

Comparison of Thiol/Disulfide Balance in Elective and Emergency Cesarean Sections: A Prospective, Observational Study

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ABSTRACT Objective: The initial development of the fetus occurs in a low-oxygen environment. From the beginning of the second trimester, a high amount of oxygen is required to meet the growth requirements such that placenta becomes metabolically active. Under these conditions, oxidative stress (OS) can develop during pregnancy and may result in disorders such as miscarriage and preeclampsia. Although several methods have been used to examine the OS levels of mother and fetus, the current method is based on assessing the thiol/disulfide balance. In the present study, we investigated the thiol/disulfide balance in pregnant women undergoing emergent and elective cesarean sections (CS). **Material and Methods:** A total of 166 pregnant women, 83 in the emergency CS group and 83 in the elective CS group, were included in this observational study. We measured the disulfide, native thiol, and total thiol levels in blood samples collected from the umbilical artery of cords during CS. **Results:** The native thiol/total thiol ratio was significantly higher and native thiol, total thiol, disulfide, disulfide/native thiol ratio, and disulfide/total thiol ratio were lower in the elective CS group compared with the emergency CS group. Forty pregnant women received general anesthesia (GA), whereas 43 women were administered spinal anesthesia (SA) in the elective CS group. Women who received GA had significantly lower native thiol/total thiol ratio. Moreover, they reported a significantly higher total thiol, disulfide, disulfide/native thiol, disulfide/total thiol, and native thiol/total thiol ratios compared with women who had SA. **Conclusion:** Oxidative stress increases in emergency CS, accompanied by a significant change in the thiol/disulfide balance in favor of disulfides in emergency CS. Although OS levels increased in emergency CS, there was no difference between the groups in terms of neonatal Apgar scores.

Keywords: Thiols; disulfides; oxidative stress; cesarean section; anesthesia

During pregnancy, oxygen demand and consumption keep varying, depending on the metabolic needs of the mother and fetus. High metabolic activities during pregnancy are accompanied by increased oxygen radical production, leading to a disturbance in the balance of oxidant and antioxidant systems during all phases of pregnancy.¹

Oxidative stress (OS) occurs owing to the disturbance in the balance of anti-oxidant defenses and reactive oxygen species (ROS).^{2,3} ROS damage the cell membranes and react with several molecules, thereby resulting in cell toxicity and injury.

At lower levels, ROS are essential and play a beneficial role as a second messenger to maintain cell homeostasis by controlling cell differentiation, cell growth and progression, immunity, and apoptosis. ROS generated du-

ring pregnancy are usually detoxified in the placenta. However, increased levels of ROS due to an imbalance in the anti-oxidant system causes loss of cellular function and cell damage.² Increased OS due to this imbalance has a significant effect on the pathophysiology of diseases in pregnancy.^{2,4,5}

Several studies in the past have analyzed OS during the delivery stage in terms of delivery type, different anesthesia methods, and whether the cesarean section was elective or emergency.⁶⁻¹⁰ Moreover, OS and antioxidant status were evaluated both in utero and in neonatal cord blood using different test methods in previous studies.^{11,12}

Fetal distress refers to the condition where sufficient quantity of oxygen is not available to the fetus. It can occur due to multiple causes such as low oxygen levels in the mother's blood and umbilical cord compression leading to reduced blood flow. Fetal distress, due to any reason, increases the level of OS.¹³ Under fetal distress, emergency cesarean section (CS) under spinal anesthesia (SA) or general anesthesia (GA) is generally performed. Several studies have shown that OS increases during both normal vaginal delivery and CS.¹⁴⁻¹⁷

Different methods are being used to detect the level of OS during pregnancy, such as OSindex (OSI), erythrocyte malondialdehyde (MDA) concentration estimation, and glutathione peroxidase (GPX) activity assessment. Research is continuing to develop a practical and highly sensitive method. On the contrary, fetal distress is followed by external fetal heart rate monitorization.¹⁸ More studies are required to investigate the levels of fetal distress, OS, and neonatal status together and to determine standard values.¹⁹

We, therefore, planned this observational study to detect the levels of OS in pregnant women who underwent emergency CS due to fetal distress.

Nowadays, a novel method described by Erel and Neselioglu that analyzes the thiol/disulfide balance is being used to detect OS via measurement of total, native thiol, and disulfide levels.²⁰

Thiols are organic compounds and include a sulfhydryl group (-SH). Thiols are converted via ROS to form disulfides; disulfide bridges can then

be reduced back to thiols. This cycle continues in a balanced state known as the dynamic thiol/disulfide balance.²⁰ An analysis of the literature revealed that this novel and practical method has not been used widely to detect levels of OS during elective and emergency CS.

Primarily, we investigated the fetal OS level in emergency and elective CS, thereby contributing to the literature on this subject by using this new method of Erel and Neselioglu.

Secondly, we evaluated whether Apgar scores of newborns and the level of OS were different in elective and emergency CS, under GA and SA.

MATERIAL AND METHODS

ETHICAL STANDARDS

Ethical approval for this observational prospective study was provided by the Clinical Trials Ethics Committee of Ahi Evran University (date: 04/07/2017, decision no: 2017/12/116).

