Journal of Psychiatric Research 79 (2016) 57–60

Contents lists available at ScienceDirect

Journal of Psychiatric Research

journal homepage: www.elsevier.com/locate/psychires

# Depression in pregnancy is associated with decreased glutathione peroxidase activity in fetal cord blood.

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ARTICLE INFO

*Article history:*
Received 14 March 2016
Received in revised form
9 April 2016
Accepted 25 April 2016

*Keywords:*
Depression
Pragnancy
Antioxidant
Fetal cord
Umbilical cord
Glutathione peroxidase
Myeloperoxidase

ABSTRACT

The investigation of fetal cord blood (FCB) during child delivery has created a novel topic in the field of psychiatric research. The umbilical vein receives nutrients and oxygen from the mother's circulation and transports them to the fetal circulation. Investigating fetal cord blood during delivery is beneficial for understanding the fetal environment. Depression in pregnancy is associated with medical and emotional burdens. In this study, we aimed to investigate glutathione peroxidase (Gpx) and myeloperoxidase (MPO) activity in the FCB of depressed mothers and healthy controls. Our study included 45 depressed mothers and 59 healthy controls. The FCB samples were collected from the umbilical vein during delivery. We found that Gpx levels were significantly decreased in the FCB of depressed mothers than healthy controls, medians were 0.14 U/ml and 0.16 U/ml respectively, Z: −3.567 and $p < 0.001$. MPO levels were similar in both groups, medians were 1.0 U/L and 1.2 U/L respectively, Z: −1.837 and p:0.066. Depression in pregnancy may be associated with decreased antioxidant levels, and this condition may cause an oxidative load, which may lead to improper brain development. Future studies should be performed in larger samples to clarify our preliminary results.



## 1. Introduction

Recently, the investigation of fetal cord blood (FCB) during the delivery has created a novel topic in the field of psychiatric research. A vein and two arteries exist in the fetal cord. The umbilical vein receives nutrients and oxygen from the mother's circulation and transports them to the fetal circulation. This function is vital for the fetus to survive (Kiserud and Acharya, 2004). Investigating fetal cord blood during child delivery is beneficial for understanding the fetal environment; it may provide a better picture of how maternal psychiatric or medical diseases may affect the intrauterine conditions of the fetus. To the best of our knowledge, depression in pregnancy is associated with not only medical but also emotional burdens for both the mother and the fetus. Intrauterine growth retardation, low birth weight, and shortened duration of pregnancy are a few of the consequences of depression during pregnancy (Uguz et al., 2013a).

Oxidative balance defines the equilibrium between antioxidants and oxidants (Camkurt et al., 2016b). Disruption of the oxidative balance, such as increases in oxidants or decreases in antioxidants, may have a deteriorating effect on the body, particularly on the brain (Güneş et al., 2016). Brain tissue consumes a high amount of oxygen and contains excitatory neurotransmitters. Consisting of a high amount of lipids, the brain is a potential substrate for oxidation. In this context, investigating antioxidants or oxidants in FCB during child delivery will be helpful to discover the fetal environment and exposition (Ng et al., 2008).

Glutathione peroxidase (Gpx) is a major antioxidant enzyme that neutralizes lipid peroxides and hydrogen peroxide. With this critical function, Gpx prevents the body from suffering oxidative damage. Gpx activity and glutathione levels have been investigated in major depression. Decreased, unchanged, or increased Gpx activities have been reported thus far (Bilici et al., 2001; Gawryluk

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http://dx.doi.org/10.1016/j.jpsychires.2016.04.008
0022-3956/

et al., 2011; Sarandol et al., 2007).

The main function of myeloperoxidase (MPO) is the synthesis of hydrochlorous acid to defend the body against pathogens. Being an oxidant and inflammatory enzyme, MPO could be useful to understand the oxidative status of a tissue. Several studies have been performed to identify changes in MPO levels in psychiatric disorders. Vaccarino et al. (2008) argued that MPO could be used as a marker for immune activation. Likewise, Selek et al. (2015) noted MPO levels to be higher in depressed bipolar patients.

Few studies have been performed on FCB. Current data suggest that maternal generalized anxiety disorder and obsessive compulsive disorder are associated with decreased brain derived neurotrophic factor (BDNF) and increased tumor necrosis factor alpha (TNFa) levels (Uguz et al., 2013b, 2014). The umbilical vein represents the systemic circulation of the fetus, which is closely associated with the brain tissue of the fetus. In this study, we aimed to investigate the Gpx and MPO levels in the FCB of depressed mothers to understand the oxidant-antioxidant status of the fetal environment.

