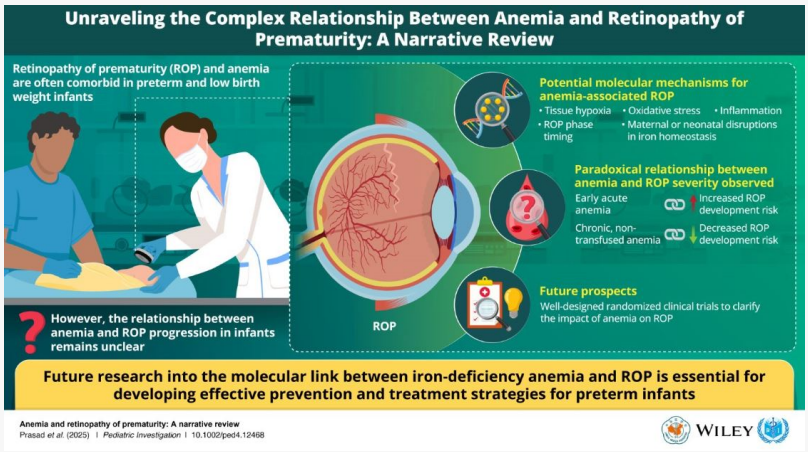
Pediatric Investigation Review Explores the Link Between Anemia and Retinopathy of Prematurity

The review article examines the relationship between anemia and retinopathy of prematurity, focusing on iron deficiency and underlying molecular mechanisms



Anemia is a common condition in preterm infants and is closely linked to the development of ROP. Iron deficiency exacerbates hypoxia and oxidative stress, contributing to abnormal retinal vessel growth. Understanding the molecular mechanisms behind anemia

BEIJING, CHINA, June 20, 2025 /EINPresswire.com/ -- Anemia is a common condition in premature infants, particularly those at risk for retinopathy of prematurity (ROP). While the relationship between anemia and ROP risk remains complex, recent studies have explored potential mechanisms linking anemia to ROP progression. Now, a Pediatric Investigation review evaluates existing literature on iron deficiency and its molecular mechanisms in ROP development, highlighting the need for further targeted clinical trials to clarify the role of anemia in ROP.

Retinopathy of prematurity (ROP) is a major cause of vision impairment in preterm infants, particularly those born weighing ≤1,250 g. Anemia is commonly observed in these infants, with nearly 90% of extremely low birth weight (ELBW) infants requiring at least one blood transfusion. The primary cause of anemia in this population is frequent blood draws needed for medical monitoring during critical illness. Additionally, preterm infants miss the crucial third trimester of pregnancy, during which 70% of maternal iron is transferred to the fetus, placing them at an increased risk for iron deficiency. As anemia and ROP frequently co-occur in infants, understanding the potential link between these two conditions is essential for improving clinical outcomes and treatment strategies.

A recent review published online in Pediatric Investigation on 03 February 2025 explores the complex association between anemia and ROP, focusing on the role of iron deficiency and its

potential molecular mechanisms in ROP development. The review highlights several factors that may underlie this association, including tissue hypoxia, oxidative stress, inflammation, and the timing of anemia onset relative to the different phases of ROP—all of which contribute to retinal damage. “Given the high prevalence of anemia and iron deficiency in preterm infants, understanding these mechanisms is vital for improving prevention and treatment strategies for ROP,” explains corresponding author Dr. Ellen C. Ingolfsland from the Department of Pediatrics, Division of Neonatology, University of Minnesota, USA.

The review begins with the discussion on the potential role of iron deficiency in the development of ROP. Anemia reduces oxygen delivery to the retina, and iron deficiency further exacerbates hypoxia by inhibiting the prolyl hydroxylase domain, which normally activates hypoxia-inducible factor 1-alpha (HIF-1α), a protein essential for the body’s response to low oxygen levels or hypoxia. Under conditions of hypoxia and iron deficiency, HIF-1α is translocated to the nucleus, where it activates the transcription of angiogenic factors such as vascular endothelial growth factor (VEGF). While VEGF promotes normal angiogenesis under physiological conditions, its overexpression in ROP leads to pathological neovascularization, contributing to the abnormal retinal vessel growth characteristic of the condition.

In addition to hypoxia, oxidative stress and inflammation play significant roles in the development of ROP. Preterm infants, with lower antioxidant levels, are more vulnerable to reactive oxygen species (ROS) produced during oxidative metabolism. The accumulation of ROS in the retina, particularly during the first phase of ROP, damages endothelial cells and delays retinal vasculature development. Anemia and iron deficiency further increase ROS production, accelerating retinal damage. Additionally, anemia triggers a proinflammatory response, leading to higher levels of cytokines such as interferon-gamma and tumor necrosis factor-alpha, which further exacerbate retinal injury.

Furthermore, the review highlights a paradox in the relationship between anemia and ROP severity. It suggests that early anemia, particularly in the first few weeks of life, is associated with a significantly increased risk for ROP development. Whereas chronic, non-transfused anemia may decrease this risk with iron deficiency having a protective effect. This paradox is likely due to the timing, severity, and treatment of anemia, which vary across clinical settings. The review points out that transfusion protocols and iron supplementation strategies differ significantly between neonatal intensive care units, complicating efforts to determine the precise role of anemia in ROP.

“In light of these findings, our review emphasizes the need for well-designed randomized controlled trials to clarify the impact of anemia on ROP and to explore the molecular mechanisms involved. Such studies should consider factors such as the timing, severity, and management of anemia, along with other confounding factors like comorbidities,” explains Dr. Ingolfsland.

Overall, while anemia remains a common and significant issue for preterm infants, its exact role

in the development and progression of ROP is still not fully understood. “Our review calls for further focused research to better understand the molecular mechanisms linking iron deficiency anemia to ROP. Addressing this knowledge gap is essential for developing more effective prevention and treatment strategies that could improve clinical outcomes for vulnerable premature infants,” concludes Dr. Ingolfsland.

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Reference
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Dr. Ellen C. Ingolfsland is an Assistant Professor in the Division of Neonatology and a faculty member in the Department of Pediatrics at the University of Minnesota. She earned her MD from the University of Minnesota Medical School, where she also completed her residency in Pediatrics and fellowship in Neonatal-Perinatal Medicine. Dr. Ingolfsland specializes in neonatal-perinatal medicine, with expertise in the care of preterm and critically ill neonates, including general neonatology. She has been recognized as a "Top Doctor" by Minneapolis - St. Paul Magazine and continues to contribute to the field of neonatology.

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