

Antioxidant Status and Oxidative Stress in Anemic Pregnancy: A Trimester-Wise Review of Serum Markers and Urinary F2-Isoprostanes: A review

Gopi Krishna Chowdary¹, Dr. Ashish Anjankar², Dr. Roshan Kumar Jha³, Ranjit Ambad⁴

¹ Ph.D Scholar, Dept. of Biochemistry, Jawaharlal Nehru Medical college, Sawangi, Wardha.

² Professor Dept. of Biochemistry, Jawaharlal Nehru Medical college, Sawangi, Wardha. Email: ashish.anjankar@gmail.com

³ Assistant Professor Dept. of Biochemistry, Jawaharlal Nehru Medical college, Sawangi, Wardha.

Email: rosissan47@gmail.com

⁴ Professor Dept. of Biochemistry, Jawaharlal Nehru Medical college, Sawangi, Wardha. Email: ambad.sawan@gmail.com

Corresponding author:

Gopi Krishna Chowdary, Email: gopichowdary001@gmail.com

ABSTRACT

Background: Pregnancy is accompanied by increased oxidative stress due to elevated metabolic demands and reactive oxygen species (ROS) generation. In anemic women, impaired antioxidant defense further exacerbates oxidative imbalance, contributing to adverse maternal and fetal outcomes. Serum oxidative stress markers, including superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), and malondialdehyde (MDA), alongside urinary F2-isoprostanes, provide insight into systemic and lipid peroxidation status.

Material and Methods: A comprehensive review of PubMed and Scopus literature up to 2024 was conducted using keywords “oxidative stress,” “pregnancy,” “anemia,” “SOD,” “MDA,” “CAT,” “GPx,” and “F2-isoprostanes.” Studies assessing trimester-wise changes were included.

Conclusion: Evidence indicates progressive oxidative stress across pregnancy, with anemia amplifying alterations in enzymatic antioxidants and elevating urinary F2-isoprostanes. Integration of serum and urinary biomarkers offers a more complete assessment of oxidative status. These markers hold promise for early prediction of complications and for guiding antenatal interventions.

KEYWORDS: Oxidative stress, SOD, MDA, GPx, catalase, F2-isoprostanes, anemia, pregnancy

How to Cite: Gopi Krishna Chowdary, Dr. Ashish Anjankar, Dr. Roshan Kumar Jha, Ranjit Ambad, (2025) Antioxidant Status and Oxidative Stress in Anemic Pregnancy: A Trimester-Wise Review of Serum Markers and Urinary F2-Isoprostanes: A review, Vascular and Endovascular Review, Vol.8, No.2s, 258-260.

INTRODUCTION

Pregnancy involves significant physiological and metabolic adaptations, resulting in increased oxidative stress due to rising oxygen demand and mitochondrial activity (1). While controlled oxidative stress is essential for implantation and placental development, excess reactive oxygen species (ROS) cause cellular injury, contributing to adverse outcomes such as preeclampsia, intrauterine growth restriction (IUGR), and preterm birth (2,3).

Anemia, a major global health problem affecting nearly 40% of pregnant women, further aggravates oxidative stress (4,5). Reduced hemoglobin levels impair oxygen delivery and alter antioxidant capacity, making anemic women more vulnerable to oxidative imbalance (6).

Enzymatic antioxidants such as superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) play central roles in detoxifying ROS, while malondialdehyde (MDA) serves as a marker of lipid peroxidation (7,8). Depletion of these enzymes and increased MDA levels reflect systemic oxidative stress, which has been associated with complications including preeclampsia and IUGR (9,10).

Urinary F2-isoprostanes, derived from free radical-induced peroxidation of arachidonic acid, represent reliable markers of oxidative stress and lipid peroxidation (11). They are chemically stable, quantifiable by mass spectrometry, and widely considered superior to MDA or thiobarbituric acid reactive substances (TBARS) in reflecting in vivo oxidative injury (12,13).

Trimester-specific variations in oxidative stress have been documented. Oxidative stress is relatively low in the first trimester, increases during the second trimester due to placental growth and maternal metabolic demand, and peaks in the third trimester (14,15). In anemic women, these changes are more pronounced, with reduced enzymatic antioxidants and elevated MDA and urinary F2-isoprostane levels (16,17).

Despite growing evidence, few studies systematically evaluate serum oxidative stress markers in conjunction with urinary F2-isoprostanes across all trimesters in anemic women. Such an integrated approach could provide a comprehensive oxidative profile, aiding early identification of women at risk of complications (18,19).

