

## Malondialdehyde Level in the Cord Blood of Newborn Infants

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### Abstract

**Objective:** In this study, we aim to demonstrate that measurement of the malondialdehyde (MDA) level in the umbilical cord blood of newborn infants born via cesarean section (C/S) and normal vaginal delivery (NVD) is indicative of oxidative stress during the perinatal period.

**Methods:** The study was conducted at Bakirkoy Training and Research Hospital between January 2006 and April 2006 on 15 newborns born via elective C/S, 15 newborns born via emergency C/S, and 15 newborns born via normal vaginal delivery. Complete blood count, total bilirubin, glucose, creatinine phosphokinase (CPK), uric acid, iron, blood gas, and malondialdehyde levels were measured in the umbilical cord blood

**Findings:** Malondialdehyde levels in the umbilical cord blood in the emergency C/S and NVD groups were found to be statistically and significantly higher than those in the elective C/S group. In the emergency C/S group, it was determined that the malondialdehyde level increased as the oxygen saturation of the umbilical cord blood increased. In the NVD group, a positive correlation was detected between the total bilirubin and malondialdehyde levels in the umbilical cord blood. In the emergency C/S group, the malondialdehyde level was recorded to be high in the infants with high level of uric acid in the umbilical cord blood.

**Conclusion:** We concluded that the malondialdehyde level in umbilical cord blood could serve as an indication of perinatal oxidative stress and that it could thus help in preventing permanent damage.

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**Key Words:** Malondialdehyde; Oxidative Stress; Newborn; Cord Blood; Cesarean Section

### Introduction

Oxidative stress occurs during many pathological processes in an organism. Free oxygen radicals are

neutralized by the antioxidant system and a balance is maintained.

When this balance is impaired, however, tissue damage may result. It is known that increasing

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free oxygen radicals in newborns damages the cell membrane by way of lipid peroxidation, and this damage may be associated with various pathologies recorded in newborns, such as hypoxic-ischemic encephalopathy, intraventricular hemorrhage, necrotizing enterocolitis, and bronchopulmonary dysplasia [1,2].

Malondialdehyde (MDA) is one of the fairly reactive metabolic products resulting from the effect of free oxygen radicals on tissues and from a series of reactions during lipid peroxidation [2]. The plasma MDA level is a sensitive indicator of lipid peroxidation and thus of oxidative stress [1,3]. The perinatal period is a significant period which affects the rest of the newborn's life. Although the relation between mother-related factors (the presence of systemic diseases such as preeclampsia, and hypertension), birth-related factors (low gestational age, low Apgar score, presence of hypoxic-ischemic encephalopathy, etc.), and exposure of newborns to oxidative stress has been discussed in previous studies, there is an insufficient number of studies that have been conducted on this issue [4].

This study, aims to investigate the relationship between MDA levels and mother-related, and newborn-related factors, which may affect these levels. It also measures complete blood count, blood gas, and biochemical values in the umbilical cord blood of newborn infants born via cesarean section (C/S) and normal vaginal delivery (NVD).

We assume that the MDA level in cord blood is anterogradely significant as an indicator of oxidative stress during perinatal period.

## Subjects and Methods

This study was conducted on 15 newborns born via elective C/S, 15 newborns born via emergency C/S, and 15 newborns born via normal vaginal delivery at Bakirkoy Training and Research Hospital, Turkey which has a high birth rate.

In all cases, the following maternal factors were ascertained in the prenatal history: age, height, weight, number of pregnancies, weight gained during pregnancy, number of control examinations undergone during pregnancy, socioeconomic status, whether or not she smoked,

the presence of a systemic disease, and number and order of brothers and sisters. The following paternal factors were also ascertained: age, educational background, and occupation. In the natal history, the following factors were measured: mode of delivery, gestational age, weight at birth, height and head circumference at birth, Apgar score, the presence of meconium within the amniotic fluid, upper arm circumference, and CANS (Clinical Assessment of Nutritional Status) score. The ponderal index was also calculated. Immediately after delivery, blood was acquired from the umbilical cord remained at the side of placenta for the study. All information on the forms was prepared.

Pregnant women with diabetes mellitus, hypertension, chronic diseases, those who did not want to be included in the study, were excluded. In infants with congenital anomalies, newborns with umbilical cord abnormalities, were excluded.