Pregnant women who were followed up in the Clinic of Obstetrics and Gynecology of Ahi Evran University Training and Research Hospital between October 1, 2017, and April 1, 2018, for whom it was decided to perform CS and who met the inclusion criteria, were included in the study. We adhered to the declaration of Helsinki, which sets out ethical rules for research on human subjects. We provided information on the research to all volunteer participants and received informed consent from each of them.

STUDY POPULATION

A total of 468 pregnant women for whom it was decided to perform CS within the specified date range were evaluated for this observational study (Figure 1).

We divided the volunteers into two groups: elective CS and emergency CS. For both procedures, women were included according to the inclusion and exclusion criteria in this study. We performed a preliminary study involving 20 pregnant women in each group. The PASS version 11.0 was used for sample size (NCSS LLC; Kaysville, Utah, USA). According to the statistics, to obtain

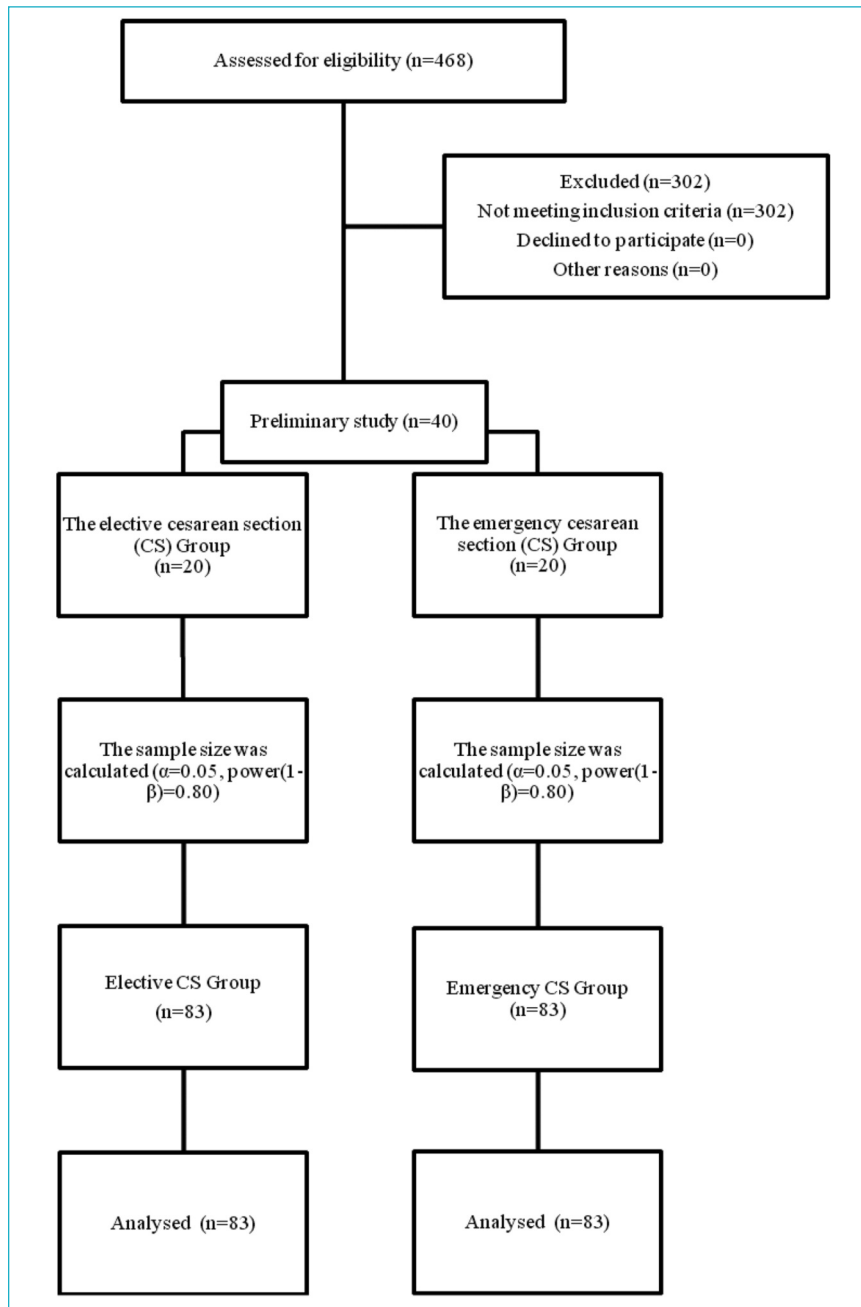


FIGURE 1: Flow diagram of study.

$\alpha=0.05$ and force $(1-\beta)=0.80$, 83 women in each group and a total of 166 pregnant women were planned to be included in the study.

INCLUSION AND EXCLUSION CRITERIA

According to the last menstrual date and ultrasonographic examination, women between 37 and 41 weeks of pregnancy with cephalopelvic disproportion, with breech presentation, and women who

were scheduled for elective CS because of prior CS were included in the elective CS group. Those pregnant at term for whom normal delivery was initially planned but then emergency CS was performed due to fetal distress, detected through fetal heart monitorization, and women with delayed delivery, who had a history of previous CS and were admitted as emergency cases were included in the emergency CS group.

