Medical Xpress

Studies establish two significant risk factors for condition that leads to early death in preterm infants

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About 50% of preterm infants develop some form of bronchopulmonary dysplasia, a breathing disorder that can cause long-term breathing and

health issues. About 20% of preterm infants develop BPD with pulmonary hypertension, the most severe subtype of the condition.

An estimated 40% of this group will die before the age of 2. However, little is known about what causes the development of BPD-PH.

"Current screening methods are limited in their ability to detect BPD, let alone the severity of the disease," said Samuel Gentle, M.D., assistant professor in the University of Alabama at Birmingham Division of Neonatology. "Since both BPD and BPD-PH are common morbidities in preterm infants, we wanted to evaluate other potential methods for earlier diagnosis."

Gentle, along with other researchers from the UAB Marnix E. Heersink School of Medicine, conducted two studies to evaluate risks and predictors of preterm infants' developing BPD-PH. Results from both studies, published in the *American Journal of Respiratory and Critical Care Medicine*, establish the duration of intermittent hypoxemia events and the time the patent ductus arteriosus vessel remained opened as potential predictors for BPD-PH in preterm infants.

Intermittent hypoxemia and BPD-PH

Preterm infants struggle to accurately control their breathing, typically due to their lungs' being underdeveloped. This can lead to intermittent hypoxemia or periodic drops in an infant's oxygen saturation level below an acceptable range.

Studies suggest that the cumulative effect of IH episodes may be detrimental to a neonate's health. The first UAB study evaluated whether characteristics of IH episodes such as frequency and duration of IH events can predict which preterm infants will later develop BPD-PH.

Results showed that infants with IH events lasting longer than one minute were twice as likely to develop BPD-PH. The frequency of the episodes did not differ between the two groups.

"If the length of IH episodes is a predictor of developing of BPD-PH, it may enable physicians to identify infants with BPD-PH earlier on," Gentle said. "We are hopeful that earlier detection translates to earlier intervention and improved outcomes in infants with this devastating disease."

Patent ductus arteriosus and BPD-PH

While in utero, a fetus does not need blood pumped to its lungs as the mother provides the fetus with oxygen. Instead, the patent ductus arteriosus vessel is one mechanism by which blood from the heart bypasses the lungs and is directed toward the body. Once a baby is born, the PDA vessel typically disappears early on during the transitional circulation period. In preterm infants, the PDA vessel stays open longer, sometimes for months.

Gentle's second study evaluated how the length of time the PDA vessel remained open affected the development of BPD-PH. Results showed that preterm infants born between 22 and 28 weeks with BPD-PH more frequently had a PDA that remained opened beyond 28 days. Additionally, a persistent PDA duration was linked with BPD-PH-related death. This was more frequent than in infants with only BPD.

Observational studies have shown that babies with a PDA that stays open longer are more likely to develop BPD. Additional studies have shown that intervention, such as prescribing acetaminophen or ibuprofen, can help close the PDA but does not necessarily prevent development of BPD.

"There is considerable practice variation as to whether doctors should intervene and close persistent PDAs," Gentle said. "Our results provide evidence that taking a conservative approach to PDA intervention beyond four weeks after birth may increase infants' risk of developing BPD-PH."

Gentle also notes that the question remains whether a persistent PDA is what causes BPD-PH or developing BPD-PH leads to a PDA that remains open longer. He says longitudinal monitoring of PDA, including echocardiograms before 28 days postpartum, could help provide additional markers that could be used as determinants of development.

More information: Samuel J. Gentle et al, Intermittent Hypoxemia and Bronchopulmonary Dysplasia with Pulmonary Hypertension in Preterm Infants, *American Journal of Respiratory and Critical Care Medicine* (2022). DOI: 10.1164/rccm.202203-0580OC

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