Early Prediction of Mortality risk in Neonatal Sepsis Using Combined Assessment of Lactate Dehydrogenase and Malondialdehyde

By

Rania Mohamed Abdou[1], Mohamed Tarif Hamza[2], Asmaa Aboud Nasr[3], Mohamed Omar Abd El Aal Dawoud[1]

Pediatrics[1,] Clinical Pathology[2] department, Faculty of medicine Ain shams University.
Pediatrics department El Minia hospital Ministry of Health[3]

[1]Corresponding author: Rania Mohamed Abdou

e- mail: Raniaabdou@med.asu.edu.eg

Abstract:

Background: Neonatal sepsis continues to be a leading contributor to illness and death among newborns, especially in low and middle - income countries (LMICs). Early risk stratification is critical for initiating life-saving interventions; however, conventional biomarkers often lack sufficient prognostic accuracy. **Aim:** The study aimed to assess and compare the prognostic accuracy of serum lactate dehydrogenase (LDH) and malondialdehyde (MDA), as biomarkers of cellular injury and oxidative stress, with CRP in predicting mortality in neonates with sepsis.
Methods:
A prospective cross-sectional study was carried out from November 2022 to April 2023 on 64 newborns diagnosed with sepsis and admitted to the Level III Neonatal Intensive Care Unit at Ain Shams Pediatrics Hospital in Cairo. Serum levels of LDH, MDA, and CRP were measured on Day 1 (baseline) and Day 7 (follow-up). Receiver operating characteristic (ROC) curves were used to evaluate the predictive performance of each biomarker by comparing levels between surviving and non-surviving infants.

Results: revealed that elevated baseline levels of both LDH and MDA were significantly related with increased mortality ($p < 0.05$). MDA demonstrated the highest prognostic accuracy (AUC: 0.948) with 100% sensitivity and 89.3% specificity. LDH also showed strong predictive value (AUC: 0.854) with slightly lower specificity (78.6%). CRP displayed high specificity (87.8%) at baseline but lower sensitivity (58.3%) that declined by Day 7.

Conclusion: MDA and LDH are valuable prognostic biomarkers in neonatal sepsis, with MDA showing superior performance.

Keywords: Neonatal sepsis; Malondialdehyde (MDA); Lactate dehydrogenase (LDH); Oxidative stress; Prognostic biomarkers.

Introduction:

Neonatal sepsis is a life-threatening bloodstream infection that significantly affects infants under 28 days of age, contributing to high rates of illness and mortality, particularly in low- and middle-income countries **(Seale et al., 2014)**. Despite advancements in molecular medicine and neonatal care, the accurate diagnosis of sepsis remains challenging. This difficulty arises from the subtle and nonspecific clinical signs in newborns, which often lead to misdiagnosis (**Attia et al., 2023)**. As a result, there is a critical need for reliable and objective biomarkers to improve risk stratification and predict adverse outcomes in affected neonates. The pathophysiology of neonatal sepsis involves a complex interplay between inflammatory and oxidative processes, ultimately resulting in cellular damage and organ dysfunction. The inflammatory cascade is initiated by the release of both pro-inflammatory and anti-inflammatory cytokines, such as C-reactive protein (CRP) and procalcitonin (PCT) (**Boscarino et al., 2023)**. However, traditional inflammatory biomarkers have notable limitations, including a lack of specificity and the potential for elevated levels in non-septic conditions, such as maternal fever or meconium aspiration. This overlap complicates the differentiation between true infection and colonization, reducing effective intervention in neonates with sepsis (**Tang et al., 2022)**. Oxidative stress, defined by an imbalance between reactive oxygen species (ROS) and the body's antioxidant defenses, plays a significant role in the progression of neonatal sepsis. Excessive ROS production can overwhelm the immature antioxidant systems of newborns, leading to lipid peroxidation, protein oxidation, and DNA damage (**Giuffrè et al., 2015)**. Among the emerging biomarkers, lactate dehydrogenase (LDH) and malondialdehyde (MDA) show promise for interpreting oxidative damage and the underlying pathophysiology of sepsis (**Panizzolo et al., 2023)**. LDH, an intracellular enzyme, serves as a key indicator of tissue damage and anaerobic metabolism resulting from hypoperfusion and hypoxia. Elevated LDH levels are associated with increased disease severity, organ dysfunction, and mortality in sepsis patients, offering valuable insights into systemic injury (**Lu et al., 2018)**. Similarly, MDA, a byproduct of lipid peroxidation, reflects oxidative stress-induced damage to cell membranes. Increased MDA levels during septic episodes are triggered by infection and contribute to endothelial dysfunction, impaired microcirculation, and heightened vascular permeability, all of which worsen outcomes in sepsis patients (**Helan et al., 2022)**. Therefore, measuring MDA and LDH in cases of neonatal sepsis may help identify high-risk neonates earlier, enhance diagnostic accuracy, and enable timely interventions, ultimately improving survival rates.