Women with newly diagnosed or chronic hypertension, diabetes mellitus, and bleeding diathesis, preeclampsia or eclampsia; those who were smoking; those suspected to have infections such as chorioamnionitis; those with multiple pregnancies; those with intrauterine growth retardation (IUGR) and fetal malformation; those who used antioxidant treatments such as vitamin E during pregnancy and were on low-molecular-weight heparin or acetyl salicylic acid treatment were excluded.

PROCEDURE

When pregnant women were brought to the operation room for CS, an intravenous 500 mL/h 0.9% NaCl infusion was initiated. All women were followed up with non-invasive blood pressure (NIBP), electrocardiography (ECG), and peripheral oxygen saturation (SpO_2) monitorization before the operation.

After evaluating women's emergency, difficulty, and history of anesthesia, the type of anesthesia was determined by a joint decision taken by the pregnant woman, obstetrician, and the anesthesiologist. The anesthesia was performed in the Anesthesiology and Reanimation Clinic of Ahi Evran University Training and Research Hospital by the anesthesiologist responsible for obstetric surgery, using standard procedures.

STANDARD GENERAL ANESTHESIA

For standard GA, propofol (2-3 mg/kg) and rocuronium bromide (0.6 mg/kg) were used. Intubation was performed 2 min after the induction, following which surgical procedures were started. It was used with 4 L/min 50% O_2 -air mixture until the baby was born.

STANDARD SPINAL ANESTHESIA

A 26-G spinal needle (Atrocan; Braun, Germany) was inserted at the L3-L4 or L4-L5 vertebral level, and 10 mg heavy bupivacaine was administered. After controlling the development of sensory block at the T6 level with a pinprick test, the surgical procedure was started. Oxygen (2 L/min) was administered through a nasal mask during the operation.

In both methods, the umbilical cord was clamped, and the placenta was delivered after the baby was delivered. The placenta was removed from the surgical site to obtain blood samples.

MATERIALS

After the delivery of the placenta, two samples were drawn from the umbilical arteries of the cord. The first blood sample collected using a heparinized injector was investigated with an epoc Bgem Test Card (Epocal Inc., Ottawa, Canada). Arterial pH, the arterial partial pressure of carbon dioxide ($PaCO_2$) (mmHg), the arterial partial pressure of oxygen (PaO_2) (mmHg), glucose (mg/dL), lactate (mmol/L), and hemoglobin (g/dL) were also measured.

The second blood sample was collected to determine the total, native thiol, and disulfide. The samples were centrifuged and stored at $-80^\circ C$ until analyzed. Native thiol ($\mu\text{mol/L}$), total thiol ($\mu\text{mol/L}$), and disulfide ($\mu\text{mol/L}$) were measured using the method described by Erel and Neselioglu, and disulfide/native thiol (%), disulfide/total thiol (%), and native thiol/total thiol (%) ratios were calculated.²⁰

The age and gestational age of pregnant women, and first- and fifth-minute Apgar scores of the newborn, and the type of anesthesia administered were recorded.

STATISTICAL ANALYSES

For statistical analyses, PASW (Predictive Analytics Software) version 18.0 (SPSS Inc., Chicago, IL, USA) was used. Descriptive statistics are presented as numbers and percentages (n [%]) for categorical variables, and mean and standard deviation ($\text{mean} \pm \text{SD}$), median, and interquartile (median [Q1-Q3]) are used for numeric variables.

The suitability of variables for normal distribution was investigated using visual (histogram and probability graphs) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk tests).

In binary comparisons for univariate analyses between the elective and emergency CS groups, Student's t -test or the Mann-Whitney U test was

used for numeric variables showing normal distribution or without normal distribution. The Chi-square test was used for categorical variables. For correlations between numeric variables without normal distribution, Spearman’s rho test was used. Less than 5% type 1 error level was interpreted as statistically significant.

RESULTS

A total of 166 CS, 83 elective CS and 83 emergency CS, were examined in the study. Cesarean sections were performed under GA (n=77, 46.4%) and under SA (n=89, 53.6%). The median of maternal age was 27 years (23-30) and the mean of gestational weeks was 39±1. The median of maternal BMI was detected to be 27.69 kg/m² (25.80-30.67).

Values of maternal age detected in the elective CS were higher than those recorded in the emergency CS (28 [24-33], 25 [23-29], p=0.019, respectively).

Values of the maternal BMI in the elective CS group were lower than those recorded in the emergency CS (27.24 [25.39-29.3], 28.69 [26.04-32.18], p=0.027, respectively).

The comparison of thiol/disulfide balance in the arterial cord and blood gas values in groups are given in Table 1.

There was a negative correlation between the native thiol value, total thiol value, and lactate value in the emergency CS group (p=0.043 and p=0.037, respectively).

In the elective CS group, a statistically significant positive correlation was seen between the disulfide value, the disulfide/native thiol ratio, the disulfide/total thiol ratio, and the lactate value (p=0.002, p=0.001, and p=0.001, respectively).

