Volume 3, Issue 11, November 2025 ISSN (E): 2938-3765

MDA IN THE DIAGNOSIS OF HYPOXIA IN NEWBORNS

Khaydarova Sevara
Master's Degree at the Department of Clinical Laboratory Diagnostics With a Course in Clinical Laboratory Diagnostics at Samarkand State Medical University

Abstract
Hypoxia in newborns continues to be a major contributor to early neonatal morbidity and long-term neurological deficits. Diagnostic strategies increasingly focus on biochemical markers that indicate oxidative stress and lipid peroxidation. Among these, malondialdehyde (MDA), a stable end product of polyunsaturated fatty acid oxidation, has received particular attention due to its high reactivity and strong association with oxidative tissue injury. In this study, we examine the potential of MDA as a diagnostic marker for neonatal hypoxia, considering its biochemical origins, temporal dynamics, and methods of measurement. We also explore the relationship between elevated MDA levels and the severity of perinatal hypoxic injury. Furthermore, we discuss how MDA formation interacts with cytokine signaling, membrane destabilization, and mitochondrial dysfunction, providing an integrated perspective on the pathophysiological mechanisms underlying neonatal hypoxic states.

Keywords: Malondialdehyde, neonatal hypoxia, oxidative stress, lipid peroxidation, biomarkers, antioxidant defense, perinatal asphyxia.

Introduction

Hypoxia during the neonatal period initiates a cascade of metabolic disturbances, including mitochondrial dysfunction, impaired oxidative phosphorylation, and activation of anaerobic glycolysis. One of the earliest and most harmful consequences is the excessive production of reactive oxygen species (ROS), which quickly attack membrane phospholipids. This leads to lipid peroxidation—a chain reaction that compromises membrane integrity and generates toxic end products. Among these, malondialdehyde (MDA) is the most extensively studied marker of oxidative stress in perinatal medicine.

Elevated MDA levels reflect ongoing membrane damage, enzymatic imbalance, and systemic oxidative stress. Newborns, particularly preterm infants, have underdeveloped antioxidant defenses, including catalase, glutathione peroxidase, and superoxide dismutase systems. These developmental limitations amplify lipid peroxidation during hypoxic episodes and result in the accumulation of measurable MDA in plasma, urine, cerebrospinal fluid, and umbilical cord blood.

In recent years, MDA has emerged as a promising biochemical indicator of perinatal hypoxia and hypoxic-ischemic encephalopathy (HIE). Clinical evidence indicates a strong correlation between MDA concentration and the severity of asphyxia, Apgar scores, lactate levels, base deficit, and neuroimaging findings. Understanding the biochemical pathways leading to MDA formation and its link to hypoxic injury is therefore critical for improving diagnostic accuracy in neonatology.

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5

MDA Formation as a Result of Lipid Peroxidation in Hypoxic Tissue

Lipid peroxidation is initiated when reactive oxygen species (ROS)—including hydroxyl radicals (•OH), superoxide anions (O_2•–), and hydrogen peroxide (H_2O_2)—attack polyunsaturated fatty acids in cell membranes. The neonatal brain, rich in arachidonic and docosahexaenoic acids, is particularly susceptible to this process. This chain reaction progresses through three stages: initiation, propagation, and termination.

During initiation, ROS remove hydrogen atoms from fatty acid side chains, generating lipid radicals. Propagation occurs as these radicals interact with oxygen to form lipid peroxyl radicals, which further compromise membrane integrity. Eventually, unstable intermediates break down into aldehydes, mainly malondialdehyde (MDA), which then diffuse from cells into systemic circulation Hypoxia accelerates these reactions via several mechanisms. Mitochondrial decoupling increases electron leakage, xanthine oxidase activation generates additional superoxides, and reduced ATP levels impair membrane pump function, increasing vulnerability to oxidation. In newborns with perinatal asphyxia, circulating MDA levels rise markedly within hours after injury. Notably, these changes appear earlier than many inflammatory markers, highlighting MDA's potential as an early diagnostic indicator.