Methodology

Study Design and Setting

This prospective cross-sectional study was directed over a six-month period, from November 2022 to April 2023, in the Level III Neonatal Intensive Care Unit at Ain Shams Pediatrics Hospital—a regional tertiary referral center in Cairo, Egypt, which manages over 1,200 neonatal admissions annually.

Study Population

A total of 64 neonates with clinical sepsis were recruited using convenience sampling. All neonates admitted to the NICU during the study period who met the inclusion criteria were eligible for enrollment. The patients were followed up throughout their NICU stay until discharge or death. Based on their outcomes, the studied neonates were finally classified into two groups: a clinically improved group (survivors) and a hospital mortality group (non-survivors).

Sample Size

The study estimated the sample size using PASS 15 software, with a power of 80% and a significance level of 0.05. Based on a previous study by **Lorente et al., 2012**, the minimum sample size was 64 neonates, this calculation includes a 10% allowance for potential attrition.

Inclusion Criteria

Neonates were eligible for inclusion if they met the following criteria:

1. Were aged ≤28 days, and
2. A clinical and laboratory diagnosis of sepsis was defined by the existence of at least 2 of the following signs:
    - Temperature instability (>38°C or <36°C)
    - Tachycardia or bradycardia
    - Respiratory distress (e.g., tachypnea, grunting, chest retractions)
    - Feeding intolerance along with laboratory confirmation via

      C-reactive protein (CRP) ≥10 mg/L

      Positive blood culture

Exclusion Criteria

Neonates were excluded if they experienced the following criteria:

- Confirmed congenital anomalies

- A history of major surgical intervention within 72 hours prior to enrollment
- Evidence of perinatal asphyxia (Apgar score < 5 at 5 minutes accompanied by clinical signs of end-organ dysfunction)

Classification: The studied neonates were subclassified into a clinically improved group (survivors) and a hospital mortality group (non-survivors).

Ethical Considerations

- **Ethical Approval:** The study protocol was approved by the Research Ethics Committee of Ain Shams University Hospital (Reg. No. FWA000017585; Approval Number: FMASU MS 871/2022/2023).
- **Consent:** Informed consent was obtained from the parents or legal guardians of all enrolled neonates prior to participation.
- **Conflict of Interest:** The authors declare no conflict of interest related to this study or its publication.
- **Confidentiality:** All patient data and study information were confidential.
- **Financial Disclosure:** No funding was received for the conduct of this study or its publication.

Collection of Data

Data were prospectively collected using a consistent form included the following:

- Demographics: Gestational age, birth weight, sex
- Maternal History: Presence of premature rupture of membrane, urinary tract infection
- Clinical Presentation: Signs and symptoms on admission
- Laboratory Findings: Complete blood count, CRP, blood cultures, LDH, and MDA levels
- Clinical Interventions: Use of antibiotics, vasopressors, and mechanical ventilation
- Outcomes: Clinical improvement (survivors) or in-hospital mortality (non survivors)

Biomarker Assessment

Venous blood samples were obtained at two time points.