There was a negative correlation between the native thiol/total thiol ratio and the lactate value in the elective CS group (p=0.001).

In the elective CS group, in those who received GA, Apgar 5 score, pH, hemoglobin, and the native thiol/total thiol ratio were lower compared with patients who received SA (Table 2).

TABLE 1: Comparison of thiol-disulfide homeostasis in arterial cord blood in elective and emergency cesarean section (CS).

	Elective CS (n=83)	Emergency CS (n=83)	p
Anesthesia type, n (%)			
General	40 (48.2)	37 (44.6)	0.641 ^a
Spinal	43 (51.8)	46 (55.4)	
Age	28±5 28 (24-33)	26±5 25 (23-29)	0.019 ^b
Gestational weeks	39±0 39 (39-39)	39±1 39 (38-40)	0.110 ^b
BMI (kg/m ²)	28.09±4.36 27.24 (25.39-29.3)	29.3±4.49 28.69 (26.04-32.18)	0.027 ^c
Apgar 1-min	8±1 8 (8-9)	8±1 9 (8-9)	0.751 ^b
Apgar 5-min	10±1 10 (9-10)	10±1 10 (9-10)	0.615 ^b
pH	7.37±0.03 7.37 (7.35-7.39)	7.35±0.06 7.35 (7.31-7.38)	0.003 ^b
PaCO ₂ (mmHg)	39.63±5.35 39.5 (36.4-42.5)	40.45±6.95 38.5 (35.6-46.7)	0.863 ^b
PaO ₂ (mmHg)	29.48±8.72 31 (23.4-35)	24.76±8.94 23.5 (20.7-29.3)	0.001 ^c
Glucose (mg/dL)	60±9 61 (55-67)	68±12 67 (59-74)	<0.001 ^b
Lactate (mmol/L)	1.77±1.56 1.4 (1.25-1.66)	1.66±0.61 1.48 (1.33-1.75)	0.043 ^b
Hemoglobin (g/dL)	13.71±1.39 13.6 (12.8-14.6)	15.11±2.14 14.9 (13.3-16.6)	<0.001 ^b
Native thiol (µmol/L)	444.54±47.01 434.8 (409.7-485)	471.32±41.88 472.2 (451.9-491.5)	0.001 ^b
Total thiol (µmol/L)	490.88±62.12 493 (443-545)	529.12±59.47 528 (501-561)	<0.001 ^b
Disulfide (µmol/L)	23.46±9.43 24.75 (17.5-31.2)	29.02±11.9 30.45 (20.75-36.9)	0.001 ^c
Disulfide/Native thiol (%)	5.18±1.83 5.36 (3.87-6.45)	6.07±2.26 6.43 (4.96-7.64)	0.006 ^c
Disulfide/total thiol (%)	4.65±1.52 4.84 (3.59-5.72)	5.34±1.83 5.7 (4.51-6.63)	0.009 ^c
Native thiol/total thiol (%)	90.83±3.2 90.33 (88.57-92.82)	89.34±3.65 88.6 (86.87-90.98)	0.007 ^b

^a Chi-square test. ^b Mann-Whitney U test. ^c Student’s t-test.

BMI: Body mass index. PaCO₂: The arterial partial pressure of carbon dioxide.

PaO₂: The arterial partial pressure of oxygen.

All data are presented as n (%), [mean±SD] and [median (Q1-Q3)].

In the emergency CS group, in those who received GA, age, pH, hemoglobin, and native

TABLE 2: Comparison of lactate and thiol-disulfide homeostasis in arterial cord blood according to the type of anesthesia use during elective cesarean section (CS).

	Elective CS (n=83)		p
	General anesthesia	Spinal anesthesia	
	(n=40)	(n=43)	
Age	27±5 28 (23-30)	29±5 28 (25-33)	0.101 ^b
Gestational weeks	39±0 39 (39-39)	39±1 39 (39-39)	0.519 ^b
BMI (kg/m ²)	27.34±3.23 27.12 (25.35-28.37)	28.79±5.14 27.34 (25.56-30.3)	0.297 ^b
Apgar 1-min	8±1 8 (8-9)	8±1 9 (8-9)	0.201 ^b
Apgar 5-min	9±1 9 (9-10)	10±1 10 (9-10)	0.006 ^b
pH	7.36±0.03 7.36 (7.34-7.38)	7.38±0.03 7.38 (7.36-7.39)	0.001 ^b
PaCO ₂ (mmHg)	40.89±4.24 40.5 (38.1-43.4)	38.47±6.03 38.3 (35.3-40.6)	0.024 ^b
PaO ₂ (mmHg)	32.6±8.12 34.25 (26.4-38.1)	26.59±8.32 28.4 (21-33.6)	0.001 ^c
Glucose (mg/dL)	59±9 61 (50-66)	61±8 60 (56-67)	0.449 ^b
Lactate (mmol/L)	2.06±2.19 1.42 (1.34-1.53)	1.49±0.36 1.35 (1.22-1.84)	0.185 ^b
Hemoglobin (g/dL)	13.09±1.01 12.95 (12.4-13.85)	14.27±1.45 14.3 (13.2-15.4)	<0.001 ^b
Native thiol (μmol/L)	455.66±45.5 457.7 (409.6-490.35)	434.2±46.54 433.4 (412.6-469.9)	0.085 ^b
Total thiol (μmol/L)	508.97±60.69 512 (458-554.5)	474.05±59.27 482 (438-512)	0.015 ^b
Disulfide (μmol/L)	26.79±9.29 28.15 (18.85-32.83)	20.36±8.55 22.05 (13.1-26.45)	0.002 ^c
Disulfide/native thiol (%)	5.79±1.69 6.04 (4.28-7.16)	4.62±1.8 4.73 (3.48-5.75)	0.003 ^c
Disulfide/total thiol (%)	5.15±1.38 5.39 (3.95-6.26)	4.19±1.51 4.32 (3.25-5.16)	0.003 ^c
Native thiol/total thiol (%)	89.74±2.76 89.22 (87.49-92.11)	91.85±3.27 91.35 (89.69-93.5)	0.002 ^b