## 2. Methods

### 2.1. Participants

The participants were women giving birth by elective caesarean section at the Obstetric Clinic of Kahramanmaraş Sütçü İmam University. The reasons for choosing elective caesarean section were as follows: 1) the duration of the operation is standard and similar for all patients; 2) the collection of blood samples is performed by a fellow obstetrician; 3) the procedure has a shorter duration than a vaginal birth; and 4) there is a chance to minimalize complications during the delivery. The study sample included 45 women with a diagnosis of major depression alone, according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV), and 59 women without any psychiatric diagnosis (controls) who met the study criteria. The inclusion criteria for the study were as follows: voluntary participation to the study and a current age between 18 and 40 years. Patients with a history of medical illnesses (e.g., endocrine abnormalities, cardiovascular and pulmonary system diseases, neurological disease, and metabolic disease), a history of pregnancy-related complications, any malformation in newborn infants, a history of maternal infection, active maternal infections, mental retardation, multiple pregnancies, intrauterine growth restriction, low birth weight, preterm delivery or emergency caesarean section, those who reported smoking or alcohol consumption during pregnancy, those who had used systemic corticosteroids during pregnancy, those who had used any psychotropic medications during pregnancy, and those whose infants had developed hypoxia during delivery were excluded. The study was conducted in a similar methodology as Uguz et al. (2013b) research. The Beck Depression Scale was applied to all patients to determine the severity of depression (Beck et al., 1996). Study performed according to the Helsinki declaration. Kahramanmaraş Sütçü İmam University's ethical committee approved our study (approval date: 22.02.2016; number: 16), which was performed in the same methodology as our previous research, and we used 33 patient samples and 37 healthy control samples collected during our previous study (Camkurt et al., 2016a). We increased the sample size to 45 for patients and 59 for healthy controls. Blood samples were collected from the umbilical vein during delivery and then centrifuged at 4000 rpm for 10 min. Samples were stored at −80 °C until the biochemical analysis.

### 2.2. MPO analysis

MPO activity was determined by a modification of the O-dianisidine method. The assay mixture, in a cuvette of 1 cm path length, contained 0.3 mL 0.1 M phosphate buffer (pH 6.0), 0.3 mL 0.01 M $H_2O_2$, 0.5 mL 0.02 M O-dianisidine (freshly prepared) in deionized water, and 10 μL serum in a final volume of 3 mL. The serum was added last, and the change in absorbance at 460 nm was monitored for 10 min. All measurements were carried out in duplicate. One unit of MPO is defined as that giving an increase in absorbance of 0.001 per minute, and specific activity is given as u/ml (Freehold, 1972).

### 2.3. Gpx analysis

The Beutler method was used for GSH-Px activity measurement. The role of GSH-Px is to catalyze the oxidation of reduced glutathione (GSH) to oxidized glutathione (GSSG) by means of H2O2. In the presence of H2O2 with t-butyl hydroperoxide, GSSG formed by GSH- Px is reduced to GSH with the help of glutathione reductase and NADPH. GSH-Px activity is determined by reading the difference of absorbance spectrophotometrically at 340 nm during the oxidation of NADPH to NADP (Beutler, 1975).

### 2.4. Statistical analysis

Statistical analysis was performed using the Statistical Package for Social Sciences, version 11.5 (SPSS, Inc., Chicago, IL). The normality of continuous variables was assessed using the Shapiro-Wilk's W-test, Kolmogorov Smirnov test, histogram and steam and leaf graphs.

The mean and standard deviation and interquartile ranges used to demonstrate investigated data. Relationships between the categorical variables were evaluated using the Chi-square test. A student's *t*-test was used to compare the mean differences for the normally distributed continuous variables between the two groups, t value shown accordingly. The Mann-Whitney *U* test was used to compare the two groups when the assumption of normality was not fulfilled, Z value shown accordingly. While investigating data associations, correlation coefficients and their significance the Spearman test (for non-normally distributed variables) and the Pearson test (for normally distributed variables).

## 3. Results

Patients and controls were similar in age. The means were 29.04 and 30.51, respectively. The p value was 0.188. Furthermore, the babies' head circumference (mean of patients: 35.62 cm; mean of controls: 35.59 cm) and length (mean of patients: 50.98 cm; mean of controls: 51.31 cm) were similar in both groups. The babies' weights were significantly lower in the patients than the controls (means were 3288 gr and 3518 gr, respectively; $p = 0.004$). The patients' Beck Depression Scale scores were significantly higher than those of the controls ($p < 0.001$; see Table 1).

Gpx levels were significantly lower in patients than in the healthy controls (medians were 0.14 U/ml and 0.16 U/ml, respectively; $p < 0.001$). The interquartile values for patients and controls were as follows: 0.13 u/ml and −0.15 U/ml, and 0.15 U/ml and −0.18 U/ml, respectively. MPO levels were similar in both groups ($p = 0.066$; Table 2).

We found a moderate correlation between Gpx levels and Beck scores (r: −0.456; $p < 0.001$), weak correlation between Beck scores and weight of the babies (r: 0.364; $p < 0.001$) and weight and Gpx levels (r:−2.888; p:0.003).