1. Day 1 (Baseline): At the time of sepsis diagnosis
2. Day 7 (Follow-Up): Seven days after baseline to assess dynamic changes and prognostic value

Serum LDH levels were measured using a standardized enzymatic assay on the Roche/Hitachi Cobas® C501 chemistry analyzer. MDA levels were measured by an available enzyme-linked immunosorbent assay (ELISA) kit (Elabscience®, Catalog No. E-EL-H5543). All measurements were performed in accordance with the manufacturer's protocol under controlled laboratory conditions.

Statistical Analysis

Data analysis was conducted using IBM SPSS Statistics for Windows, Version 27.0 (IBM Corp., Armonk, NY, USA). Continuous variables were assessed for normality and presented as mean ± standard deviation (SD) or median with interquartile range (IQRs), as appropriate. Categorical variables are expressed as frequencies and percentages.

Comparisons between survivors and non-survivors were performed as follows.

- For continuous variables; Independent t-tests or Mann–Whitney U tests
- For categorical variables; Chi-square tests or Fisher's exact tests

The diagnostic performance of LDH and MDA in predicting mortality was estimated using a receiver operating characteristic (ROC) curve analysis. For every biomarker, the area under the ROC curve (AUC) was calculated. The optimal cutoff values were determined by the Youden index. Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were among the calculated diagnostic indices. The DeLong's test compared the AUCs between the biomarkers. Statistical significance was put at $P < 0.05$.

Results:

The study included 64 neonates, with a slight male predominance (53.1%). Cesarean section was the primary mode of delivery (79.7%). The mean gestational age was 36.89 weeks, with 76.6% of the neonates born at full term (≥37 weeks). Premature rupture of membranes (PROM) was observed in 21.9% of neonates. Maternal demographic data indicated that most participants were under 35 years of age. A slightly higher proportion resided in rural areas (53.1%) and 54.7% were housewives. Reported consanguinity was relatively low, present in only 10.9% of cases (table 1).

Table 1: Demographic and Clinical Data of the Studied Patients (n = 64)

Variable	Category	Number	percent
Mother's Age in years	≥ 35 years	19	29.7%
	< 35 years	45	70.3%
Residency	Urban	30	46.9%
	Rural	34	53.1%
Occupation	Employed	29	45.3%
	Housewife	35	54.7%
Consanguinity	positive	7	10.9%

Mode of Delivery	Normal Vaginal Delivery (NVD)	13	20.3%
	Cesarean Section (C.S.)	51	79.7%
Sex of Neonate	Female	30	46.9%
	Male	34	53.1%
Gestational Age (weeks)	Mean ± SD	36.89 ± 2.19	--
	Range	36 - 42	--
PROM*	positive	14	21.9%
UTI*(in mothers)	Positive	5	7.8%

*PROM= premature rupture of membrane - *UTI = urinary tract infection

Table 2: Comparison of Demographic and Perinatal Characteristics Between Survivors and Non-Survivors

Parameter		Survivors	Non survivors	Test value	P-value
		N=49	N= 15		
Sex of neonate	Female	23 (46.9%)	7 (46.7%)	0.000*	0.985
	Male	26 (53.1%)	8 (53.3%)		
Mode of delivery	NVD	8 (16.3%)	5 (33.3%)	2.052*	0.152
	C.S.	41 (83.7%)	10 (66.7%)		
Gestational age	Mean ± SD	37.18 ± 2.12	36.93 ± 2.22	1.979•	0.052
PROM	Positive	8 (16.3%)	6 (40.0%)	3.766*	0.061
UTI	Positive	3 (6.1%)	2 (13.3%)	0.829*	0.363

P-value >0.05: Non-significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS) *: Chi-square test; •: Independent t-test

Table 3**: Comparison of Demographic and Perinatal Characteristics Between Survivors and Non-Survivors**

Parameter		**Survivors**	**Non survivors**	**Test value**	**P-value**
		N=49	**N= 15**		
Sex of neonate	Female	23 (46.9%)	7 (46.7%)	0.000*	0.985
	Male	26 (53.1%)	8 (53.3%)		
Mode of delivery	NVD	8 (16.3%)	5 (33.3%)	2.052*	0.152
	C.S.	41 (83.7%)	10 (66.7%)		
Gestational age	Mean ± SD	37.18 ± 2.12	36.93 ± 2.22	1.979•	0.052

PROM	Positive	8 (16.3%)	6 (40.0%)	3.766*	0.061
UTI	Positive	3 (6.1%)	2 (13.3%)	0.829*	0.363

P-value >0.05: Non-significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS) *: Chi-square test; •: Independent t-test

Table 3 data comparing demographic and perinatal characteristics between neonates who survived and those who did not found no significant differences in factors such as sex, mode of delivery, gestational age, PROM, and maternal UTI.