^a Chi-square test. ^b Mann-Whitney U test. ^c Student's t-test.
 BMI: Body mass index. PaCO₂: The arterial partial pressure of carbon dioxide.
 PaO₂: The arterial partial pressure of oxygen.
 The data are presented as n (%), [mean±SD] and [median (Q1-Q3)].

thiol were lower, and PaCO₂ were higher compared with the patients who received SA (Table 3).

TABLE 3: Comparison of lactate and thiol-disulfide homeostasis in arterial cord blood according to the type of anesthesia used during emergency cesarean section (CS).

	Emergency CS (n=83)		p
	General anesthesia	Spinal anesthesia	
	(n=37)	(n=46)	
Age	25±4 24 (22-28)	27±5 27 (24-31)	0.027 ^b
Gestational weeks	39±1 39 (39-40)	39±1 40 (38-40)	0.153 ^b
BMI (kg/m ²)	28.91±3.78 28.15 (26.15-30.82)	29.62±5 29.41 (26.04-32.32)	0.573 ^b
Apgar 1-min	8±1 9 (8-9)	8±1 9 (8-9)	0.866 ^b
Apgar 5-min	10±0 10 (9-10)	10±1 10 (9-10)	0.931 ^b
pH	7.33±0.04 7.33 (7.3-7.36)	7.36±0.06 7.37 (7.34-7.39)	0.001 ^b
PaCO ₂ (mmHg)	42.6±6.67 41.8 (36.2-48.8)	38.73±6.76 37.75 (34.5-43.1)	0.025 ^b
PaO ₂ (mmHg)	26.48±9.8 25.3 (21.2-29.9)	23.38±8.04 22.6 (20.3-28.3)	0.117 ^c
Glucose (mg/dL)	70±14 66 (61-78)	66±11 67 (58-72)	0.359 ^b
Lactate (mmol/L)	1.59±0.6 1.48 (1.33-1.58)	1.72±0.61 1.55 (1.37-1.77)	0.232 ^b
Hemoglobin (g/dL)	14.44±2.13 14.1 (13.2-14.9)	15.65±2.01 15.7 (13.6-16.6)	0.004 ^b
Native thiol (μmol/L)	463.96±48.57 459 (449.8-479.4)	477.24±35.04 485.2 (456.8-495.1)	0.021 ^b
Total thiol (μmol/L)	523.05±73.88 526 (491-555)	534±44.99 537 (503-569)	0.280 ^b
Disulfide (μmol/L)	29.69±14.53 32.65 (19.65-38.1)	28.48±9.4 26.73 (22.75-33.4)	0.649 ^c
Disulfide/native thiol (%)	6.22±2.67 7.09 (4.87-7.93)	5.95±1.89 5.4 (5.01-6.74)	0.593 ^c
Disulfide/total thiol (%)	5.43±2.2 6.21 (4.44-6.85)	5.27±1.48 4.87 (4.55-5.94)	0.689 ^c
Native thiol/total thiol (%)	89.17±4.4 87.7 (86.38-91.13)	89.48±2.96 90.27 (88.18-90.9)	0.178 ^b

^a Chi-square test. ^b Mann-Whitney U test. ^c Student's t-test.
 BMI: Body mass index. PaCO₂: The arterial partial pressure of carbon dioxide.
 PaO₂: The arterial partial pressure of oxygen.
 Data are presented n (%), [mean±SD] and [median (Q1-Q3)].

DISCUSSION

In the present study, we compared the OS levels between pregnant women undergoing emergency

and elective CS by examining the balance of thiol/disulfide with the new method described by Erel and Neselioglu.²⁰ Our results showed that OS in women undergoing emergency CS was more prominent than in those in the elective CS group.

The oxidant and antioxidant balance undergoes a continuous change during pregnancy due to the changes in maternal hormonal balance, and changes in fetal and maternal metabolic needs. Evidence from the literature suggests that OS level varies during different trimesters in pregnancy.^{1,21} For example, higher OS levels have been reported in preterm deliveries.²² In our study, only 37 to 41 weeks of pregnancies were included to ensure standardization.

