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## THE ROLE OF OXIDANT STRESS IN THE DEVELOPMENT OF PREMATURE CHILDBIRTH

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## THE ROLE OF OXIDANT STRESS IN THE DEVELOPMENT OF PREMATURE CHILDBIRTH

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### **Resume**

**Objective.** To evaluate the role of lipid peroxidation processes and antiradical protection of cells in pregnant women at risk for preterm birth.

**Material and methods.** 66 pregnant women with habitual miscarriage (32-36 weeks) were examined. The control group consisted of 14 women with a physiological course of pregnancy at the same time of gestation.

**Results.** The level of malonic dialdehyde (MDA), catalase and ceruloplasmin using the enzyme immunoassay method was studied. Revealed changes in AOS parameters in pregnant women with a risk for PL indicate their important role in the regulation of the vital activity of the organism.

**Conclusion.** Comparison of the data allowed us to believe that the enhancement of the processes of lipid peroxidation and the inhibition of the activity of the antioxidant system may be a factor contributing to the development of pregnancy complications during PL

**Keywords:** preterm labor, superoxide dismutase activity, antioxidant system.

## РОЛЬ ОКСИДАНТНОГО СТРЕССА В РАЗВИТИЕ ПРЕЖДЕВРЕМЕННЫХ РОДОВ

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### **Резюме**

**Цель исследования.** Оценка роли процессов липопероксидации и антирадикальной защиты клеток у беременных с риском на преждевременные роды (ПР).

*Материал и методы. Обследованы 66 беременных женщин с привычным невынашиванием (32-36 нед). Контрольную группу составили 14 женщин с физиологическим течением беременности в эти же сроки гестации.*

*Результаты. Изучен уровень малонового диальдегида (МДА), каталазы и церулоплазмينا использованием иммуноферментного метода. Выявленные изменения показателей АОС у беременных с риском на ПР указывают на их важную роль в процессах регуляции жизнедеятельности организма*

*Заключение. Усиление процессов ПОЛ и угнетение активности антиоксидантной системы могут явиться фактором, способствующим развитию осложнений беременности при ПР.*

*Ключевые слова: преждевременные роды, перекисное окисление липидов, антиоксидантная система.*

## БАРВАҚТ ТУҒРУҚНИНГ РИВОЖЛАНИШИДА ОКСИДАНТ СТРЕССНИНГ ЎРНИ

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### *Резюме*

*Мақсад. Липопероксидация ва ҳужайранинг антирадикал ҳимоясини барвақт туғилишига хавфи бўлган аёлларда ролини баҳолаш.*

*Материал ва усуллар. Барвақт туғилиш хавфи бор ҳомиладорлар (66та) (32 - 36 ҳафта) ва (14та) физиологик кечувчи ҳомиладор аёллар текширилди.*

*Натижалар ва хулоса. Липидларнинг перекись оксидланиш жараёни ва антиоксидант тизимнинг активлигини пасайиши барвақт туғруқларнинг асоратланишига хавф омили бўлади.*

*Калит сўзлар: барвақт туғруқ, липидларнинг перекись оксидланиши, антиоксидант тизим.*

### **Relevance**

In the modern literature, a key role in the pathogenesis of preterm labor is assigned to the systemic inflammatory response syndrome, in which reactions occur that lead to metabolic disorders in the mother's body [6]. Since metabolic disorders change the balance between oxidative and reduction processes in peripheral blood and tissues, preterm labor is often accompanied by the manifestation of symptoms typical of

chronic oxidative stress - the accumulation of lipid peroxidation products, products of covalent protein modification, a decrease in the efficiency of energy-converting mitochondrial membranes, and an increase in the number of damage to the nuclear and mitochondrial DNA [1,3,4,5]. With an increase in the effect on the body of various factors of a chemical or physical nature, LPO processes are greatly enhanced and the formation of ROS increases. When the balance of these two processes is disturbed, oxidative stress develops, which can manifest itself at the cellular, tissue and organismal levels, which leads to the development of many pathological processes [7,8,9]. To date, in the works devoted to the problem of preterm birth, there are insufficient data on the LPO-AOS system, on the basis of which it is possible to accurately determine the contribution of oxidative stress processes that occur in the mother-placenta-fetus system.

**The aim of this** study was to assess the role of lipid peroxidation and antiradical cell protection in pregnant women at risk of preterm labor.

### **Material and methods**

We examined 66 pregnant women with a history of recurrent miscarriage (risk group for premature birth) in the dynamics of the gestational period (32-36 weeks). The control group consisted of 14 women with physiological pregnancy during the same gestational period. Pregnant women underwent general clinical and laboratory research methods. The age of the examined pregnant women ranged from 21 to 28 years. Analysis of the frequency and nature of extragenital diseases in the examined women showed a high frequency of their occurrence, in particular, ARVI-81%, pathology of ENT organs -24%, diseases of the gastrointestinal tract -30.5%, diseases of the urinary system-35.5%.

Determination of the level of diene conjugates (DC) and malondialdehyde (MDA) was carried out by spectrophotometric methods [2,8]. For the quantitative determination of peroxides (OxyStat), total antioxidant status (TAS) and superoxide dismutase (SOD) activity, we used a COBAS-411 immunoassay analyzer from ROSH and reagents from the same company.

Statistical analysis of the data was carried out using parametric statistical methods using Microsoft Office Excel (version 2007, Microsoft Corporation, USA, 2007) and Statistica software package for statistical analysis (version 5.5 A, StatSoft Inc., USA, 1999).