Table4: Sepsis biomarkers Among Neonatal Survivors During the 1st and 7th day follow up

Survivors (n=49)		Day 1	Day7	Test value	P-value
CRP	Median (IQR)	24 (12 – 48)	2 (2 – 3)	6.761*	<0.001
	Range	6 – 96	1 – 6		
LDH	Mean ± SD	625.41 ± 134.11	306.07 ± 108.33	7.316**	<0.001
	Range	250 – 833	112 – 485		
MDA	Median (IQR)	19.52 (16.9 – 25.54)	4.06 (3.77 – 4.99)	5.314*	<0.001
	Range	5.6 – 65.26	2.94 – 7.74		

*Wilcoxon signed-rank test ** Paired t-test

The table shows significant reductions in key biomarkers CRP, LDH, and MDA in neonatal survivors from day 1 to day 7, indicating improvements in inflammation and oxidative stress in follow up.

Table5: Sepsis biomarkers Among Neonatal Non-Survivors During the 1st and 7th day follow up

Non survivors (n=15)		Day1	Day7	Test value	P-value
CRP	Median (IQR) Range	96 (96 – 96) 6 – 96	4.5 (2 – 6) 2 – 12	8.614	<0.001
LDH	Mean ± SD range	780.75 ± 71.43 708 – 915	429.00 ± 69.58 288 – 502	10.631	<0.001
MDA	Mean ± SD range	33.86 (31.74 – 45.4) 26.91 – 60.49	7.21 (6.76 – 7.96) 5.02 – 8.76	9.314	<0.001

The table reveals that three key sepsis-related biomarkers—CRP, LDH, and MDA—in non-surviving neonates show a significant decline from day 1 to day 7, indicating transient biochemical improvement before clinical deterioration or death.

Table 6: Comparison between patients' survivors and mortality patients regarding CRP, LDH and MDA at 1st baseline

Item		survivors	Non-survivors	Test value	P-value
		No. = 49	No. = 15		
1st baseline sample					
CRP	Median (IQR) Range	24 (12 – 48) 6 – 96	96 (96 – 96) 6 – 96	-3.008‡	0.003
LDH	Mean ± SD Range	625.41 ± 134.11 250 – 833	780.75 ± 71.43 708 – 915	-3.171•	0.003
MDA	Median (IQR) Range	19.52 (16.9 – 25.54) 5.6 – 65.26	33.86 (31.74 – 45.4) 26.91 – 60.49	-3.408‡	0.001

P-value >0.05: Non-significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS) •: Independent t-test; ‡: Mann Whitney test

Table 7: Comparison between patients' survivors and mortality patients regarding CRP, LDH and MDA at follow up sample after 7 days

Item		survivors	Non-survivors	Test value	P-value
		No. = 49	No. = 15		
Follow up after 7 days sample					
CRP	Median (IQR) Range	2 (2 – 3) 1 – 6	4.5 (2 – 6) 2 – 12	-2.300‡	0.021
LDH	Mean ± SD Range	306.07 ± 108.33 112 – 485	429.00 ± 69.58 288 – 502	-3.073•	0.004
MDA	Median (IQR) Range	4.06 (3.77 – 4.99) 2.94 – 7.74	7.21 (6.76 – 7.96) 5.02 – 8.76	-3.977‡	0.000

P-value >0.05: Non-significant (NS); P-value <0.05: Significant (S); P-value< 0.01: highly significant (HS) •: Independent t-test; ‡: Mann Whitney test

Table (6 and 7) demonstrates that, at baseline, non-survivor' levels of CRP, LDH, and MDA were significantly higher than survivors. At follow-up after 7 days, CRP levels decreased but remained significantly higher in non-survivors. LDH levels remained elevated in non-survivors in comparison to survivors. The MDA levels at follow-up were significantly higher in non-survivors.

