Research Article

Cord Blood Malondialdehyde Level in Newborns as Indicator of Oxidative Stress

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Abstract
Objective: Malondialdehyde (MDA) is one of the eminentderivatives of lipid peroxidation, and it can be used as amarker of cell membrane injury. The aim of this study was to assess the cord blood MDA level in newborn infants, as indicator of oxidative stress during the perinatal period. **Subjects and Methods**: This study was conducted on ٦٠ (٥٢ full term and ٨ preterm) newborns divided into ٣ groups including ٢٠ normal vaginal delivery (NVD), ٢٠ elective caesarean section (CS) and ٢٠ emergency CS in the delivery room and NICU of Dairout Hospital during the periodfrom May ٢٠١٢ to November ٢٠١٢. Cord blood samples were used to measure MDA levels by the thiobarbituric acid (TBA) colorimetric assayusing commercial kit (Biodiagnostics, Egypt, catalog No. ٠٠١- ٠٠٢). **Results:** There was insignificant difference between the groups regarding comparison of most demographic data and anthropometric measures. Though, there was significant difference between the groups as regards preterm birth (٣٠٪ in emergency CS versus ٢٪ and ٠٪ for vaginal delivery and elective CS respectively). There was significant difference between the groups regarding MDA level (p=٠.٠٠١)where higher MDA level was found in CS groups. Significant negative correlation between cord blood MDA level and gestational age, birth weight, head circumference, Apgar score at ٥ minutes and pO٢ level was detected in emergency CS group. As well, significant positive correlation was found between MDA level in the cord blood and uric acid in emergency CS group. **Conclusion:** Measurement of umbilical cordMDA level may have a role in the prophecy and/or treatment of anticipated oxidative stress and the resultant cellular destruction.

Keywords: Malondialdehyde (MDA), oxidative stress, perinatal hypoxia.

Introduction
Oxidative stress (OS) results from an imbalance between reducing agents and enzymes implicated in the elimination of free radicals (FRs) and/or reactive oxygen species (ROS). Antioxidant systems include enzymes such as superoxide dismutase, catalase and glutathione peroxidase, macro-molecules such as ceruloplasmin and ferritin and small molecules such as ascorbic acid, alpha-tocopherol, beta carotene and reduced glutathione[١]. The consequence of OS on fetal structure involves the activation of a complex array of genes involved in inflammation, coagulation, fibrinolysis, cell cycle and signal transduction [٢]. Moreover, it is now known that ROS are important for fertilization and developing [٣].

FRs may be generated by different mechanisms such as ischemia reperfusion, hypoxia, neutrophil and macrophage activation and free fatty acid and prosta-glandinmetabolism[٤]**.** In reasonablequantity and in existence of a good antioxidant capacity, FRs areconstantlyproduced and are crucial for cell metabolism and fetal growth. However, when overproduced they are toxic with an attack of all classes of biological macromolecules, polysac-charides, nucleic acid, lipids and proteins[٥]**.** FRs cause various diseases owing to their high capability to damage vital biological systems[٦]**.**

As oxidative stress plays an important role in the pathomechanism of the hypoxic ischemic damage to the tissues, oxidative stress markers are promising as pro-spectivepredictive and prognostic tools[٧]. The MDA level is a sensitive indicator of lipid peroxidation and hence of oxidative stress[٨]. The fetal tissues, which are adapted to a low oxygenation during intrauterine development, are subjected to a rapid change in oxygen-concentration after delivery. Birth itself is a strong oxidative stress. Oxidativestress, excess of free radicals and their reactive metabolites, play an important role in the pathogenesis of FRs diseases in both adults and neonates[٩]. The neonatal brain has a high concentration of unsaturated fatty acids, low molecular weight iron, high rate of oxygen consu-mption and low concentrations of antioxidants which make it sensitive to damage[١٠]. Lipid peroxidation (LPO) is implicated in the pathogenesis of a numberof diseases and clinical conditions[١١]. Quantification of primary lipid peroxidation products isdifficult due to their unstable nature. Thus, theassessment of lipid peroxidation is usually performed by analyzing secondaryoxidation products such as MDA[١٢].MDA is one of the well-known secondary products oflipid peroxidation and it can be used as an indicator of cell injury[١٣].

The aim of this study was to assess the cord blood Malondialdehyde (MDA) level in newborn infants, as indicator of oxidative stress during the perinatal period and its relation to some mother and newborn-related factors.

Subjects and Methods

Subjects:

This study was performed in Dairout Hospital during the period from May ٢٠١٢ to November ٢٠١٢. It was conducted on ٢٠ newborns born via elective CS, ٢٠ newborns born via emergency CS, and ٢٠ newborns born via NVD. Neonates delivered from pregnant women with diabetes mellitus, pregnant women with hypertension, mothers with chronic diseasesincluding renal diseases, hyper-cholesterolemia, liver diseases, asthma and thyroid disorders were excluded from this study. Moreover, neonates with congenital anomalies, neonates with perinatal problems such as hypoglycemia and newborns with umbilical cord abnormalities were excluded as well. All neonates were subjected to careful prenatal, natal and post natal history takingalong with thorough clinical examination.

