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Histological Changes of Bronchopulmonary Dysplasia and Pulmonary Hypertension: An Autopsy Series of 42 Preterm Infants

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HISTOLOGICAL CHANGES OF BRONCHOPULMONARY DYSPLASIA AND PULMONARY HYPERTENSION: AN AUTOPSY SERIES OF 42 PRETERM INFANTS

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Background: Bronchopulmonary Dysplasia (BPD), a significant cause of perinatal morbidity and mortality, leads to disrupted pulmonary vascular growth and ultimately pulmonary hypertension (PH). The diagnosis of BPD is made by oxygen requirement for at least first 28 days of life. We hypothesized that histologic changes of BPD are evident before 28 days of age.

Methods: All live born preterm infants born <37 weeks of gestational age (GA), who received an autopsy between 2010 and 2017 at Children's Hospital of Michigan or Hutzel Women's Hospital, were identified by autopsy records. Infants with major congenital defects were excluded. Clinical data were extracted from electronic medical records. Autopsy specimens of lung and heart tissue were examined by a single pathologist, and classified according to presence or absence of defining features of BPD and PH.

Results: Of the 42 preterm infants that met the study criteria, 79% were <32 weeks GA, 55% were male, 55% were African American, 33% were SGA, and 17% were twins. Infants that died at <28 days of life were statistically more likely to be African American and receiving high frequency ventilation and were less likely to have preterm premature rupture of membranes (PPROM) and an echocardiogram obtained as part of their clinical workup.

Of infants <32 weeks GA, 61% died at <28 days of age; histological BPD was observed in 25% of infants and PH was observed in 65%. Of infants <32 weeks GA, 39% died at ≥28 days; histological BPD was observed in 92% and histological PH was observed in 85% of subjects.

Of infants ≥32 weeks GA, 78% died at <28 days of age; histological BPD was observed in 0% of infants and PH was observed in 71%. Of infants ≥32 weeks GA, 22% died at ≥28 days; histological BPD and PH were both observed in 50% of subjects.

Histological changes of BPD observed in 5 infants born <32 weeks GA who died before 28 days of age were identified as early as 6.73 days of age. Histologic PH was identified in 4 of the 5 infants with the earliest evidence being observed in an infant that died at 6.73 days of age.

Conclusion: Histologic changes consistent with BPD and PH were evident in 25% and 65% respectively of postmortem lung samples from infants born <32 weeks GA who received less than 28 days of cumulative oxygen support. These findings suggest that there is a need to develop better clinical criteria and dedicate future research to seeking biomarkers for BPD in extremely preterm infants before 32 weeks GA. Because timely intervention is key to minimizing long-term effects of the disease, research that further refines the timeline of BPD's pathogenesis is essential. By identifying infants at risk through reliable biomarkers and initiating preventative measures before 28 days of life, clinicians may prevent long-term morbidity and mortality related to BPD.

Keywords: Bronchopulmonary dysplasia, pulmonary hypertension, death, extremely preterm infants, autopsy, histology, prematurity, respiratory distress syndrome