA (7-9,12,13,18,23). Our study revealed that BPD occurred 26 times more frequently among premature infants born between 26- and 29-weeks GA compared to those born between 30 and 31 weeks GA. Premature birth disrupts the continuum of intrauterine lung development, leading to a heightened prevalence of BPD in extremely premature infants. This can be attributed to their delivery at a stage of lung development characterized by either late canalicular or early saccular

phases, where alveolarization and distal microvascular growth are still in the early stages (2). Given these findings, it is evident that preventing BPD requires obstetric interventions aimed at either limiting or delaying premature delivery.

Other risk factors for BPD have been identified in the literature but were not observed in our study. These include genetic predisposition, lower BW, male gender, Patent Ductus Arteriosus, breastfeeding, blood transfusion, fluid balance and sepsis (2,4,8,12,18,23).

This study is limited by its retrospective and observational design, which hinders the ability to definitively establish a causal relationship between the investigated risk factors and BPD. Additionally, the retrospective nature of data collection may introduce biases due to missing or imprecise information. Some essential data, such as the exact duration of MV, the composition of enteral and parenteral nutrition, and daily fluid intake, were not specified in the records.

Despite these limitations, this study represents the largest national investigation into the prevalence of BPD among very preterm infants, regardless of severity. Additionally, it stands as the inaugural attempt to identify predictive factors of BPD in our country, to our knowledge.

Conclusions

Our study revealed a high prevalence of BPD in very preterm infants and identified several independent risk factors for BPD, including maternal hypertensive disorders, IUGR, chorioamnionitis, MV, and GA less than 30 weeks. Early prevention of BPD starting from the antenatal period through birth and hospitalization is crucial to minimize exposure to modifiable risk factors such as MV and infections. Personalized targeted prevention strategies, based on an understanding of predictive factors and BPD progression patterns, should be considered for high-risk preterm infants.

Abbreviation

BPD: Bronchopulmonary dysplasia
MV: mechanical ventilation
GA: gestation age
PMA: postmenstrual age
IUGR: intrauterine growth restriction
NICU : neonatal intensive care unit
FiO2: Fraction of Inspired Oxygen
CPAP : Continuous Positive Airway Pressure
RR: Relative risks
CIs : 95% confidence intervals
BW: birth weight
VILI : ventilator-induced lung injury

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