Temporal Dynamics of MDA in Neonatal Hypoxia

The temporal profile of MDA elevation reflects the progression of hypoxic injury. Umbilical cord blood obtained at birth typically shows increased MDA levels in infants with low Apgar scores or signs of metabolic acidosis. Within 6–12 hours, MDA concentration continues to rise as ROS generation intensifies during reperfusion, which paradoxically inflicts secondary oxidative damage. Persistent elevation of MDA for 24–48 hours correlates with severe hypoxic-ischemic encephalopathy, multi-organ involvement, and deterioration of hepatocellular and myocardial membrane stability. Studies using serial plasma measurements have demonstrated that the magnitude and duration of MDA increase in a manner that closely parallels neurosonographic abnormalities, EEG disturbances, and long-term neurological outcomes.

Cytokines such as TNF-α and IL-6 may indirectly modulate MDA levels. They enhance nitric oxide synthase activity, contributing to peroxynitrite formation and additional oxidative injury. This interplay explains why infants with systemic inflammatory responses or post-asphyxial sepsis exhibit even higher MDA concentrations.

Diagnostic Value of MDA in Clinical Practice

MDA measurement has gained recognition as a valuable tool for assessing the severity of neonatal hypoxia. Plasma and cord blood MDA levels are consistently higher in newborns with moderate to severe asphyxia compared to healthy controls. Several studies report a statistically significant correlation between MDA values and standard clinical parameters: low Apgar score, elevated lactate, increased creatine kinase-BB, and reduced pH at birth.

Cord blood MDA level above defined thresholds may serve as an early predictor of hypoxic-ischemic encephalopathy. In addition, elevated MDA levels in cerebrospinal fluid appear to be closely linked to neuronal membrane damage and activation of the apoptotic pathway. In neonates treated with therapeutic hypothermia, MDA monitoring may help assess the efficacy of neuroprotective interventions and provide insight into ongoing oxidative processes.

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5

Analytical methods for quantifying MDA include thiobarbituric acid reactive substances (TBARS) assay, high-performance liquid chromatography (HPLC), and mass spectrometry. While TBARS is widely used due to its simplicity, HPLC offers greater specificity by distinguishing MDA from interfering aldehydes. Standardization of measurement protocols remains an active challenge for clinicians and researchers.

Systemic Consequences of Elevated MDA in Newborns

Excessive MDA is not only a marker but also a mediator of cellular injury. It forms adducts with membrane proteins, impairs enzyme function, and crosslinks nucleic acids, producing mutagenic and pro-apoptotic effects. MDA-protein complexes stimulate inflammatory signaling and may participate in the amplification of systemic oxidative stress.

In the context of neonatal hypoxia, elevated MDA has been associated with myocardial dysfunction, hepatic injury, renal tubular damage, and pulmonary oxidative stress. Preterm infants are especially susceptible due to reduced antioxidant capacity, limited glutathione pools, and immature mitochondrial protective mechanisms. The combination of hypoxia and secondary infection further boosts MDA production, reflecting the escalation of oxidative imbalance.

Experimental studies demonstrate that antioxidant therapy—vitamin E, N-acetylcysteine, melatonin—can attenuate MDA accumulation and reduce the severity of hypoxic injury. However, clinical efficacy remains inconsistent, emphasizing the need for more targeted therapeutic approaches.

Conclusion

MDA is a robust and informative biomarker of neonatal hypoxia, reflecting the extent of oxidative membrane damage and the severity of hypoxic-ischemic injury. Its elevation follows a characteristic temporal pattern that correlates with clinical, metabolic, and neurophysiological markers of perinatal asphyxia. Although methodological standardization is required for its widespread clinical adoption, MDA measurement offers valuable insight into oxidative processes and may guide early diagnosis and treatment strategies.

