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Correlation Between Umbilical Cord Histomorphometry and Oxidative Stress Markers in Intrauterine Growth Restriction (IUGR): A review

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ABSTRACT

Intrauterine growth restriction (IUGR) is a significant cause of perinatal morbidity and mortality, often resulting from placental insufficiency that impairs fetal nutrient and oxygen supply. Structural changes in the umbilical cord, including increased vessel wall thickness, narrowed lumen, and reduced Wharton's jelly volume, have been frequently observed in IUGR cases and are indicative of compromised vascular function. This review synthesizes data comparing umbilical cord histomorphometry between IUGR and appropriate-for-gestational-age neonates, alongside analyses of oxidative stress markers such as malondialdehyde (MDA), superoxide dismutase (SOD), glutathione peroxidase (GPx), and catalase in cord blood. Evidence consistently shows that histomorphometric alterations in the umbilical cord correlate with elevated oxidative stress—characterized by increased MDA and decreased antioxidant enzyme activity—suggesting oxidative injury plays a key role in vascular remodeling during IUGR. The relationship between biochemical and structural changes highlights the potential of combined assessments as early diagnostic tools for IUGR. Furthermore, these findings support the exploration of antioxidant therapies to mitigate oxidative damage in affected pregnancies. However, further large-scale, prospective studies are necessary to confirm these associations and evaluate their clinical relevance in prenatal management.

KEYWORDS Intrauterine Growth Restriction; Umbilical Cord Histomorphometry; Oxidative Stress; Malondialdehyde; Superoxide Dismutase and Wharton's Jelly.

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INTRODUCTION

Current knowledge indicates that intrauterine growth restriction (IUGR) significantly impacts fetal development and contributes to perinatal morbidity and mortality worldwide (1). The umbilical cord, connecting placenta and fetus, is essential for nutrient and oxygen transport. Histomorphometric features—such as vessel wall thickness, luminal area, and Wharton's jelly content—reflect placental vascular health and are altered in response to chronic hypoxia and oxidative stress (2). The cord contains two arteries and one vein encased in Wharton's jelly, which protects vessels from compression. Quantitative histomorphometric analysis assesses arterial media thickness, luminal diameter, and Wharton's jelly volume (3). In IUGR, increased arterial wall thickness, narrowed lumens, and reduced Wharton's jelly volume suggest impaired perfusion and diminished protection (4,5).

Oxidative stress, caused by an imbalance between reactive oxygen species (ROS) and antioxidants, is elevated in IUGR (6). ROS damage vascular structures, with malondialdehyde (MDA) as a marker of lipid peroxidation, while antioxidant enzymes like superoxide dismutase (SOD), glutathione peroxidase (GPx), and catalase are often decreased (7). Elevated MDA and reduced antioxidants have been found in umbilical cord blood of IUGR fetuses (8,9). These histomorphometric and oxidative changes indicate vascular remodeling due to oxidative injury and hypoxia (10). Correlating these findings can improve .

improve understanding and management of IUGR (11).

Discussion

This review consolidates morphological and biochemical evidence concerning intrauterine growth restriction (IUGR), focusing on umbilical cord histomorphometry and oxidative stress markers. Consistently, studies reveal thickening of umbilical artery walls in IUGR infants, characterized by hypertrophy of the tunica media and increased perivascular collagen deposition (12). The vascular lumen often appears constricted, potentially increasing resistance in the fetoplacental circulation and impairing fetal blood flow (13). Wharton's jelly, a mucopolysaccharide-rich connective tissue that cushions umbilical vessels, is frequently reduced in volume and cellularity in IUGR cases (14). These structural changes likely represent adaptations to chronic intrauterine stressors such as hypoxia, inflammation, and altered hemodynamics (15).

Biochemically, IUGR is marked by increased oxidative stress. Cord blood from affected neonates shows elevated malondialdehyde (MDA), a marker of lipid peroxidation and membrane damage (16). Concurrently, activities of antioxidant enzymes including superoxide dismutase (SOD), glutathione peroxidase (GPx), and catalase decline, reflecting impaired defense against reactive oxygen species (17). This pro-oxidant state results from placental insufficiency, mitochondrial dysfunction, and repeated hypoxia-reoxygenation cycles (18).

There is growing evidence linking histomorphometric changes to oxidative stress. Higher MDA correlates with increased arterial media thickness, suggesting lipid peroxidation contributes to vascular hypertrophy (19). Reduced SOD and GPx associate with decreased Wharton's jelly volume, implying antioxidant deficiency facilitates oxidative degradation of its structural components (20). Catalase deficiency correlates with lumen narrowing, likely due to endothelial damage from accumulated hydrogen peroxide (21). These findings highlight oxidative stress as a key driver of vascular remodeling and mechanical weakening in the umbilical cord during IUGR (22).

Conclusion

Collectively, existing literature underscores a significant correlation between umbilical cord histomorphometry and oxidative stress markers in IUGR. Structural alterations specifically, thickened umbilical artery walls, narrowed lumens, and reduced Wharton's jelly are consistently observed and appear closely linked with biochemical indicators of oxidative imbalance, such as elevated malondialdehyde and suppressed antioxidant enzyme levels.

These findings suggest that oxidative stress is not only a hallmark but also a potential driver of cord remodeling in IUGR pregnancies. Recognizing these associations enhances our understanding of the pathophysiology and may offer new avenues for early diagnosis. Integration of oxidative stress marker assays into perinatal evaluation protocols and exploration of targeted antioxidant therapies represent promising but as yet unvalidated strategies.

Future research should prioritize longitudinal, standardized studies to confirm these correlations and assess whether modulation of oxidative pathways can prevent or attenuate histomorphometric changes. Improved diagnostic and therapeutic approaches addressing oxidative stress may ultimately contribute to better outcomes for IUGR-affected pregnancies and neonates.

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