During pregnancy, conditions such as hypertension, preeclampsia, and eclampsia increase the chances of developing OS.²³ For example, elevated OS levels were detected in pregnant women with IUGR.²⁴ In the present study, pregnant women with fetuses with IUGR were not included. In addition, pregnant women with an acute infection that would affect oxidant levels were not included.

A study by Paamoni-Keren et al. assessed the glutathione (GSH) concentration in 48 pregnant women to compare OS levels between normal deliveries and CS. It was observed that the newborns of pregnant women with elective CS were less exposed to OS than infants born to women with normal deliveries.⁶ In another study, the effect of normal delivery and CS on thiol-disulfide homeostasis was investigated, and it was determined that OS was lower in infants born through normal deliveries compared with infants born via CS.²⁵

The study by Paamoni-Keren et al. enrolled pregnant women, of whom 12 received GA and 10 were administered SA in the elective CS group.⁶ However, in this study, the amount of oxygen given by mask during SA and the drugs used during GA were not described. In this study, no difference was detected between the groups in terms of pO_2 and GSH. In our research, we found that total thiol and disulfide levels increased in the GA group. At the same time, we reported high $PaCO_2$ and PaO_2 values. The difference in the results obtained in our study and that conducted by Pa-

moni-Keren et al. could be attributed to the differences in anesthesia procedures.

In another study, 47 pregnant women who were planned to undergo CS were divided into three groups according to three different anesthesia methods, and OS levels were compared between the groups.⁹ Blood samples were collected from the umbilical artery and parameters such as total antioxidant status (TAS), total oxidant status (TOS), oxidative stress index (OSI), along with blood gas parameters were measured. There was no statistical significance between the groups in terms of TAS and TOS; however, a difference in terms of OSI was present. In this study, arterial blood gas parameters, such as pH, $PaCO_2$, PaO_2 , SaO_2 , HCO_3 , glucose, lactate, and hemoglobin were found to be similar in all groups. With respect to OS, it was concluded that GA was preferable over epidural anesthesia. In our study, we compared pregnant women receiving GA and SA in the elective CS group and found that $PaCO_2$, PaO_2 , total thiol, disulfide, disulfide/native thiol, disulfide/total thiol, and native thiol/total thiol ratios were higher in women receiving GA compared with those receiving SA. There was no difference between glucose and lactate values. We believe the difference in the results of the two studies is due to various drugs used to induce anesthesia. In another study, women were ventilated with 1% sevoflurane and a 50% O_2/N_2O mixture after intubation, whereas in our study, women were ventilated with 1% sevoflurane and a 50% O_2 /air mixture until the baby was delivered.⁹ In the study by Karabayirli et al., SA was administered with 2 mL 0.5% levobupivacaine and 20 μ g fentanyl. However, in our study, SA was administered with 10 mg heavy bupivacaine. In the comparative study, no O_2 was administered with a nasal cannula, whereas we provided patients with 2 L/min O_2 .⁹

In the study by Yalcin et al., effects of different oxygen concentrations on OS during SA were compared in 80 pregnant women who underwent elective CS.⁸ Women were administered 21% O_2 (air group) and 40% O_2 (OXgen group). TAS, TOS, and OSI were examined in the blood samples from the umbilical artery. TAS level in the OXgen group

and TOS and OSI levels in the air group were found to be elevated. In our study, 2 L/min O₂ was administered with nasal cannula to women who underwent emergency or elective CS under SA.

Lurie et al. compared OS levels between 21 elective and 21 emergency CS cases.¹⁰ Amniotic fluid, umbilical cord plasma, and erythrocyte MDA concentrations, and GPX activity were investigated. Compared with elective CS, it was found that MDA concentrations increased in emergency CS, which was performed because of fetal distress. In our study, an examination of umbilical cord blood revealed the OS level to be higher in the emergency CS group, similar to Lurie et al.'s findings. However, no difference was detected between the groups in terms of neonatal Apgar scores.

In the current study, no correlation between umbilical artery pH and GPX activity and MDA concentration in the amniotic fluid was detected. However, we found an inverse correlation between amniotic fluid protein, cord erythrocyte GPX, amniotic fluid MDA, cord plasma MDA, cord erythrocyte MDA values, and umbilical artery pH.¹⁰ Moreover, we did not detect any correlation between the pH value of arterial cord blood and disulfide, the disulfide/native thiol ratio, the disulfide/total thiol ratio, and the native thiol/total thiol ratio in either group. However, a statistically significant negative correlation between the native thiol, total thiol, and lactate in the emergency CS group was observed upon examining lactate values. A positive relation was found between disulfide, the disulfide/native thiol ratio, the disulfide/total thiol ratio, and lactate in the elective CS group, whereas a negative relationship was observed between the native thiol/total thiol ratio and lactate in the elective CS group.