Immediately after birth, the umbilical cord study for citrate tube 2 ml, complete blood count tube of 2 ml, heparinized blood was drawn into the tube of 1 ml. For MDA, citrated blood plasma from the tube separated. The MDA was, stored at -70 degrees. The MDA levels were determined spectrophotometrically at the Istanbul University Cardiology Institute of Biochemistry Lab.

Before starting the study, we received hospital ethics committee approval (dated 04/06/2005, number 2005/11).

"SPSS for Windows 10.0", Anova, Tukeys' b, and Cruscal Wallis tests were used for the comparison of data. Correlation analyses were performed by Pearson.

## Findings

In our study, of the 45 total newborns, 20 (44, 4%) were female, and 25 (55, 6%) were male. 41 (91, 2%) were term, and 4 (8, 8%) were preterm; 41 (91, 2%) were AGA (Appropriate for Gestational Age), 2 (4, 4%) were SGA (Small for Gestational Age), and 2 (4, 4%) were LGA (Large for Gestational Age). Meconium within the amniotic fluid was recorded in 3 (6.6%) newborns. Of the 4 preterm babies, 2 were born via emergency C/S and 2 were born via elective C/S (maternal

**Table 1:** Characteristics of newborns

Parameters	NVD group No (%)	Elective cesarean group No (%)	Emergency cesarean group No (%)	Total No (%)
<b>Gender</b>				
Female	7 (46.7)	6 (40)	7 (46.7)	20 (44.4)
Male	8 (53.3)	9 (60)	8 (53.3)	25 (55.6)
<b>Birth Time</b>				
Term	15 (100)	13 (86.7)	13 (86.7)	41 (91.2)
Preterm	---	2 (16.3)	2 (13.3)	4 (8.8)
<b>Type</b>				
AGA	15 (100)	15 (100)	11 (73.3)	41 (91.2)
LGA	--	--	2 (13.3)	2 (13.3)
SGA	--	--	2 (13.3)	2 (13.3)
<b>Meconium</b>				
N/A	15 (100)	15 (100)	12 (80)	41 (93.4)
Available	--	--	3 (20)	3 (6.6)

AGA: Appropriate for Gestational Age/ SGA: Small for Gestational Age/ LGA: Large for Gestational Age/  
NVD: Normal Vaginal Delivery

request, due to a history of prenatal death). The SGA and LGA babies and all of the babies who had meconium within the amniotic fluid were delivered via emergency C/S (Table 1).

No statistically significant difference could be found between the NVD, elective C/S, and emergency C/S group in terms of mother's age, years of education, height, weight prior to pregnancy, weight after pregnancy, weight gained during pregnancy, control examinations undergone during pregnancy, systolic arterial pressure during pregnancy, or diastolic arterial pressure (Table 2).

The mean pregnancy week in the group born via normal vaginal delivery ( $40.13 \pm 0.35$  week) was found to be statistically and significantly higher than that of the elective cesarean group

( $38.80 \pm 1.26$  week) ( $P < 0.05$ ). No statistically significant difference was recorded compared to the elective cesarean group ( $39.60 \pm 1.45$  week) ( $P > 0.05$ ).

No statistically significant difference could be found between the groups regarding the baby's birth weight ( $3227,33 \pm 263,67$ g,  $3177,33 \pm 352,08$ g,  $3187,33 \pm 624,65$ g;  $P > 0.05$ ), birth height ( $49.00 \pm 1.25$ cm,  $48.73 \pm 1.98$ cm,  $50.27 \pm 2.52$ cm;  $P > 0.05$ ), head circumference ( $34.47 \pm 1.13$ cm,  $34.47 \pm 1.20$ cm,  $35.43 \pm 1.41$ cm;  $P > 0.05$ ), arm circumference at birth ( $10.43 \pm 0.7$ cm,  $10.10 \pm 0.54$ cm,  $10.53 \pm 1.37$ cm;  $P > 0.05$ ), ponderal index ( $2.74 \pm 0.22$ ,  $2.74 \pm 0.18$ ,  $2.65 \pm 0.26$ ;  $P > 0.05$ ), or CANS score ( $26.33 \pm 1.35$ ,  $26.67 \pm 1.45$ ,  $26.13 \pm 2.72$ ;  $P > 0.05$ ).