Samples:

Umbilical cord blood samples were taken after delivery in the delivery room. The blood was drawn into ٣ tubes. About ٢ ml of blood was drawn in EDTA tube for CBC assessment, ١ ml heparinized blood for detection of blood gases and ٢ ml of blood in one empty tube for determination of other serum laboratory parameters including MDA. Serum was separated, collected and stored at -٧٠^{o}C after measurement of serum bilirubin, glucose level and serum uric acid immediately. No special treatment was required to this serum.This stored serum was later used forevaluating MDA cord blood levels.

Complete blood picture (CBC) was evaluated by automated blood counter (Electronic counter Sysmex KX-٢١N). As well, serum bilirubin, glucose level and serum uric acid were analyzed using automated biochemistry analyzer (Mindray BS-٨٠٠). Moreover, blood gases were measured to all subjects using (Radiometer ABL٨٠٠ BASIC).

Malondialdehyde level:

Malondialdehyde levels were measured by the thiobarbituric acid reactive substances (TBARS) colorimetric assay, by using commercial kit from Biodiagnostics Company, Egypt, with catalog No. ٠٠١-٠٠٢ according to the manufacture instructions. The MDA-thiobarbituric (TBA) reaction depends on the formation of a pink colored complex between MDA as the stable end-product of lipid peroxidation with TBA, which have a proportional maximum absorption at ٥٣٢ nm (٥٣٠-٥٤٠nm)[١٤,١٥].

Statistical Analysis:

The results were presented as mean ± standard deviation (SD). The significance

of the mean difference between groups was assayed by the student *t*-test and was correlated by using Pearson correlation coefficient.p-value equal or less than ٠.٠٥ is statistically significant. Qualitative data were presented as percent (%). Results were expressed as tables and figures. Graphs were done by Excel Microsoft Office ٢٠١٠.

Results

In our study, ٣٤(٥٦.٧٪) of the ٦٠ total newborns were females, ٢٦(٤٣.٣٪) were males and ٥٢(٨٦.٧٪) werefull term infants. Meconium within amniotic fluid was recorded in ٢(٣.٣٪) newborns delivered by CS. There was insignificant difference regarding length, weight, mid arm circumference or ponderal index in the three groups included in the study, but there was significant difference between the groups as regard Apgar score at ٥ min., gestational age and head circumference with p=٠.٠٥; ٠.٠١ and <٠.٠٠١ respectively (Table ١). The cord blood level of MDA was significantly higher in CS groups than in NVD group with p=<٠.٠٠١(Table ٢). There was insignificant correlation between MDA level and mother age, baby length or sex in the studied groups; but there was significant negative correlation between cord blood MDA and gestational age, head circumference, weight, ponderal index and Apgar score at ٥ min in emergency CS group(p=<٠.٠٥) (Table ٣). There was a positive significant correlation between cord blood total bilirubin level and MDA in NVG group(r=٠.٨١, p=<٠.٠٠١) (Table ٤). Additionally, strong negative significant correlations between cord blood hematocrate HCT (r=-٠.٩٣, p=<٠.٠٠١), hemoglobin (Hb) (r=-٠.٨٣, p=<٠.٠٠١) as well as pO٢ (r=-٠.٧١, p=<٠.٠٠١) and MDA in emergency CS group are demonstrated. Also a significant positive correlation between cord blood uric acid and MDA level in emergency CS group was observed (r=٠.٨٩, p=<٠.٠٠١)(Table ٤).

Discussion

The role of OS in various pathological processes is until now a subject of research[٨]. Yet, therelation between insufficient newborn's antioxidant defense system and newborn pathologies is the mostimportant[١٦]. Thus, it is important to explore and investigate diverse markers of OS. An increase of MDA level as a marker of OS has been investigated in a variety of pathological conditions[١٧]. Regarding MDA values, we assessed MDA in the cord blood as a marker of lipid peroxidation. It was taken immediately after birth. The means of MDA levels in emergency and elective CS groups was ٣.٣٥±٠.٦ nmol/ml and ١.٥±٠.٥ nmol/ml respectively. It was found to be significantly higher compared to that in NVD group (١.١±٠.٤nmol/ml) (P<٠.٠٠١). That may be due to an increasein theoxygen saturation of the umbilical cord blood in these conditions. These findings are in agreement with those of Kumar et al., ٢٠٠٨ and Kirimi E et al., ٢٠١٠[١٨,١٩]. But, these finding are in disagreement with those of Mocatta et al., ٢٠٠٤ and Gulbayzar et al., ٢٠١١[٢٠,٨] who found that cord blood MDA levels in babies delivered via elective CS were lower compared to those of babies born via NVD. It was asserted that this divergence between different studies was due to the different CS indications[٢١].

