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Understanding G6PD Deficiency and Oxidative Stress in Pregnancy: A Review of F2-Isoprostanes in Anemic and Non-Anemic Women

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ABSTRACT

Background: Glucose-6-phosphate dehydrogenase (G6PD) maintains redox balance by generating NADPH for glutathione recycling. Pregnancy increases oxidative stress, which is further aggravated by anemia. Excessive oxidative stress is associated with complications such as preeclampsia, intrauterine growth restriction (IUGR), and preterm birth. Urinary F2-isoprostanes, reliable markers of lipid peroxidation, offer a non-invasive measure of oxidative burden.

Material and Methods: This review examined studies on trimester-wise changes in oxidative stress, G6PD activity, and urinary F2-isoprostanes among anemic and non-anemic pregnant women. Articles were retrieved from PubMed using keywords "G6PD," "oxidative stress," "pregnancy," and "F2-isoprostanes."

Conclusion: Evidence shows that reduced G6PD activity increases oxidative stress in pregnancy, with urinary F2-isoprostanes rising progressively across trimesters. Anemic women exhibit significantly higher oxidative stress than non-anemic counterparts. Combining enzymatic and urinary biomarkers may improve early risk assessment and guide antenatal interventions to reduce adverse fetomaternal outcomes.

KEYWORDS: G6PD, oxidative stress, F2-isoprostanes, pregnancy, anemia

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INTRODUCTION

Pregnancy is characterized by profound metabolic and physiological adaptations, including increased oxygen consumption and mitochondrial activity, resulting in elevated production of reactive oxygen species (ROS) (1). While moderate ROS levels contribute to placentation, excess oxidative stress has been implicated in preeclampsia, preterm birth, and IUGR (2,3).

Anemia, affecting nearly 40% of pregnant women globally, worsens oxidative stress by limiting oxygen delivery and depleting antioxidant reserves (4,5). Glucose-6-phosphate dehydrogenase (G6PD) plays a crucial protective role through the pentose phosphate pathway, producing NADPH required for maintaining reduced glutathione (6). Deficiency or reduced activity of G6PD impairs antioxidant defense, leading to cellular vulnerability under oxidative conditions (7,8).

Among biomarkers of oxidative stress, urinary F2-isoprostanes—stable products of free radical-mediated peroxidation of arachidonic acid—are considered the most reliable indicators of in vivo lipid peroxidation (9). They are chemically stable, quantifiable by mass spectrometry, and unaffected by dietary artifacts, unlike malondialdehyde (MDA) or thiobarbituric acid reactive substances (10,11). Importantly, urinary F2-isoprostanes increase progressively with gestational age, reflecting the physiological rise in oxidative stress (12).

Evidence suggests that anemic women show higher urinary F2-isoprostanes and lower G6PD activity compared with non-anemic women, correlating with poor pregnancy outcomes (13,14). However, systematic trimester-wise analyses integrating both markers are limited. Given the prevalence of anemia and G6PD deficiency in many regions, identifying biomarker-based predictors of oxidative stress is vital for early risk stratification (15).

This review synthesizes available literature on G6PD activity, oxidative stress, and urinary F2-isoprostanes across trimesters in anemic and non-anemic pregnant women, highlighting their role in predicting maternal and neonatal complications.

MATERIAL AND METHOD

A literature search was conducted in PubMed, Scopus, and Web of Science for studies on G6PD deficiency and oxidative stress in pregnant women, focusing on F2-isoprostanes in anemic and non-anemic populations. The search used the following Boolean terms:

("G6PD deficiency" OR "glucose-6-phosphate dehydrogenase deficiency")

AND (pregnancy OR "pregnant women")

AND ("oxidative stress" OR "reactive oxygen species" OR ROS)

AND ("F2-isoprostanes" OR "8-iso-PGF2α")

AND (anemia OR "iron deficiency anemia" OR IDA OR "non-anemic")

The search was restricted to English-language, human studies published, and reference lists of relevant articles were screened for additional studies.

DISCUSSION

Oxidative stress plays a central role in pregnancy-related complications (1,2). G6PD ensures redox stability by maintaining NADPH levels for glutathione regeneration (6). Reduced G6PD activity in anemic women enhances vulnerability to ROS, aggravating lipid peroxidation (7,8).

Urinary F2-isoprostanes are gold-standard markers for oxidative stress (9,10). Studies show a trimester-dependent increase, with highest levels observed in the third trimester (11,12). Anemic women consistently demonstrate higher urinary F2-isoprostanes compared to non-anemic women, suggesting that anemia magnifies oxidative imbalance (13,14).

Clinically, elevated F2-isoprostanes and low G6PD activity have been linked with preeclampsia, preterm delivery, and IUGR (15–17). Their combined use may serve as a predictive tool for high-risk pregnancies, supporting interventions such as antioxidant supplementation and enhanced monitoring (18). However, limitations include heterogeneity in assays and a lack of longitudinal studies comparing anemic and non-anemic cohorts across all trimesters (19,20).

Future research should focus on standardizing urinary F2-isoprostane assays and integrating them with enzymatic antioxidant measures to improve early prediction of adverse outcomes (21–23). Translational studies are needed to validate their clinical application and potential as screening tools in antenatal care (24–26).

CONCLUSION

Pregnancy involves increasing oxidative stress, which is amplified in anemic women due to impaired antioxidant defenses. G6PD activity is crucial for redox balance, while urinary F2-isoprostanes serve as reliable non-invasive markers of lipid peroxidation. Both rise progressively with gestation, with higher values in anemic women correlating with adverse maternal and neonatal outcomes. Their combined evaluation offers promise for early risk identification and prevention strategies. Incorporating these biomarkers into antenatal screening could improve maternal health outcomes. Large-scale prospective studies are essential to establish standardized protocols and validate their predictive utility.

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