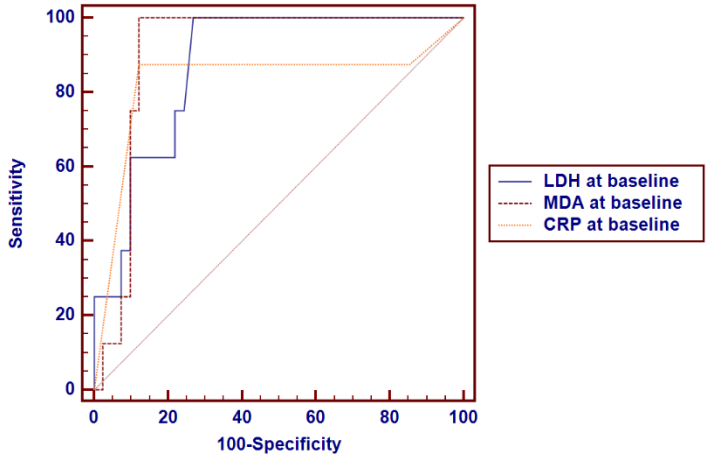

Figure 1: Roc curve for LDH, MDA and CRP and baseline sample

Figure (1) of ROC analysis demonstrated the strong prognostic utility of the baseline biomarkers. **LDH on day 1** (cutoff >706 U/L) predicted mortality with perfect sensitivity (100%) and moderate specificity (73.17%), supported by an AUC of 87.5%. **MDA** (cutoff >27.29 nmol/mL) emerged as the most robust predictor of mortality, achieving 100% sensitivity, 87.8% specificity, and the highest discriminative power (AUC: 90.9%). **CRP** (cutoff >75 mg/L) also exhibited strong prognostic value for adverse outcomes, with a balanced sensitivity (87.5%) and specificity (87.8%) and an AUC of 83.1%.

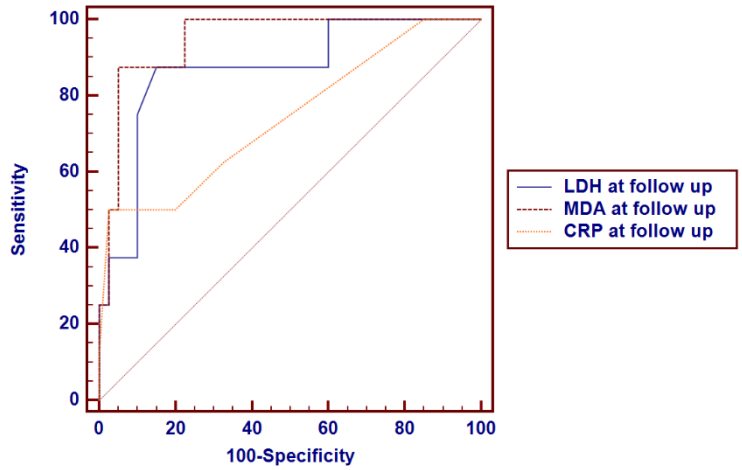

Figure 2: Roc curve for LDH, MDA and CRP after 7 days follow up from baseline sample

Figure 2 of Roc curve shows that the LDH level after 7 days of follow-up (cutoff >398 U/L) demonstrated a strong predictive capacity for mortality, with 87.5% sensitivity, 82.93% specificity,

and an AUC of 86%. MDA at follow-up (cutoff >6.59 nmol/mL) emerged as the most robust predictor of poor outcomes, achieving 87.5% sensitivity, 95.12% specificity, and exceptional discriminative power (AUC: 94.8%). In contrast, CRP at follow-up (cutoff >5 mg/L) exhibited markedly lower sensitivity (50%), but very high specificity (97.5%) and modest accuracy (AUC: 74.2%).