When we studied the effect of sex of baby on cord blood MDA levels, we found insignificant difference in their values in males compared to females (P > ٠.٠٥). These findings are in disagreement with Parmigiani et al., ٢٠٠٠[٢٢] who found that female infants had significantly lower mean value of MDA than the male infants. In the emergency CS group, the MDA level was found to besignificantly high in newborns with a low ponderal index. So, it mayserve as an indicator of intrauterine growthretardation.

A highly negative correlation was detected between MDA levels of the cord blood and both gestational age and weight of the baby in the NVD group. Thus, in newborns with low gestational age and low weight, the MDA level was found to be significantly higher. These findings are in agreement with those of Buonocore et al., ١٩٩٨[٢٣]who reported a highly significant negative correlations between MDA levels in the cord blood and birth weight (P = ٠.٠٠٠١).But, these findings are in disagreement with those of Winterbourn et al., ٢٠٠٠[٢٤]who reported that there was no significant correlation between

blood MDA and birth weight.A highly negative correlation was detected between head circumference and MDA levels of cord blood in the NVD group. Therefore, in newborns with a small head circumference, the MDA level was found to be significantly higher.

In the emergency CS group, the MDA level in the cord blood was found to be significantly higher in babies with low Hb and HCT values. These finding are in agreement with those of Sayat Gülbayzar et al., ٢٠١١[٨]. It could be thought that anemia accompanies many pathological processes of the newborn and affects prognosis negatively. This fact may be revealed through increasing MDA levels as an indicator of oxidative stress.

In the current study, a negative correlation was determined between cord blood pO^2 value and MDA level in the emergency CS group (r=-٠.٧١, p<٠.٠٠١). Accordingly, newborns with a low pO^2 level had significantly higher levels of MDA.These finding are in disagreement with those of SayatGülbayzar et al.,٢٠١١[٨]who determined a positive correlation between cord blood pO^2 value and MDA level in the emergency CS group.

Concerning the cord blood total bilirubin, in the NVD group, a positive correlation was determined between the cord blood total bilirubin level and the MDA level (r=٠.٨٣, p=٠.٠٠١). In newborns with a high total bilirubin level, the MDA level was found to be significantly high. These findings also are in accordance with those of SayatGülbayzar et al., ٢٠١١ and Yigit et al., ١٩٩٩[٨,٢٥]. Bilirubin is an effective scavenger of oxidant radicals. Known as an antioxidant, bilirubin increases in case of oxidative stress.

In our study, the MDA level of newborns in the emergency CS group was found to be statistically and significantly higher with a high level of uric acid in the cord blood.These findings also are in agreement with those of SayatGülbayzar et al.,٢٠١١[٨]who found a higher MDA levels with higher uric acid levels. Despite the damage that may be caused by oxidative stress in newborns delivered via emergency CS, it may be true that uric acid levels increase as a defense mechanism.

In conclusion, the higher MDA levels in the cord blood of newborns delivered by emergency CS than those born by NVD may indicate that CS represents an oxidative stress. Accordingly, measurement of cord blood MDA level may play a role in the prediction and consequently management of expected oxidative stress and its subsequent cellular damage.

TABLES

Table (١): Comparison between NVD,elective CS & emergency CS groups as regards demographic data and anthropometricmeasures

	NVD N=٢٠	Elective CS N=٢٠	Emergency CS N=٢٠	
	Mean±SD	Mean±SD	Mean±SD	p value
Gestational Age(week)	٣٤.٤±١.٠٤	٣٨.٤٥±٠.٧	٣٧.٣٥±١.٦	٠.٠١*
Weight (kg)	٣.٢±١.٢	٣.٠٥±٠.٣	٢.٧±٠.٥	٠.١٩
Length (cm)	٤٩.٠٣±٠.٩	٤٨.٦±١.٠٣	٤٨.٣±١.٣	٠.١١
Head circumference (cm)	٣١.٧±١.٨	٣٣.٩±١.٥	٣١.٥±٢.١	<٠.٠٠١*
Mid arm circumference (cm)	١١.٩±٠.٩	١٢.٣±٠.٩	١٢.٣±٠.٧	٠.٢٨
Ponderal index	٢.٤±٠.٣	٢.٧±٠.٣	٢.٤±٠.٤	٠.٠٩
Apgar ٥ minute	٨.٣٥±٠.٨	٩.١±٠.٦	٨.٢٥±٠.٨	٠.٠٥*

*Significant difference

Table (٢): Comparison between NVD,elective & emergency CS groups as regards laboratory data