No statistically significant difference could be

**Table 2:** Relationship between mode of delivery and mother-related information

Mother Parameters	NVD group Mean (SD)	Elective cesarean group Mean (SD)	Emergency cesarean group Mean (SD)	P- value
Age of the mother (year)	24.60 (5.51)	28.27 (4.45)	27.93 (5.83)	>0.05
Educational background (year)	5.33 (2.82)	6.13 (3.56)	5.60 (3.74)	>0.05
Weight gained at pregnancy (kg)	12.85 (5.24)	13.77 (3.06)	13.60 (4.97)	>0.05
Number of control examinations undergone during pregnancy	4.60 (2.90)	6.40 (2.75)	5.73 (2.96)	>0.05

NVD: Normal Vaginal Delivery / SD: Standard Deviation

found between the groups regarding Apgar score at the first minute ( $6.27 \pm 0.88$ ,  $6.87 \pm 0.92$ ,  $6.00 \pm 1.65$ ;  $P > 0.05$ ) or Apgar score at the fifth minute ( $8.93 \pm 0.26$ ,  $8.93 \pm 0.26$ ,  $8.60 \pm 0.51$ ;  $P > 0.05$ ).

The mean  $pO_2$  in the group born via emergency cesarean section ( $34.47 \pm 17.35$  mmHg) was determined to be statistically and significantly higher compared to that of the NVD group ( $22.30 \pm 5.55$  mmHg,  $P = 0.04$ ), whereas no statistically significant difference could be found when compared to that of the elective cesarean section group ( $39.60 \pm 1.45$ ,  $P > 0.05$ ). The mean  $HCO_3^-$  ( $24.82 \pm 3.04$  mmHg) and mean BE, ( $-0.71 \pm 2.53$  mmHg), in the group born via elective cesarean section were found to be statistically and significantly higher compared to those of the NVD ( $20.04 \pm 2.99$  mmHg,  $-3.71 \pm 3.15$  mmHg;  $P < 0.05$ ) and emergency cesarean section groups ( $20.78 \pm 3.50$  mmHg,  $-4.39 \pm 3.55$  mmHg;  $P < 0.000$ ). No statistically significant difference could be found between the groups regarding cord blood pH ( $7.31 \pm 0.14$ ,  $7.34 \pm 0.05$ ,  $7.34 \pm 0.09$ ) or  $pCO_2$  ( $22.30 \pm 5.55$  mmHg,  $47.82 \pm 9.98$  mmHg,  $40.69 \pm 10.43$  mmHg) values, ( $P = 0.2$ ).

No statistically significant difference could be found between the groups regarding cord blood glucose ( $74.20 \pm 24.19$  mg/dl,  $71.93 \pm 28.33$  mg/dl,  $85.13 \pm 53.42$  mg/dl), uric acid ( $3.62 \pm 1.11$  mg/dl,  $2.92 \pm 0.84$  mg/dl,  $17.3 \pm 51.12$  mg/dl), total bilirubin ( $1.92 \pm 0.54$  mg/dl,  $1.50 \pm 0.95$  mg/dl,  $1.52 \pm 0.65$  mg/dl), iron ( $130.80 \pm 47.08$  mg,  $153.13 \pm 29.68$  mg,  $122.53 \pm 44.01$  mg), or creatinine phosphokinase (CPK) ( $244.67 \pm 131.75$  U/L,  $211.27 \pm 107.74$  U/L,  $245.87 \pm 186.95$  U/L), values ( $P > 0.05$ ).

Mean MDA values in cord blood in the NVD and emergency cesarean section groups ( $2.03 \pm 0.42$

nmol/ml,  $2.21 \pm 0.95$  nmol/ml, respectively) were found to be statistically and significantly higher compared to that in the elective cesarean group ( $0.92 \pm 0.29$  nmol/ml,  $P < 0.001$ ).

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

No statistically significant correlation was identified between head circumference and MDA levels of cord blood in the elective cesarean section or emergency cesarean section groups (Table 3).

A negative correlation was detected between the ponderal index and the MDA level of the cord blood in the emergency cesarean section group. In newborns with a low ponderal index, the MDA level was found to be statistically and significantly higher. No statistically significant correlation was identified between ponderal index and MDA level of cord blood in the NVD and elective cesarean groups (Table 3).

In the NVD, elective C/S, and emergency C/S groups, no statistically significant correlation was determined between cord blood MDA level and pregnancy week, birth weight, birth height or arm circumference at birth (Table 3).

