

# Glutathione-Dependent System of Antioxidant Defense in the Placenta in Preterm Delivery

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Components of the antioxidant defense system in placental tissues were studied in women with normal pregnancy and full-term delivery and women with spontaneous abortions at 28-36 weeks. In women with spontaneous abortions glutathione peroxidase activity in placental tissues increased and the content of SH compounds decreased, which led to exhaustion of the antioxidant defense system. Glutathione-S-transferase activity also decreased, which attests to impaired detoxifying function of the placenta.

**Key Words:** *glutathione peroxidase; glutathione reductase; glutathione transferase; placenta; preterm delivery*

The important role of the placenta in the functioning of the mother—placenta—fetus system was confirmed by many studies. Placental failure is the leading cause of fetal pathology and death [5]. Placental failure is characterized by inadequate exchange in the mother—fetus system due to impaired placental metabolism. Activation of free radical oxidation (FRO) plays an important role in the pathogenesis of preterm delivery [4]. Hyperactivation of FRO in tissues, in particular, in the placenta is prevented by multicomponent antioxidant system ensuring binding and modification of radicals and inhibiting generation of peroxides.

We studied glutathione system and some components of the antioxidant defense in placental tissues of women with spontaneous preterm deliveries at 28-36 weeks.

## MATERIALS AND METHODS

Placental tissue from women with full-term deliveries after normal gestation and women with spontaneous preterm deliveries at 28-36 weeks was examined. Tissue samples from the central and peripheral areas of

the placenta were washed in cold normal saline and homogenized in ice-cold buffer containing 60 mM  $\text{KH}_2\text{PO}_4$  and 105 mM KCl (pH 7.4). The homogenate was centrifuged for 15 min at 10,000 rpm and 4°C. The content of sulfhydryl groups was measured spectrophotometrically using Ellman reagent [9]. Superoxide dismutase (SOD) activity was measured by NBT reduction [6], catalase activity by utilization of  $\text{H}_2\text{O}_2$  [7], glutathione peroxidase activity using tert-butyl hydroperoxide [2], glutathione reductase activity by oxidation of reduced NADP [3], and glutathione-S-transferase (GST) activity by the rate of GS-2,4-dinitrobenzene production [1]. Protein was measured by Lowry's method [8].

The results were processed using standard statistical software.

## RESULTS

No significant differences in SOD and catalase activities in placental tissue were found in women with normal pregnancy and delivery and in women with preterm delivery. However, some components of the glutathione system were changed in the latter group (Table 1). In both the central and peripheral areas of the placenta the content of nonprotein SH groups ac-

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**TABLE 1.** Parameters of Glutathione System in Placenta ( $M\pm m$ )

Parameter	Full-term delivery	Preterm delivery
Nonprotein SH groups, $10^4$ mmol/g tissue		
center	7.2 $\pm$ 0.3 (16)	5.3 $\pm$ 0.4* (11)
periphery	6.2 $\pm$ 0.3 (16)	5.1 $\pm$ 0.3* (10)
Glutathione peroxidase activity, mmol GSH/min/mg protein		
center	40.21 $\pm$ 3.39 (10)	54.31 $\pm$ 5.36*** (12)
periphery	36.67 $\pm$ 4.12 (10)	58.35 $\pm$ 4.67* (12)
Glutathione reductase activity, nmol NADPH/min/mg protein		
center	31.17 $\pm$ 1.51 (10)	36.17 $\pm$ 1.65*** (12)
periphery	29.54 $\pm$ 1.88 (10)	36.70 $\pm$ 1.58** (11)

**Note.** \* $p$ <0.01, \*\* $p$ <0.02, \*\*\* $p$ <0.05 compared to normal. The number of examinees is given in parentheses.

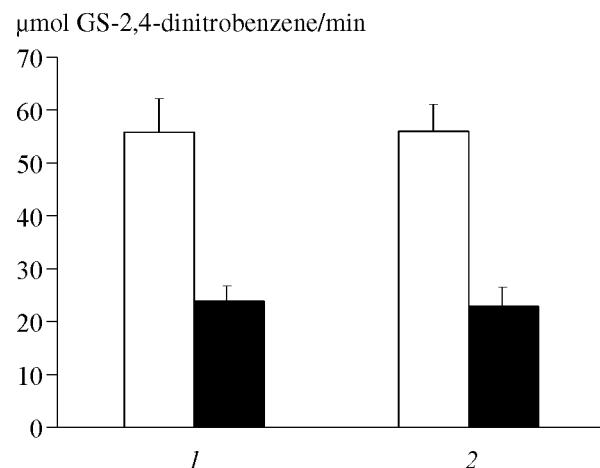
ting as free radical traps significantly decreased. Activity of glutathione peroxidase catalyzing the reaction between reduced glutathione (GSH) and hydroperoxides significantly increased. Activity of glutathione reductase reducing oxidized glutathione also increased. These data suggest that SH compounds possessing antiradical and antiperoxide activities play an important role in the placental antioxidant defense in spontaneous abortion at 28-36 weeks. Apart from neutralization of FRO products, intensified reduction of oxidized glutathione promotes mobilization of functional reserves in the placenta and maintains homeostasis of SH-containing antioxidants.

It was interesting to measure GST catalyzing conjugation of GSH with various hydrophobic substrates in the placental tissue. The placenta contains a single type of GST (GST pi) [10]. GST activity did not depend on its location in the placenta (center or periphery) (Fig. 1). Enzyme activity significantly decreases during preterm delivery, which attests to impaired detoxifying capacity of the glutathione/GST system.

Hence, spontaneous preterm delivery (at 28-36 weeks) was associated with reduced content of SH compounds in the placenta and exhaustion of the glutathione-dependent antioxidant defense system. These changes reflect impairment of nonspecific resistance of the mother—placenta—fetus system, which leads to fetal and neonatal pathologies.

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**Fig. 1.** Glutathione transferase activity (per mg protein) in central (1) and peripheral (2) areas of the placenta in normal (light bars) and preterm delivery (dark bars). All differences from normal are significant.