This review explores trimester-wise changes in serum oxidative stress markers (SOD, CAT, GPx, MDA) and urinary F2-isoprostanes in anemic pregnant women, highlighting their role in understanding disease mechanisms and their potential clinical utility.

MATERIAL AND METHOD

A literature search was conducted in PubMed, Scopus, and Web of Science for studies on oxidative stress and antioxidant status in anemic pregnant women across trimesters. Keywords included terms for anemia, pregnancy, oxidative stress, antioxidants, biomarkers, and trimester-specific analysis. The search was limited to English-language, human studies published, and reference lists of relevant articles were screened for additional studies. The search strategy combined keywords and Boolean operators as follows

(anemia OR "iron deficiency anemia" OR IDA) AND (pregnancy OR "pregnant women") AND ("oxidative stress" OR "reactive oxygen species" OR ROS) AND ("antioxidant status" OR "antioxidant capacity" OR "antioxidant enzymes" OR SOD OR CAT OR GPx) AND ("serum markers" OR "urinary biomarkers" OR "F2-isoprostanes" OR "8-iso-PGF2 α " OR "thiol/disulfide balance") AND ("first trimester" OR "second trimester" OR "third trimester" OR trimester-specific)

DISCUSSION

Pregnancy-associated oxidative stress results from increased ROS generation by the placenta and maternal tissues (1,2). Under normal conditions, antioxidant defenses balance ROS production, but anemia shifts this balance toward oxidative damage (4,6). Studies consistently demonstrate reduced SOD, CAT, and GPx activities in anemic pregnant women compared to non-anemic controls (7,8). The decline progresses with advancing gestation, reflecting exhaustion of antioxidant reserves (9). Simultaneously, MDA levels increase, indicating ongoing lipid peroxidation (10,11). These changes are more severe in moderate-to-severe anemia, correlating with hemoglobin levels and adverse outcomes (12). Urinary F2-isoprostanes are robust markers of oxidative stress and lipid peroxidation (11). Trimester-wise studies reveal rising concentrations, with highest levels during the third trimester (13,14). Anemic women exhibit consistently higher values than non-anemic peers, underscoring the amplifying effect of anemia on oxidative stress (15). Elevated F2-isoprostanes have been linked to preeclampsia, preterm delivery, and IUGR (16,17). During the first trimester, oxidative stress remains moderate but increases significantly in the second trimester due to rapid placental growth and maternal hemodynamic changes (14,18). In the third trimester, maximal oxidative stress is observed, often exceeding antioxidant defenses, particularly in anemic women (15,19). The combined assessment of serum enzymatic antioxidants and urinary F2-isoprostanes offers a comprehensive evaluation of oxidative stress. Women with low antioxidant enzyme activity and high urinary F2-isoprostanes are at increased risk of adverse outcomes (20,21). This dual biomarker approach may guide early interventions, including nutritional supplementation (iron, folate, vitamins C and E) and closer antenatal surveillance (22).

Evidence is limited by heterogeneity in study designs, variability in biomarker assays, and small cohort sizes (23).

Moreover, most studies are cross-sectional, restricting the ability to establish causal links between oxidative stress and outcomes (24). Prospective longitudinal studies with larger sample sizes are needed to validate these biomarkers (25). Standardization of urinary F2-isoprostane assays and integration with clinical indices would strengthen predictive utility (26). In summary, anemia magnifies oxidative stress during pregnancy, reflected by reduced antioxidant enzyme activity, elevated MDA, and increased urinary F2-isoprostanes. Together, these biomarkers may serve as valuable tools for monitoring maternal risk and guiding clinical care.

CONCLUSION

Pregnancy is accompanied by progressive oxidative stress, which becomes more pronounced in women with anemia due to impaired antioxidant defenses. Serum antioxidant enzymes (SOD, CAT, GPx) decrease while MDA, a lipid peroxidation marker, rises with advancing gestation. Concurrently, urinary F2-isoprostanes increase progressively across trimesters, representing a stable and reliable measure of oxidative damage.

The combined evaluation of serum and urinary markers provides a comprehensive profile of oxidative stress in anemic pregnant women. Such information can be valuable for early risk assessment, enabling clinicians to identify women at higher risk of complications like preeclampsia, preterm birth, and IUGR. Interventions such as iron supplementation, antioxidant-rich nutrition, and enhanced antenatal surveillance could be tailored to biomarker status, potentially improving maternal and neonatal outcomes.