In another study, OS was compared in 106 pregnant women undergoing vaginal delivery, elective CS, emergency CS, and prolonged action with vaginal delivery.²⁶ CS was performed under SA without giving O₂. TAS and paraoxonase 1 (PON 1) activity were investigated in mothers' blood before and after the delivery and in the cord blood after the delivery. It was stated that the postpartum low TAS levels and decreased PON 1 activity detected in

the emergency CS and prolonged action with vaginal delivery groups might be due to the increased production of free radicals. Similar to this study, we found that thiol/disulfide balance deteriorated in favor of disulfide, leading to increased OS levels in women in the emergency CS group.

LIMITATIONS

One of the limitations of the present study is that it did not evaluate the presence of uterine contractions and lack of placental perfusion in the emergency CS group. Elective CS was performed during the daytime, but emergency CS was performed at all hours of the day. Moreover, no evaluation was done according to the time of the operation. Metabolic rates of mother and fetus may be affected by daily hormonal changes, fasting periods, and anxiety levels.²⁷ We did not standardize these factors in our study. Also, maternal age and BMI in elective and emergency CS groups could not be standardized. Therefore, we plan to conduct further studies with a larger number of patients with an aim to standardize these factors.

Some studies have shown that oxytocin, when used as a delivery inducer, reduced the concentration of glutathione, an OS indicator.²⁸ In addition, there are studies that report no disturbance in the thiol/disulfide balance by oxytocin induction.²⁹ Another limitation of the present study is that the duration of the delivery action of oxytocin and its amount used were not evaluated.

CONCLUSION

According to the findings of the present study, OS increased in the emergency CS with a shift in the thiol/disulfide balance in favor of disulfide compared with elective CS. Despite the increase in OS levels in emergency CS, there was no difference between the groups in terms of neonatal Apgar scores.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or

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Authorship Contributions

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Recai Dağlı, Selda Songur Dağlı, Rukiye Nar; **Data Collection and/or Processing:** Recai Dağlı, Selda Songur Dağlı, Rukiye Nar; **Analysis and/or Interpretation:** Recai Dağlı, Selda Songur Dağlı; **Literature Review:** Recai Dağlı; **Writing the Article:** Recai Dağlı; **Critical Review:** Selda Songur Dağlı, Rukiye Nar; **References and Fundings:** Recai Dağlı; **Materials:** Recai Dağlı, Selda Songur Dağlı, Rukiye Nar.