Discussion:

Sepsis remains a global health concern, with low- and middle-income countries (LMICs) bearing a disproportionate burden accounting for 93.91% of incident cases and deaths in 2019. This underscores the urgent need for specific strategies to improve early diagnostic modalities consequently reduce neonatal morbidity and mortality (**Li et al., 2023)**. In our study, the observed demographic and clinical trends align with existing literature. The present study, involving 64 neonates, observed a slight male predominance (53.1%) among the neonates which is consistent with global epidemiological trends (**Dunn et al., 2015)**. Most mothers were under 35 years old, with 53.1% residing in rural areas and 54.7% identified as housewives. These findings highlight the influence of maternal age, residence, and occupation on neonatal outcomes (**Dunn et al., 2015)**. Although the consanguinity rate was relatively low (10.9%), which is favorable given the established association between consanguinity and congenital anomalies, rural residence remains a potential determinant of limited access to quality prenatal care and health literacy (**Jiang et al., 2020)**. The study also revealed a high cesarean section rate of 79.7%, exceeding rates reported in comparable studies. This may reflect institutional practices or systemic constraints that influence obstetric decision-making. The association between neonatal sex and delivery method is multifactorial; male neonates are more frequently delivered via cesarean section due to higher birth weights and increased incidence of fetal distress (**Magsi et al., 2022)**.

Importantly, the study draws attention to the diagnostic limitations of conventional biomarkers, such as C-reactive protein (CRP), in the early detection of neonatal sepsis. Recent advances in understanding sepsis pathophysiology suggest that oxidative stress and its associated biomarkers may provide enhanced diagnostic and prognostic value. This highlights the need for reliable, rapid, and accessible diagnostic tools, especially in LMICs (**Poggi and Dani 2018).**

In this study, serum levels of lactate dehydrogenase (LDH) and malondialdehyde (MDA) were measured in neonates with sepsis at both the acute phase (day 1) and the follow-up phase (day 7). Both biomarkers were strongly associated with poor clinical outcomes, including increased mortality, underscoring their potential as early predictors of disease severity and progression. While all three biomarkers decreased significantly over time in non survivors, this did not correlate with survival, possibly due to the severity of the initial insult or irreversible organ damage. These findings suggest that although biomarker trends are useful, they should be interpreted

alongside clinical context, and persistently elevated or delayed normalization may signal poor prognosis. Baseline profiling of these biomarkers proved valuable for risk stratification **(Mubaraki et al., 2023)**. Elevated LDH levels demonstrated 100% sensitivity in predicting mortality, though moderate specificity may limit its use as a standalone marker. LDH, a well-established indicator of tissue hypoxia and cellular injury, reflects sepsis-induced multiorgan dysfunction. This finding is consistent with previous research linking LDH to hematologic abnormalities, such as leukopenia and thrombocytopenia, in severe infections (**Van et al., 2020)**.

MDA, produced by lipid peroxidation, is a key indicator of oxidative stress in sepsis pathogenesis. In this study, MDA demonstrated superior prognostic performance, achieving perfect sensitivity and high specificity. These results are in line with growing evidence that oxidative stress markers like MDA and TBARS offer greater predictive reliability than traditional inflammatory markers, making them promising tools for early clinical decision-making and therapeutic intervention (**Boscarino et al., 2013)**.

CRP remains valuable for monitoring disease progression in neonatal sepsis. However, its sensitivity declined markedly at follow-up (50%), reinforcing its limitations as a prognostic marker. Despite this, CRP maintained high specificity for confirming inflammation and assessing treatment response, supporting its use in monitoring therapeutic efficacy rather than as a primary prognostic tool (**Saedii et al., 2022)**.

Notably, MDA emerged as the most accurate predictor of mortality, with an area under the curve (AUC) of 94.8%, outperforming both CRP and procalcitonin. This finding emphasizes the importance of oxidative stress markers in identifying pathophysiological changes before clinical deterioration occurs **(Mubaraki et al., 2023)**. LDH, with a diagnostic threshold of >398 U/L, also demonstrated strong predictive capability and clinical value, particularly in resource-limited settings where advanced oxidative stress assays may not be available. Its established role in neonatal conditions such as respiratory distress syndrome further supports its inclusion in risk assessment protocols (**Van et al., 2020)**.

