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Monitoring changes in serum 8-isoprostane concentration as a possible marker of oxidative stress in pregnancy

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ABSTRACT

Introduction: Oxidative stress represents a pathophysiological mechanism lying behind occurrence of different acute and chronic diseases. Pregnancy, mainly due to placenta rich with mitochondria, is also being associated with the state of oxidative stress. Numerous markers have been proposed in order to test oxidative stress in pregnancy state, one of them being 8-isoprostane.

The aim of this study was to analyse serum concentrations of 8-isoprostane as a possible oxidative stress marker in pregnancy.

Methods: Serum concentrations of 8-isoprostane were measured in overall population of 84 woman, between 20 and 30 years of age. Tested population was divided in 2 groups: 42 pregnant woman were classified as being either in the first or second trimester of pregnancy. In the control group healthy non-pregnant women were included. Concentration of 8-isoprostane in serum was determined by commercial 8-isoprostane EIA test kit of Cayman Chemical Company, USA.

Results: The 8-isoprostane levels were significantly increased in pregnant women in relation to healthy non pregnant women ($p<0.05$). The 8-isoprostane levels were significantly increased in second and third trimester of pregnancy ($p<0.05$).

Conclusions: According to the obtained results, 8-isoprostane might be used as a possible marker of oxidative stress in pregnancy state, but not as a biomarker for the risk of complications development in pregnancy in analysed population.

Keywords: oxidative stress, pregnancy, 8-isoprostane

INTRODUCTION

Oxidative stress generally describes a state where a cell antioxidative defence is inadequate to completely inactivate reactive oxygen compounds which are being generated due to increased production, decreased antioxidative defence, or both. The main consequence of oxidative stress is the damage of DNA, lipids and proteins, which then compromise the health of a cell or induce production of different reactive compounds leading to the death of the cells by necrosis or apoptosis. Oxidative stress can be

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monitored by the analysis of special oxidative stress biomarkers isolated from biological fluids and tissues (1).

Lipid peroxidation represents an oxidative damage seizing cell membranes, lipoproteins and other molecules containing lipids in conditions of oxidative stress existence. Peroxidation of membrane lipids caused by oxidative stress leads to changes in membrane biological characteristics, such as fluid degree change, leading to inactivation of membrane receptors and enzymes. Lipid peroxidation can lead to increased cell damage through piling of oxidative products, out of which some are chemically reactive and modify macromolecules by creating covalent bounds. Lipid peroxidation products are therefore used as oxidative stress biomarkers. Different and relatively weaker final products are created by lipid peroxidation, mostly α,β- unsaturated reactive aldehydes, such as malondialdehyde (MDA), 4-hidroxynonenal (HNE), 2-propenal (acrolein) and isoprostanes, which can be determined in plasma and urine and serve as indirect oxidative stress indicators (2).

Isoprostanes represent stabile products of lipid peroxidation, being present in all normal biological fluids and tissues in detectable quantities (3). They are created by initial peroxidation of arachidonic acid esterified by tissue lipids (4). Their in vivo synthesis, as it has been found in animal models, increases due to oxidative damage. 8-isoprostane, is one of their representatives and can serve for accurate estimate of overall F2-isoprostane endogenous production (2).

Oxidative stress is part of pregnancy physiology and, according to literature data, important factor for embryogenesis (5,6).

Numerous data suggest that lipid peroxidation products and antioxidative protection components change significantly in pregnancy (7). Increased intensity of lipid peroxidation in pregnant woman placenta (8,9) has been reported. However, antioxidative response in healthy pregnant women is present at the level that ensures the protection from increased risk and it is a part of pregnancy physiology (2).

According to the research results and data from literature in the last years, the level of oxidative stress is increased in pregnant women carrying a risk for the development of pregnancy complications or for those that already have some of the complications: hypertensia, diabetes, preeclampsia, fetal growth lagging (10-20).

Elevated levels of 8-isoprostane, as a marker of oxidative stress have been reported during normal pregnancy (21). On the other hand, isoprostanes, including 8-isoprostane have also been associated with an increased risk of an preeclampsia and a decreased proportion of female births (22,23).

Having in mind contradictory research results related to the importance of isoprostane monitoring as one of the biomarkers of oxidative stress in pregnant women, in this work, the imperative was to investigate the level of oxidative stress in the population of pregnant women in the first and in the second trimester of pregnancy, when the beginning of potential complications of oxidative stress occur. The validity of serum 8-isoprostane concentration as a biomarker for pregnancy complications risk assumptions was investigated, too.