REFERENCES

- Yüksel S, Yigit AA. Malondialdehyde and nitric oxide levels and catalase, superoxide dismutase, and glutathione peroxidase levels in maternal blood during different trimesters of pregnancy and in the cord blood of newborns. *Turk J Med Sci.* 2015;45(2):454-9. [Crossref] [PubMed]
- Burton GJ, Jauniaux E. Oxidative stress. *Best Pract Res Clin Obstet Gynaecol.* 2011;25(3): 287-99. [Crossref] [PubMed] [PMC]
- D'Autreaux B, Toledano MB. ROS as signalling molecules: mechanisms that generate specificity in ROS homeostasis. *Nat Rev Mol Cell Biol.* 2007;8(10):813-24. [Crossref] [PubMed]
- Korkmaz V, Kurdoglu Z, Alisik M, Cetin O, Korkmaz H, Surer H, et al. Impairment of thiol-disulfide homeostasis in preeclampsia. *J Matern Fetal Neonatal Med.* 2016;29(23): 3848-53. [Crossref] [PubMed]
- Marseglia L, D'Angelo G, Manti S, Arrigo T, Barberi I, Reiter RJ, et al. Oxidative stress-mediated aging during the fetal and perinatal periods. *Oxid Med Cell Longev.* 2014;2014: 358375. [Crossref] [PubMed] [PMC]
- Paamoni-Keren O, Silberstein T, Burg A, Raz I, Mazor M, Saphier O, et al. Oxidative stress as determined by glutathione (GSH) concentrations in venous cord blood in elective cesarean delivery versus uncomplicated vaginal delivery. *Arch Gynecol Obstet.* 2007;276(1):43-6. [Crossref] [PubMed]
- Nabhan AF, El-Din LB, Rabie AH, Fahmy GM. Impact of intrapartum factors on oxidative stress in newborns. *J Matern Fetal Neonatal Med.* 2009;22(10):867-72. [Crossref] [PubMed]
- Yalcin S, Aydoğlan H, Kucuk A, Yuze HH, Altay N, Karahan MA, et al. Supplemental oxygen in elective cesarean section under spinal anesthesia: handle the sword with care. *Braz J Anesthesiol.* 2013;63(5):393-7. [Crossref] [PubMed]
- Karabayırlı S, Keskin EA, Kaya A, Koca C, Erel O, Demircioğlu RI, et al. Assessment of fetal antioxidant and oxidant status during different anesthesia techniques for elective cesarean sections. *J Res Med Sci.* 2015;20(8): 739-44. [Crossref] [PubMed] [PMC]
- Lurie S, Matas Z, Boaz M, Fux A, Golan A, Sadan O. Different degrees of fetal oxidative stress in elective and emergent cesarean section. *Neonatology.* 2007;92(2):111-5. [Crossref] [PubMed]
- Gülbayzar S, Arica V, Hatipoğlu S, Kaya A, Arica S, Karatekin G. Malondialdehyde level in the cord blood of newborn infants. *Iran J Pediatr.* 2011;21(3):313-9.
- Jain S, Nair A, Shrivastava C. Evaluation of oxidative stress marker malondialdehyde level in the cord blood of newborn infants. *Int J Sci Study.* 2015;3(6):73-6.
- Raicević S, Cubrić D, Arsenijević S, Vukčević G, Zivković V, Vuletić M, et al. Oxidative stress in fetal distress: potential prospects for diagnosis. *Oxid Med Cell Longev.* 2010;3(3): 214-8. [Crossref] [PubMed] [PMC]
- Inanc F, Kilinc M, Kiran G, Guven A, Kurutas E, Cikim IG, et al. Relationship between oxidative stress in cord blood and route of delivery. *Fetal Diagn Ther.* 2005;20(5):450-3. [Crossref] [PubMed]
- Vakilian K, Ranjbar A, Zarganjfard A, Mortazavi M, Vosough-Ghanbari S, Mashaiee S, et al. On the relation of oxidative stress in delivery mode in pregnant women; a toxicological concern. *Toxicol Mech Methods.* 2009;19(2):94-9. [Crossref] [PubMed]
- Noh EJ, Kim YH, Cho MK, Kim JW, Kim JW, Byun YJ, et al. Comparison of oxidative stress markers in umbilical cord blood after vaginal and cesarean delivery. *Obstet Gynecol Sci.* 2014;57(2):109-14. [Crossref] [PubMed] [PMC]
- Hung TH, Chen SF, Hsieh TT, Lo LM, Li MJ, Yeh YL. The associations between labor and delivery mode and maternal and placental oxidative stress. *Reprod Toxicol.* 2011;31(2): 144-50. [Crossref] [PubMed]
- Ayres-de-Campos D, Spong CY, Chandraran E; FIGO Intrapartum Fetal Monitoring Expert Consensus Panel. FIGO consensus guidelines on intrapartum fetal monitoring: cardiocography. *Int J Gynaecol Obstet.* 2015;131(1):13-24. [Crossref] [PubMed]
- Visser GH, Ayres-de-Campos D; FIGO Intrapartum Fetal Monitoring Expert Consensus Panel. FIGO consensus guidelines on intrapartum fetal monitoring: adjunctive technologies. *Int J Gynaecol Obstet.* 2015;131(1):25-9. [Crossref] [PubMed]
- Erel O, Neselioglu S. A novel and automated assay for thiol/disulphide homeostasis. *Clin Biochem.* 2014;47(18):326-32. [Crossref] [PubMed]
- Oghagbon SE, Agu KC, Omorowa FE, Okolie NP, Okwumabua M, Omo-Erharbor JA. Oxidative stress parameters as markers of the different trimesters in normal pregnancy. *JASEM.* 2016;20(3). [Crossref]
- Martin A, Faes C, Debevec T, Rytz C, Millet G, Pialoux V. Preterm birth and oxidative stress: Effects of acute physical exercise and hypoxia physiological responses. *Redox Biol.* 2018;17: 315-22. [Crossref] [PubMed] [PMC]
- Harma M, Harma M, Erel O. Measurement of the total antioxidant response in preeclampsia with a novel automated method. *Eur J Obstet Gynecol Reprod Biol.* 2005;118(1):47-51. [Crossref] [PubMed]
- Cetin O, Karaman E, Boza B, Cim N, Alisik M, Erel O, et al. The maternal serum thiol/disulfide homeostasis is impaired in pregnancies complicated by idiopathic intrauterine growth restriction. *J Matern Fetal Neonatal Med.* 2018;31(5):607-13. [Crossref] [PubMed]
- Ulubas Isik D, Akdağ Reis Y, Bas AY, Unal S, Ozcan B, Mollamahmutoglu L, et al. The effect of the modes of delivery on the maternal and neonatal dynamic thiol-disulfide homeostasis. *J Matern Fetal Neonatal Med.* 2018;31(5):607-13. [Crossref] [PubMed]
- Vlachos GD, Bartzeliotou A, Schulpis KH, Partsinelos GA, Lazaropoulou C, Papadima C, et al. Maternal-neonatal serum paraoxonase 1 activity in relation to the mode of delivery. *Clin Biochem.* 2006;39(9):923-8. [Crossref] [PubMed]
- Chiba T, Omori A, Takahashi K, Tanaka K, Kudo K, Manabe M, et al. Correlations between the detection of stress-associated hormone/oxidative stress markers in umbilical cord blood and the physical condition of the mother and neonate. *J Obstet Gynaecol Res.* 2010;36(5):958-64. [Crossref] [PubMed]
- Schneid-Kofman N, Silberstein T, Saphier O, Shai I, Tavor D, Burg A. Labor augmentation with oxytocin decreases glutathione level. *Obstet Gynecol Int.* 2009;2009:807659. [Crossref] [PubMed] [PMC]
- Eryilmaz OG, Kansu-Celik H, Erel O, Erdogan S. Thiol/disulfide parameters as a novel oxidative marker in medical labor induction with oxytocin. *Horm Mol Biol Clin Invest.* 2017;29(2):61-5.