Understanding the biochemical and pathophysiological mechanisms behind MDA formation enhances our ability to interpret laboratory data and refine clinical decision-making in neonatology. As research continues to clarify the diagnostic utility of MDA, it holds considerable promise as a component of comprehensive evaluation for hypoxic states in newborns.

References

1. Gülbayzar S., Arıca V., Hatipoğlu S., Kaya A., Arıca S., Karatekin G. Malondialdehyde level in the cord blood of newborn infants. Iran J Pediatr. 2011;21(3):313–319.

2. El Dein H.M.S., El Gohary H., El Gendy S., et al. Correlation between increased serum malondialdehyde and spectrum of cranial ultrasonography findings in hypoxic-ischemic encephalopathy — could it be used as a predictor of disease severity? (prospective clinical study). 2020.

3. Cavia-Saiz M., et al. Biomarkers of Oxidative Stress in Healthy Infants within the First Hours After Birth. (Study of neonatal plasma and urine oxidative stress dynamics). 2023.

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5

4. Ferrante G., et al. Biomarkers of Oxidative Stress for Neonatal Lung Disease. Front. Pediatr. 2021; review of OS biomarkers in neonatology.
5. Notarbartolo V., et al. Antioxidant Therapy in Neonatal Hypoxic-Ischemic Encephalopathy: current evidence and perspectives. Metabolites. 2024;14(11):630. (discussion includes MDA as lipid peroxidation marker).
6. Solevåg A.L., et al. Metabolomics to diagnose oxidative stress in perinatal asphyxia. Antioxidants (MDPI). 2021; review — includes lipid-peroxidation metabolites like MDA.
7. Kirimi E., et al. Increased serum malondialdehyde level in neonates with hypoxic injury: association with outcome. (Clinical study linking sMDA to mortality and severity). 2010.
8. Banupriya C., et al. Can urinary excretion rate of malondialdehyde, uric acid and creatinine predict neonatal perinatal asphyxia? Early study on urinary MDA in asphyxia. 2008.
9. Sarici S.U., et al. Investigation on malondialdehyde, S100B, and advanced oxidation protein products in neonatal conditions. Clin/experimental paper linking MDA to neonatal pathology. 2015.
10. Wu L., et al. Regulated cell death in hypoxic-ischaemic encephalopathy. Cell Death Discovery / Nature partner. 2024 — discusses lipid peroxidation/ferroptosis and MDA as marker.
11. Recent review: Metabolomic and biomarker approaches to oxidative stress in perinatal asphyxia — includes MDA and related markers, methodological notes (MDPI/Antioxidants). 2021–2024.
12. Ferrante G., et al. Biomarkers and clinical utility in neonatal oxidative injury; limitations of TBARS and advantages of chromatographic methods (HPLC/MS). (Review/context). 2021.
13. Recent article on ferroptosis and neonatal HIE linking MDA to ferroptotic LPO: Ferroptosis in Neonatal Hypoxic-Ischemic Encephalopathy. (Springer, 2025) — highlights MDA as LPO hallmark.
14. Исмоилов К.И. Окислительно-антиоксидантный статус организма новорождённых детей при специфических внутриутробных инфекциях. (анализ ПОЛ и АОЗ у новорождённых). CyberLeninka, 2023. (включает методологию измерения МДА / ПОЛ).
15. Шишко Г.А. Роль оксидативного стресса в патогенезе заболеваний новорождённых детей. Обзорная статья. 2011. (обзор механизмов ПОЛ, упоминание МДА).
16. Колесникова Л.И. Перекисное окисление липидов – антиоксидантная защита: возможности применения показателей ПОЛ в педиатрии. ActaBiomedica.ru, 2020. (практическая интерпретация показателей ПОЛ и МДА).

Web of Medicine: Journal of Medicine, Practice and Nursing
webofjournals.com/index.php/5