REFERENCES

1. Burton GJ, Jauniaux E. Oxidative stress. *Best Pract Res Clin ObstetGynaecol.* 2011;25(3):287-99. PMID: 21130690
2. Myatt L. Review: Reactive oxygen and pregnancy. *Placenta.* 2010;31 Suppl:S66-9. PMID: 20079884
3. Redman CW, Sargent IL. Placental stress and pre-eclampsia. *Nat Med.* 2005;11(6):575-9. PMID: 15937474

4. Allen LH. Anemia and iron deficiency. *Am J Clin Nutr.* 2000;71(5 Suppl):1280S-4S. PMID: 10799405
5. Bencaiova G, Burkhardt T, Breymann C. Anemia prevalence and risk factors in pregnancy. *Eur J Intern Med.* 2012;23(6):529-33. PMID: 22726361
6. Scholl TO. Iron status during pregnancy. *Am J Clin Nutr.* 2005;81(5):1218S-22S. PMID: 15883452
7. Pathak P, Kapoor SK, Kapil U, et al. Status of oxidative stress in anemia during pregnancy. *Indian J Clin Biochem.* 2007;22(2):103-6. PMID: 23105650
8. Uotila J, Tuimala R, Aarnio T, et al. Lipid peroxidation products in pregnancy. *Am J Obstet Gynecol.* 1991;165(4):1178-82. PMID: 1957877
9. Atamer Y, Koçyiğit Y, Yokus B, et al. Lipid peroxidation, antioxidants, and cytokines in preeclampsia. *GynecolObstet Invest.* 2005;60(2):79-85. PMID: 16088176
10. Wu F, Tian FJ, Lin Y. Oxidative stress in preeclampsia. *Front Med.* 2020;14(5):528-539. PMID: 32910456
11. Morrow JD, Roberts LJ. F2-isoprostanes as oxidative stress markers. *Prog Lipid Res.* 1999;38(5-6):387-401. PMID: 10793887
12. Milne GL, Musiek ES, Morrow JD. F2-isoprostanes in oxidative stress. *J Biol Chem.* 2005;280(45):33683-6. PMID: 16000351
13. Montuschi P, Barnes PJ, Roberts LJ. Isoprostanes in human disease. *FASEB J.* 2004;18(15):1791-800. PMID: 15576482
14. Toescu V, Nuttall SL, Martin U, et al. Oxidative stress in normal pregnancy. *Obstet Gynecol.* 2002;99(4):703-9. PMID: 11914270
15. Hubel CA. Oxidative stress in preeclampsia. *Clin Exp Hypertens.* 1999;21(5-6):567-85. PMID: 10467491
16. Casanueva E, Viteri FE. Iron and oxidative stress. *J Nutr.* 2003;133(5 Suppl 2):1700S-5S. PMID: 12730476
17. Dennery PA. Oxidative stress in development. *SeminPerinatol.* 2004;28(5):351-7. PMID: 15693360
18. Poston L, Igosheva N, Mistry HD, et al. Oxidative stress in pregnancy complications. *Placenta.* 2011;32 Suppl:S66-9. PMID: 21257065
19. Wang Y, Walsh SW. Antioxidant activities in pregnancy. *Placenta.* 1998;19(7):481-90. PMID: 9757951
20. Roberts JM, Hubel CA. Oxidative stress in preeclampsia. *Am J Obstet Gynecol.* 2004;190(5):1177-8. PMID: 15167815
21. Scholl TO, Leskiw MJ, Chen X, et al. Oxidative stress and pregnancy outcomes. *Am J Clin Nutr.* 2005;82(4):801-9. PMID: 16210708
22. Raijmakers MT, Peters WH, Steegers EA, et al. Glutathione and oxidative stress in pregnancy. *Clin Chem.* 2000;46(6 Pt 2):999-1004. PMID: 10894856
23. Menon R. Oxidative stress in preterm labor. *Placenta.* 2003;24(5):497-502. PMID: 12744916
24. Lykkesfeldt J, Svendsen O. Oxidants and antioxidants in disease. *Vet J.* 2007;173(3):502-11. PMID: 16765490
25. Dalle-Donne I, Rossi R, Colombo R, et al. Biomarkers of oxidative damage. *Clin Chem.* 2006;52(4):601-23. PMID: 16484333
26. Tsukahara H. Biomarkers of oxidative stress in perinatal medicine. *Redox Rep.* 2007;12(4):179-87. PMID: 17896295