Cord Thiobarbituric Acid Reactive Substances (TBARS) as a predictor for early onset sepsis in preterm

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إهداء

إلى والدي و والدتي حفظهما الله تعالى.

إلى زوجتي الغالية رفيقة الدرب و الحياة.

إلى شهداء الوطن من المدنيين و أفراد و ضباط القوات المسلحة.

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LIST OF ABBREVIATIONS

AUC	**:**	Area under the ROC curve
BPD	**:**	Bronchopulmonary dysplasia
CAT	**:**	Catalase
CBC	**:**	Complete blood picture
CI	**:**	confidence interval
CRP	**:**	C-reactive protein
DHA	**:**	Docosahexaenioc acid
DIC	**:**	Disseminated intravascular coagulation
EOS	**:**	Early onset sepsis
FFP	**:**	Fresh frozen plasma
GBS	**:**	Group B streptococci
GERD	**:**	Gastroesophageal Reflux disease
GTPx	**:**	Glutathione peroxidase
Hib	**:**	Haemophilus influenzae type b
HIE	**:**	Hypoxic-ischemic encephalopathy
HOCl	**:**	Hypochlorous acid
ICSI	**:**	Intra-cytoplasmic sperm injection
IL	**:**	Interleukin
IUGR	**:**	Intrauterine growth restriction
IVH	**:**	Intraventricular hemorrhage
LBW	**:**	low birth weight
LOS	**:**	late-onset sepsis
LPS	**:**	Lipopolysaccharides
MABP	**:**	Mean arterial blood pressure

MDA	**:**	Malondialdehyde
MPO	**:**	Myeloperoxidase
NEC	**:**	Necrotizing Enterocolitis
PDA	**:**	Patent ductusarteriosus
PRBCs	**:**	Packed red blood cells
PROM	**:**	Preterm rupture of membranes
PVL	**:**	Periventricular leukomalacia
RDS	**:**	Respiratory distress syndrome
RNS	**:**	Reactive nitrogen species
ROC	**:**	Receiver operating characteristic curve
ROP	**:**	Retinopathy of prematurity
ROS	**:**	Reactive oxygen species
SOD	**:**	Superoxide dismutase
TBARS	**:**	Thiobarbituric acid reactive species
TNF-alpha	**:**	Tumor necrosis factor alpha
VLBW	**:**	very low birth weight

ABSTRACT

Background:

Neonatal sepsis (NS) promotes unbalanced production of oxidant and anti-oxidant substances, causing excess of free oxygen radicals which may lead to tissue damage. NS carries high risk of morbidity and mortality, thus identification of biomarker to optimize early diagnosis and therapeutic interventions is highly desirable.

Objectives:

To detect cord blood thiobarbituric acid reactive substance (TBARS) in preterm neonates with maternal risk factor for sepsis as predictors of early onset neonatal sepsis (EOS).

Methodology:

Cord TBARS was measured in 80 preterm neonates with antenatal risk factors for EOS, and classified into two groups: sepsis (n=25) and no-sepsis (n=55).

Results:

TBARS was significantly higher in sepsis than no-sepsis groups 10.50 (6.5 □ 20.5) vs 3.00 (2.2 - 3.8) nmol/ml, (p=0.000). TBARS was significantly higher in culture proven sepsis than negative culture patients. TBARS was significantly higher in died neonates than survivors.

Conclusion:

Cord TBARS in preterm neonates with maternal risk factor for sepsis can be used as diagnostic and prognostic biomarker for EOS.

INTRODUCTION

Neonatal sepsis is a single most important cause of neonatal deaths worldwide, accounting for over half of them. If diagnosed early and treated aggressively it is possible to save most cases of neonatal sepsis **(Khinchi et al, 2010).**

Neonatal sepsis is defined as a clinical syndrome characterized by signs and symptoms of infection with or without accompanying bacteremia in the first month of life **(Sankar et al., 2008)**.

Neonatal sepsis can be classified into two sub-types depending upon whether the onset of symptoms is before 72 hours of life (early onset) or later (late onset). Surviving infants can have significant neurologic squeals as a consequence of central nervous system involvement, septic shock or hypoxemia secondary to severe parenchymal lung disease **(Baley and Goldfark, 2001).**

Early onset sepsis (EOS), with an onset during the first 72 hours of life is caused by organisms prevalent in the maternal genital tract or in the labour room and maternityoperation theatre. The Risk factors for EOS include prematurity, low birth weight, premature and prolonged rupture of membranes, maternal fever, uroinfection and chorioamnionitis **(Chacko and Sohi 2005).**

The incidence of EOS was 20.7 per 1000 live births and it constituted 55.4% of overall sepsis **(Baley and Goldfark, 2001).**

Early diagnosis and treatment are vital to improve outcomes. Preterm neonates developing infection commonly have nonspecific clinical symptoms, and in the absence of reliable infection markers during the first hours of life, pediatricians often start early antibiotic treatment in newborn infants with risk factors for infection, exposing a considerable number of patients to unnecessary treatment **(Santana et al., 2001).**

It is well known that during inflammatory response oxidative damage occurs, and it seems that this is relevant to sepsis development. Oxidative damage could modify all biomolecules including DNA, lipids, and proteins **(Krueger et al., 2001).**

The oxidized molecules could be measured in biological fluids, being protein carbonyls (as a marker of protein oxidation) and thiobarbituric acid reactive species (TBARS, as a marker of lipid oxidation), the most frequently oxidative stress markers measured in humans. These markers are present in animal models **(Døllner et al., 2001).**

Oxidizing agents can alter lipid structure, creating lipid peroxides that result in the formation of malondialdehyde (MDA), which can be measured as Thiobarbituric Acid Reactive