METHODS

In this case-control study, serum 8-isoprostane concentrations were analysed in both pregnant and nonpregnant women. All 84 blood samples from Gradačac and near region, Bosnia and Herzegovina, were collected in the biochemical laboratory of Gradačac hospital during two months, and 8-isoprostane serum levels were investigated. Average age of tested population was between 20 and 30 years. Main experimental group was divided into two subgroups: 42 women in the first and 42 women in the second trimester of pregnancy. Pregnant women in the test group were controlled by specialists from Gynecological department of Gradačac hospital, Bosnia and Herzegovina. All of them were users of prenatal vitamins and folic acid. The total of 42 healthy fertile non pregnant women were used as control group.

From all patients recruited, informed consent was obtained. Exlusion criteria for both test and the control group were chronic diseases, inflammatory processes and infections. This study has been approved by the Hospital Ethic committee.

8-isoprostane concentration was detected with EIA kit, Cayman Chemical Company. This assay is based on competition between 8-isoprostane and

conjugate 8-isoprostane-acetylcholinesterase (8-isoprostane indicator) for a limited number of 8-isoprostane specific rabbit antiserum binding sites. Because the concentration of 8-isoprostane indicator is constant, while the concentration of 8-isoprostane varies, the amount of 8-isoprostane indicator that is able to bind to antiserum is inversely proportional to the concentration of 8-isoprostane in the sample.

Statistical analysis

The results were evaluated by T-test. For performed test, $p<0.05$ was considered as statistically significant. For statistical analyses we used SPSS 15.0 software (SPSS Inc., USA).

RESULTS

Concentration of 8-isoprostane in serum was found to be significantly higher in pregnant woman when compared to control group ($p<0.0001$) (Figure 1).

There was statistically significant difference between serum 8-isoprostane average values in the first trimester pregnant women and in the control group ($p<0.0001$) (Figure 2).

Statistically significant differences of serum 8-isoprostane concentration were also found in second trimester pregnant women and in the control group ($p<0.0001$) (Figure 3).

When concentrations of 8-isoprostane levels were compared between the first and the second trimes-

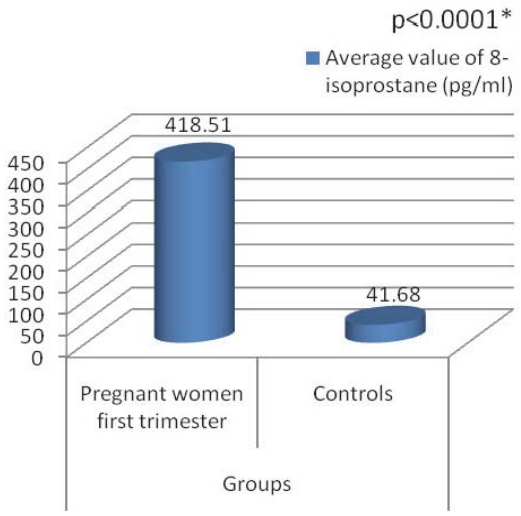

FIGURE 2. - 8 - isoprostane average values for the first trimester pregnant women and the control
*p – significancy (if p<0.05 then there is significant correlation between investigated parameters)

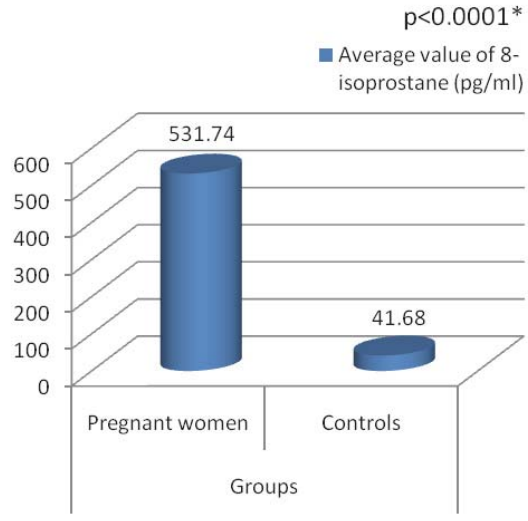

FIGURE 1. - 8 - isoprostane average values for pregnant women and control group
*p – significancy (if p<0.05 then there is significant correlation between investigated parameters)