### **Result and discussion**

The high conjugation of mitochondrial membranes in the placenta under conditions

of oxidative stress in PR is of a dualistic nature, on the one hand, contributing to the generation of ROS, which act as a PR trigger when the antioxidant capacity of the mother-placenta-fetus system is exceeded, on the other hand, it provides an adequate supply of energy necessary for the placenta to perform its functions. In this regard, the possibility of determining the antioxidant capacity before the onset of the critical moment of irreversible development of the PR state is of great importance. In pregnant women at risk of PR, already at 32-36 weeks, the level of malondialdehyde (MDA), as can be seen from the presented research results, increases, which adversely affects the state of low and especially low density lipoproteins (LP), leading to the appearance of oxidized forms of these proteins ( OLP). Under oxidative stress, these proteins undergo carbonylation with the participation of aldehyde and carbonyl derivatives of fatty acid peroxidation. Oxidized LP (OLP) form spatial structures similar to bacterial wall lipopolysaccharides (LPS) and possess the same activating effect on Toll-like receptors, in particular, TLR 4. In macrophage cells, after the binding of OLP to TLR4, the NF-regulatory pathway is activated. kB and, ultimately, the synthesis of pro-inflammatory cytokines and a new round of even more powerful generation of reactive oxygen species. In addition, the JAN and ERK2 signaling pathways are activated in the cell, activating proinflammatory defense responses. The emerging positive feedback loop, leading to an avalanche-like course of the inflammatory process, plays a decisive role in the achievement of reactive oxygen species threshold values, leading to the induction of preterm labor in pregnant women. The state of the protective antioxidant system (AOS) in the mother's blood, the main component of which is the enzyme catalase, is of key importance in preventing this situation.

**Table Indicators of LPO and AOS system in pregnant women at risk of preterm birth**

<b>Studied indicators</b>	Physiologically flowing pregnancy n = 14	Pregnant women at risk of preterm birth n = 66
Diene conjugates (DC), $\mu\text{m} / \text{l}$	18,34 $\pm$ 1,67	33,72 $\pm$ 3,45*
Malonic dialdehyde (MDA) $\mu\text{mol} / \text{L}$	4,48 $\pm$ 0,31	8,45 $\pm$ 0,71*
OxyStat indicators, $\mu\text{mol} / \text{l}$	149,98 $\pm$ 11,67	607,54 $\pm$ 18,52*
General antioxidant status, $\text{mol} / \text{l}$	1,33 $\pm$ 0,11	2,24 $\pm$ 0,12*

Superoxide dismutase activity (SOD), units / l	134,17±11,74	224,78±18,01
Ceruloplasmin, mg / dl	36,24±3,23	89,43±7,42*
Catalase nmol / l	589,45±14,04	989,71±14,56*

Note: \* - reliability of differences  $P < 0.05$

The level of the enzyme  $\beta$ -catalase, in our studies, in pregnant women with a risk of PR is increased by only 68%, while the level of malondialdehyde (MDA) is increased by 88%, which determines the direction of further development of events. This explains the significance of differences in the level of malondialdehyde (MDA) for the studied groups of pregnant women at risk of PR, since this parameter is dependently controlled by catalase activity. Thus, it can be concluded that at the risk of PR at 32-36 weeks of gestation, low catalase values in blood plasma are a negative predictor factor for the maintenance of pregnancy.

Note that significant differences in SOD activity between control and pregnant women with a risk of PR does not contradict the data on catalase activity, but, on the contrary, is complementary to them, since in the opposite case the level of peroxide generated by SOD from the perhydroxyl radical would be lower than the critical one for the moment of manifestation of the PR threat and the premature birth itself.

In our case, the same level of increase in SOD and catalase provides the onset of PR.

It is known that, in addition to ferroxidase activity and copper-binding function, ceruloplasmin has a noticeable antioxidant activity and is involved in the neutralization of peroxides. It dismutates superoxide radicals and is an antioxidant that prevents lipid peroxidation. It was found that, in contrast to SOD, which is in the cells of tissues and blood, ceruloplasmin functions in plasma and intercepts free radical forms of oxygen, protecting lipid-containing biostructures from their damaging effects. In this regard, ceruloplasmin is considered as a component of the antioxidant biological system, playing the role of a universal extracellular "scavenger" of free radicals. In the mechanism of its antioxidant effect, the ability to limit the oxidation of  $Fe^{2+}$  to  $Fe^{3+}$  and thereby weaken the processes of free radical oxidation, which requires ions of non-heme iron, is important. The analysis of the obtained research results showed an increase in the activity of ceruloplasmin in pregnant women with a risk of PR by an average of 2.5 times when comparing pregnant women with the physiological course of gestation.

## Conclusions

Thus, a comparison of clinical and biochemical data suggests that an increase in LPO processes and inhibition of the antioxidant system activity may be a factor contributing to the development of pregnancy complications at a risk of PR. The revealed changes in AOS indices in pregnant women at risk for PR indicate their important role in the processes of regulation of the body's vital activity. It is rather difficult to explain the diversity of the revealed changes occurring in the body of a woman with PD due to the multifaceted nature of the pathological process in response to the onset of intoxication. The action of external prooxidants, increased oxygen consumption, ionizing and ultraviolet radiation, air, water and food pollution, lack of natural antioxidants (vitamins E, K, A, selenium, etc.), congenital insufficiency of antioxidant defense enzymes, other conditions can lead to tension in the antioxidant defense system of the body and cause the so-called "oxidative stress", which manifests itself at the molecular and cellular levels.

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