In the NVD, elective C/S, and emergency C/S groups no statistically significant correlation was detected between cord blood MDA level and Apgar score at the first minute ( $r = -0.03$ ,  $P = 0.9$ ;  $r = 0.12$ ,  $P = 0.6$ ;  $r = -0.010$ ,  $P = 1$ ) and Apgar score at the fifth minute ( $r = -0.37$ ,  $P = 0.2$ ;  $r = 0.18$ ,  $P = 0.5$ ;  $r = -0.107$ ,  $P = 0.7$ ), respectively.

A positive correlation was determined between cord blood  $pO_2$  value and MDA level in the

**Table 3:** Correlation between cord blood malondialdehyde level and findings in newborns

Malondialdehyde	NVD		Elective cesarean		Emergency cesarean	
	r	p	r	p	R	p
Pregnancy week	0.03	0.9	0.22	0.4	-0.68	0.8
Birth weight	-0.35	0.2	0.22	0.4	-0.01	1
Birth height	-0.46	0.1	0.06	0.8	0.27	0.4
Head circumference at birth	-0.63	0.02	0.21	0.4	-0.18	0.5
Arm circumference	-0.51	0.06	0.29	0.3	0.05	0.86
Ponderal Index	0.09	0.8	0.23	0.4	-0.55	0.05

NVD: Normal Vaginal Delivery

emergency cesarean section group ( $r=0.65$ ,  $P=0.02$ ). In newborns with a high  $pO_2$  level, the MDA level was found to be statistically and significantly higher.

In the NVD, elective C/S and emergency C/S groups, no statistically significant correlation was determined between cord blood MDA level and cord blood pH ( $r=0.30$ ,  $P=0.3$ ;  $r=0.13$ ,  $P=0.6$ ;  $r=0.51$ ,  $P=0.07$ ),  $PCO_2$  ( $r=-0.16$ ,  $P=0.5$ ;  $r=0.18$ ,  $P=0.5$ ;  $r=-0.48$ ,  $P=0.1$ ),  $HCO_3$  ( $r=0.16$ ,  $P=0.2$ ;  $r=0.49$ ,  $P=0.6$ ;  $r=-0.13$ ,  $P=0.7$ ) or BE ( $r=-0.05$ ,  $P=0.9$ ;  $r=-0.20$ ,  $P=0.5$ ;  $r=-0.83$ ,  $P=0.8$ ) values, respectively.

In the emergency cesarean section group, a negative correlation was determined between the cord blood hemoglobin (Hb) and hematocrit (Hct) levels and the MDA level, respectively ( $r=0.79$ ,  $P=0.001$ ;  $r=-0.76$ ,  $P=0.002$ ). In newborns with low Hb and Hct levels, the MDA level was found to be statistically and significantly higher.

In the NVD group, a positive correlation was determined between the cord blood total bilirubin level and the MDA level ( $r=0.59$ ,  $P=0.03$ ). In newborns with a high total bilirubin level, the MDA level was found to be statistically and significantly higher.

In the elective cesarean section group, a positive correlation was determined between the cord blood CPK level and the MDA level ( $r=0.53$ ,  $P=0.04$ ). In newborns with a high CPK level, the MDA level was found to be statistically and significantly higher.

A positive correlation was determined between the cord blood uric acid level and the MDA level in the emergency cesarean section group ( $r=0.71$ ,  $P=0.006$ ). In newborns with a high level of uric acid, the MDA level was found to be statistically and significantly higher.

## Discussion

The role of oxidative stress in various significant pathological processes has recently become a subject of research. An increase of MDA as an indicator of oxidative stress has been researched in various pathological contexts both in adults and children [5]. However, the fact that newborn's antioxidant defense system could be insufficient

makes the relationship between damage due to oxidative stress and newborn pathologies more important [2].

With the determination of MDA level as one of the biochemical parameters of this stress, oxidative stress damage that might occur in the organism could be graded, albeit partially.

In the emergency C/S group, the MDA level was found to be statistically and significantly high in newborns with a low ponderal index; thus, it may serve as an indicator of intrauterine growth retardation. On the other hand, in the emergency C/S group, the MDA level was found to be statistically and significantly higher in babies with low Hb and Hct values in the cord blood. There are no studies in the literature on this subject, so this study will surely contribute in this regard. Accordingly, 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 their study, Macotta et al [7] found that cord blood MDA levels in babies delivered via elective cesarean section were lower compared to those of babies born via normal vaginal delivery. Yigit et al [8] also determined that cord blood MDA levels in babies born via spontaneous vaginal delivery were higher compared to those of babies born via cesarean section. However, in another study, the role of perinatal distress on the production of oxygen radicals and on lipid peroxidation was demonstrated by an increased MDA level, regardless of gestational age, in babies delivered via cesarean section compared to babies born via spontaneous vaginal delivery [1].