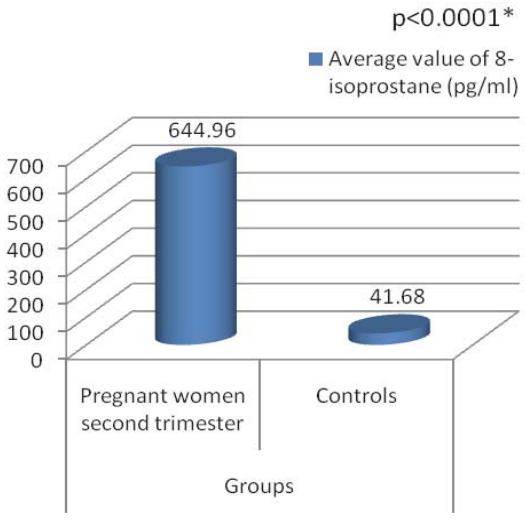

FIGURE 3. - 8 - isoprostane average values for the second trimester pregnant women and the control
*p – significancy (if p<0.05 then there is significant correlation between investigated parameters)

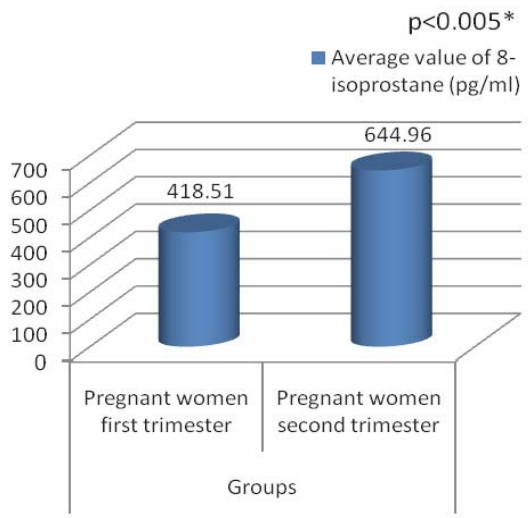

FIGURE 4. - 8 - isoprostane average values for the first trimester and the second trimester pregnant women
*p – significancy (if p<0.05 then there is significant correlation between investigated parameters)

ter, statistically significant increase in 8-isoprostane concentration was found in the second trimester pregnant women compared to the first trimester pregnant women ($p<0.005$) (Figure 4).

DISCUSSION

Level of oxidative stress is important factor in embryogenesis, as well as in pregnancy and normal birth. Under conditions of oxygen deficiency in tissues (10), stimulation of neovascularisation process and induced angiogenesis occurs in pregnancy, which itself is the result of hypoxia. On the other hand, overproduction of pro oxidants and increased oxidative stress lead to increased lipid peroxidation and accumulation of increased lipid peroxidation biomarkers in placenta (4). This occurs due to decreased intracellular space and disordered metabolism. The consequence of increased oxidative stress is apoptosis which results in embryo fragmentation and fetal embryopathies (24).

Numerous studies suggest that 8-isoprostane as an oxidative stress indicator is increased in pregnancy and in pathological states of pregnancy (11-20), while a few suggest no differences in its levels during development of pregnancy (4). This seems to be in accordance with results obtained in our study where higher level of 8- isoprostane was detected in both, first and second trimester pregnant woman when compared to controls, proving out the fact that pregnancy by itself is a state of oxidative stress (7,8). As described earlier, results of recent studies also showed that detecting high levels of oxidative stress early in pregnancy, during first two trimesters, is associated with later complications (22,23). In this study we found high level of oxidative stress in early stage of pregnancy, during first two trimesters while we have no results in the third trimester and pregnancy complications. This is one of study drawbacks together with possible analytical problems based on cross reactions of 8-isoprostane with other F2-isoprostane metabolites, which can be formed in vivo in the examined sample.

CONCLUSIONS

In this work, statistical difference between concentration of serum 8-isoprostane was found between the test group and the control group, between pregnant women in the first and in the second trimester of pregnancy and the control group, as well as between pregnant women in the two different trimesters of pregnancy. Patients in later stage of pregnancy have higher serum concentrations of 8-isoprostane than women in earlier stage.

Evidentially, pregnancy is by itself state of higher level of oxidative stress. 8-isoprostane is useful biomarker of oxidative stress in pregnancy, but at least in this work, in tested Bosnian population, it could not be established that it is useful marker for risk for pregnancy complications.

COMPETING INTERESTS

The authors declare no competing interests.

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