Finally, the study suggests that LDH, MDA, and CRP levels can be effectively integrated into neonatal sepsis management to enable early triage and timely intervention. MDA is preferred for mortality prediction in tertiary care settings, allowing clinicians to identify high-risk neonates who may benefit from aggressive and timely interventions. Meanwhile, LDH and CRP serve as practical alternatives in low-resource environments. These findings support the adoption of a multimodal biomarker approach to improve the early diagnosis, risk stratification, and management of neonatal sepsis, particularly in settings with limited resources (**Lungu et al., 2020)**.

Conclusion: This study emphasizes the importance of malondialdehyde (MDA) and lactate dehydrogenase (LDH) biomarkers in

neonatal sepsis as they are strongly associated with mortality and adverse clinical outcomes. MDA is the most reliable predictor of mortality, highlighting the role of oxidative stress in sepsis pathophysiology. LDH provides insights into tissue injury and hypoxia, particularly with limited diagnostic access. C-reactive protein (CRP) track disease progression and inflammation. Integrating these biomarkers into early clinical assessments can improve neonatal outcomes.

Recommendation:

The recommendation is to incorporate MDA testing into standard diagnostic protocols for neonatal sepsis, particularly for mortality risk prediction. LDH and CRP levels can be used as supportive biomarkers to assess disease severity and monitor treatment response. Serial measurements of CRP and LDH levels can improve prognostic accuracy and guide treatment decisions. Combining biomarker panels (MDA + LDH + CRP) can enhance early risk stratification and optimize neonatal care pathways. Larger, multicenter studies are needed to validate these findings and develop clinical guidelines.

Limitation of the study: This study has several limitations, including a small sample size, a single-center design, and a limited follow-up duration.

Author's contribution:

Rania Mohamed Abdou: Conceived the study idea, designed the methodology, supervised data collection, and led manuscript writing.

Mohammed Tarif Hamza: Laboratory assessments

Asmaa Aboud Nasr: Facilitated patient recruitment, contributed to data entry.

Mohammed Omar Abd El Aal Dawoud: Assisted in data interpretation and statistical analysis.

References:

Attia Hussein Mahmoud, H.; Parekh, R.; Dhandibhotla, S.; Sai, T.; Pradhan, A.; Alugula, S.; Cevallos-Cueva, M.; Hayes, B.K.; Athanti, S.; Abdin, Z.; et al. (2023): Insight into Neonatal Sepsis: An Overview. *Cureus*; *15*, e45530

Boscarino G, Migliorino R, Carbone G, Davino G, Dell'Orto VG, Perrone S, Principi N, Esposito S. (2023): Biomarkers of Neonatal Sepsis: Where We Are and Where We Are Going. Antibiotics (Basel) ;12(8):1233. doi: 10.3390/antibiotics12081233. PMID: 37627653; PMCID: PMC10451659.)

Dunn L, Prior T, Greer R, Kumar S.(2015): Gender specific intrapartum and neonatal outcomes for term babies. Eur J Obstet Gynecol Reprod Biol.; 185:19-22. doi: 10.1016/j.ejogrb.2014.11.035. Epub 2014 Dec 2. PMID: 25496846

Giuffrè, M. Rizzo, G. Scaturro et al, (2015) : Oxidative stress markers at birth: analyses of a neonatal population, Acta Histochemica, ; 117(4-5): pp. 486–91,

Helan M, Malaska J, Tomandl J, Jarkovsky J, Helanova K, Benesova K, Sitina M, Dastych M, Ondrus T, Pavkova Goldbergova M, Gal R, Lokaj P, Tomandlova M, Parenica J. (2022): Kinetics of biomarkers of oxidative stress in septic shock: A pilot study. *Antioxidants (Basel)*. 11(4):640. doi: 10.3390/antiox11040640.