	NVD N=٢٠	Elective CS N=٢٠	Emergency CS N=٢٠	
	Mean±SD	Mean±SD	Mean±SD	p value
MDA (nmol/ml)	١.١±٠.٤	١.٤±٠.٥	٣.٣٥±٠.٦	<٠.٠٠١*
Uric acid(mg/dl)	٣.٣±٠.٤	٣.٥±٠.٨	٣.٩±٠.٩	٠.٠١*
Glucose level(mg/dl)	٨٢.٦±١٣.١	٨٦.٢±١٦.٢	٨١.٠٥±١٤.٤	٠.٥
Total bilirubin(mg/dl)	٠.٩±٠.٣	٠.٩٨±٠.٤	١.١±٠.٢	٠.٠٥*
HCT %	٤٣.٦±٢.٨	٤٤.٥±٢.٨	٤١.٧±٢.٤	٠.٠٠٥*
Hb(gm/dl)	١٤.٧±٠.٩٩	١٤.٨٥±٠.٨	١٣.٩٩±١.١	٠.٠١*
pO٢ (mmHg)	٢٢.٣٠±٥.٥٥	٣٩.٦٠±١.٤٥	٣٤.٤٧±١٧.٣٥	<٠.٠٠١*
pCO٢(mmHg)	٤٠.٥٥±٣.١	٣٥.٤٥±٤.٦	٣٥.٥±٣.٤	<٠.٠٠١*
HCO٣ (mmHg)	٢٠.٤±١.٧	٢٣.٥±١.٩	١٩.٤٥±١.٤	<٠.٠٠١*
PH	٧.٣±٠.١	٧.٤±٠.٠٣	٧.٣±٠.٢	٠.١

*Significant difference

Table (٣): Correlation between cord blood malondialdehyde level and findings in newborns

Malondialdehyde	NVD N=٢٠		Elective CS N=٢٠		Emergency CS N=٢٠	
	r	p	r	p	r	p
Gestational age (week)	-٠.١٦	٠.٥	٠.٤٣	٠.٠٦	-٠.٥٣	٠.٠٢*
Mother age (year)	-٠.١٩	٠.٤	-٠.١٧	٠.٥	٠.١٠	٠.٧
Weight gain during pregnancy (kg)	٠.٠٤	٠.٩	-٠.١٥	٠.٥	-٠.٥٠	٠.٠٣*
Sex	٠.٢٠	٠.٣	-٠.٠٣	٠.٩	٠.٢٤	٠.٢
Weight (kg)	٠.٠٤	٠.٨	٠.١٨	٠.٤	-٠.٧٧	<٠.٠٠١*
length (cm)	-٠.١٣	٠.٦	-٠.١٠	٠.٧	٠.١٤	٠.٥
Head circumference (cm)	-٠.٧٩	<٠.٠٠١*	٠.٠٩	٠.٧	-٠.٤٨	٠.٠٣*
Mid arm circumference (cm)	-٠.٠٩	٠.٧	٠.٥٠	٠.٠٢*	-٠.٢٧	٠.٢
Ponderal index	-٠.٤٠	٠.٠٧	٠.٢٣	٠.٣	-٠.٨٨	<٠.٠٠١*
UPGAR ٥ minute	٠.١٠	٠.٧	-٠.١٦	٠.٥	-٠.٥٤	٠.٠١

*Significant difference

Table (٤): Correlation between cord blood malondialdehyde level and laboratory data in newborns

Malondialdehyde	NVD N=٢٠		Elective CS N=٢٠		Emergency CS N=٢٠	
	r	p	r	p	r	p
Uric acid (mg /dl)	-٠.٥٣	٠.٨	٠.٠٩	٠.٧	٠.٨٩	<٠.٠٠١*
Glucose level (mg /dl)	-٠.٢٤	٠.٣	٠.٣٠	٠.٢	-٠.٢٣	٠.٣
Total bilirubine (mg /dl)	٠.٨١	<٠.٠٠١ *	٠.٠٣	٠.٩	-٠.١٥	٠.٥
HCT %	-٠.٤١	٠.٠٧	-٠.١٢	٠.٦	-٠.٩٣	<٠.٠٠١*
Hb (gm/dl)	-٠.٣٥	٠.١	٠.١٩	٠.٤	-٠.٨٣	<٠.٠٠١*
pO٢ (mmHg)	-٠.٤٦	٠.٠٦	-٠.٣٦	٠.١	-٠.٧١	<٠.٠٠١*
pCO٢ (mmHg)	٠.١٧	٠.٥	٠.٠٤	٠.٩	٠.١٧	٠.٥
HCO٣ (mmHg)	-٠.١٥	٠.٥	-٠.٣٧	٠.١	٠.٣٨	٠.١
PH	-٠.٥٥	٠.٠١*	-٠.٠٦	٠.٨	-٠.٢٦	٠.٣

*Significant difference

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