In another study, it was shown that the MDA level in cord blood was increased in babies delivered via cesarean section compared to that of babies born via spontaneous vaginal delivery.

It was asserted that this divergence from previous studies was due to the different cesarean indications of the cases [4]. In our study, mean cord blood MDA levels in the NVD and emergency C/S groups were found to be statistically and significantly higher compared to that of the elective C/S group.

In their study, Kaya et al [9] evaluated the presence of oxidative stress in babies with presentation abnormality, compared cord blood

MDA level and blood gas, and found that MDA level was a more sensitive indicator than blood gas. In another study, Casey et al [10] attempted to reveal the status of the factors in the perinatal period and cord blood MDA level. The Apgar score was used to assess the physical condition of the newborn immediately after delivery. Buonocare et al [1] found a significant reverse correlation between Apgar score and cord blood MDA level. However, Yigit et al [8] identified no correlation between plasma MDA level at the first hour and Apgar score. Bilgili et al [5] determined that the cord blood MDA level was higher in cases where the Apgar scores at the first and fifth minutes were lower than 7. In their study, it was indicated that, in evaluating oxidative stress, the determination of MDA in the cord blood was more significant than determining MDA in the plasma at the first hour [4]. In our study, in all three groups, no statistically significant correlation was determined between Apgar scores at the first and fifth minutes and cord blood MDA level. These differences between studies may be associated with the limitations of the Apgar score in predicting birth asphyxia and neurological morbidity [11,12].

In our study, the mean oxygen saturation in the cord blood of the group delivered via emergency C/S was statistically and significantly higher compared to that of the NVD group, and it was determined that, in the emergency C/S group, the MDA level increased as oxygen saturation increased. Accordingly, it may be concluded that the exposure of a newborn, which remains under stress as during an emergency C/S, to oxidative stress may increase through the activation of mechanisms allowing increased oxygen saturation.

There have been various studies conducted to help reduce perinatal stress. In their study, Singh et al [13] indicated that during the antenatal period, Phenobarbital administered within the first six hours to term or near-term babies who had hypoxic-ischemic encephalopathy decreased plasma MDA levels. Bolisetty et al [14] demonstrated that the short-term usage of multiple antioxidants by preterm pregnant women reduced the oxidative stress of the mother and baby at delivery. It has long been known that biliary pigments and biliverdin prevent cell membranes from experiencing lipid peroxidation

[14,15]. Bilirubin is an effective scavenger of oxidant radicals. Known as an antioxidant, bilirubin increases in case of oxidative stress. Yigit et al [16] found MDA concentrations in infants with hyperbilirubinemia to be remarkably high. This fact was seen as the response of babies to oxidative stress. As a result of Yigit et al study, the presence of a complex interaction between bilirubin and the level of MDA was emphasized. It was asserted that hyperbilirubinemia in newborns might play a defensive role against oxidative stress because the antioxidant mechanisms are not fully developed [16]. In our study, a positive correlation between the cord blood total bilirubin level and the MDA level was identified in the NVD group. The MDA level was found to be statistically and significantly higher in newborns with a high total bilirubin level.

In their study, Schrod et al [17] determined that among newborns with a gestational age between 22-42 weeks, the uric acid levels in the group with a cord blood pH level below 7 were lower compared to that of the other group with no severe acidosis. It is thought that uric acid is the protective antioxidant of the mucosa, preserving the respiratory tracts of newborns in the initial weeks of life [17]. In our study, the MDA level of infants in the emergency C/S group was found to be statistically and significantly higher in newborns with a high level of uric acid in the cord blood. We did not evaluate the uric acid/MDA ratio. Despite the damage that may be caused by oxidative stress in newborns delivered via emergency C/S, it may be true that uric acid levels increase as a defense mechanism.

If there are elective conditions at birth, oxidative stress is less. If there are emergency conditions at birth, it is higher. Thus, emergency births increase both risks and complications.

## Conclusion

We think that the MDA level in umbilical cord blood is an important indicator of perinatal oxidative stress. Thus, determining the MDA level in cord blood will aid us in the prevention and treatment of permanent damage that may occur.



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**Conflict of Interest:** The authors declare that they have no competing interests.

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