Jiang HL, Lu C, Wang XX, Wang X, Zhang WY. (2020): Cesarean section does not affect neonatal outcomes of pregnancies complicated with preterm premature rupture of membranes. Chin Med J (Engl). 5;133(1):25-32. doi: 10.1097/CM9.0000000000000582. PMID: 31923101; PMCID: PMC7028204

Li J, Xiang L, Chen X, Li S, Sun Q, Cheng X, Hua Z. (2023): Global, regional, and national burden of neonatal sepsis and other neonatal infections, 1990-2019: findings from the Global Burden of Disease Study 2019 Eur J Pediatr. 2023 May;182(5):2335-2343. doi: 10.1007/s00431-023-04911-7. Epub 2023 Mar 7. PMID: 36879151.

Lorente L, Martín MM, Abreu-González P, Domínguez-Rodríguez A, Labarta L, Díaz C. (2012): Malondialdehyde serum levels in patients with septic shock: Correlation with mortality. Intensive Care Med. 2012;38(4):683-689.

Lu J, Wei Z, Jiang H, Cheng L, et al. (2018): Lactate dehydrogenase is associated with 28-day mortality in patients with sepsis: A retrospective observational study *J Surg Res*. ;228:314-321. doi: 10.1016/j.jss.2018.03.035.

Lungu N, Jura AM, Popescu DE, Horhat FG, Manea AM, Boia M.(2020): Understanding the Difficulties in Diagnosing Neonatal Sepsis: Assessing the Role of Sepsis Biomarkers. J Crit Care Med (Targu Mures). 2024 Oct 31;10(4):316-328. doi: 10.2478/jccm-2024-0039. PMID: 39829727; PMCID: PMC11740700.

Magsi S, Qureshi SG, Rajput F, Zia B, Magsi I.(2022): Frequency of cesarean section in premature rupture of membranes. Pak J Med Health Sci.;16(8):74. doi: 10.53350/pjmhs2216874

Mubaraki MA, Faqihi A, AlQhtani F, Hafiz TA, Alalhareth A, Thagfan FA, Elshanat S, Abdel-Gaber RA, Dkhil MA. (2023): Blood Biomarkers of Neonatal Sepsis with Special Emphasis on the Monocyte Distribution Width Value as an Early Sepsis Index. Medicina (Kaunas). 4;59(8):1425. doi: 10.3390/medicina59081425. PMID: 37629715; PMCID: PMC10456917.

Panizzolo M, Martins VH, Ghelli F, Squillacioti G, Bellisario V, Garzaro G, Bosio D, Colombi N, Bono R, Bergamaschi E. (2023): Biomarkers of oxidative stress, inflammation, and genotoxicity to assess exposure to micro- and nanoplastics: A literature review. *Ecotoxicol Environ Saf.* 15; 267:115645. doi: 10.1016/j.ecoenv.2023.115645.

Poggi C,&Dani C. (2018): Sepsis and Oxidative Stress in the Newborn: From Pathogenesis to Novel Therapeutic Targets. Oxid Med Cell Longev. 2;2018:9390140. doi: 10.1155/2018/9390140. PMID: 30174784; PMCID: PMC6098933

Saedii AA, Ahmed AMM, Mohamed OM, Bahaa El-deen MA, Abdel-Hakim MA-R. (2022): Diagnostic value of biomarkers in neonatal sepsis at neonatal intensive care unit at Minia University Hospitals. Egypt J Hosp Med.;89(2):6138–44

Seale AC, Blencowe H, Manu AA, Nair H, Bahl R, Qazi SA, Zaidi AK, Berkley JA, Cousens SN, Lawn JE., pSBI Investigator Group. (2014): Estimates of possible severe bacterial infection in neonates in sub-Saharan Africa, south Asia, and Latin America for 2012: a systematic review and meta-analysis. Lancet Infect Dis.;14(8):731-741

Tang Y.-H., Jeng M.-J., Wang H.-H., Tsao P.-C., Chen W.-Y., Lee Y.-S. (2022): Risk factors and predictive markers for early and late-onset neonatal bacteremic sepsis in preterm and term infants. J. Chin. Med. Assoc;85:507–513. doi: 10.1097/JCMA.0000000000000681.\

Van Anh TN, Kiem Hao T, Huu Hoang H (2020): The role of plasma lactate dehydrogenase testing in the prediction of severe conditions in newborn infants: a prospective study. Res Rep Neonatol.;10:31–35. doi:10.2147/RRN.S25450