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Differences in Malondialdehyde and Catalase Activity Levels Between Abortion and Normal Pregnancy

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The imbalance between antioxidant and free radical in pregnancy causes pathological changes that can lead to pregnancy complications such as abortion. Catalase is one of the antioxidant enzymes that works as a binder of free radical. The increase in free radical is characterized by an increase in biochemical markers of malondialdehyde. The aim of this study was to evaluate the mean difference of catalase activity and malondialdehyde level in abortion and normal pregnancy. This study was an observational study with cross-sectional design. A total of 42 pregnant women before 20 weeks of gestation were enrolled (14 threatened abortion, 14 normal pregnancy and 14 incomplete abortion). Subjects were taken from the maternity ward of Dr. M. Djamil and Dr. Reksodiwiryo Hospital in Padang, Indonesia. The intravenous blood samples were measured by spectrophotometry. The mean difference was statically analyzed by ANOVA test. The mean level of malondialdehyde in subjects with incomplete abortion, threatened abortion and normal pregnancy were 4.02±0.36, 3.46±0.39 and 2.83±0.21 nmol mL^{-1} ($p<0.001$), respectively. The mean level of catalase activity in subjects with incomplete abortion, threatened abortion and normal pregnancy were 51.10±12.20, 66.46±9.11 and 78.26±8.88 IU mg^{-1} ($p = 0.002$), respectively. The mean level of catalase activity was lower in abortion than normal pregnancy. The mean level of malondialdehyde was higher in abortion than normal pregnancy. The imbalance of catalase and malondialdehyde concentration were associated with abortion.

Key words: Malondialdehyde, catalase, threatened abortion, incomplete abortion, normal pregnancy

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INTRODUCTION

Abortion is defined as a termination of a pregnancy before 20 weeks of gestation or when the fetal weight is less than 500 g. Clinically, the most frequent abortion encountered in the hospital is incomplete abortion. Patients usually come with bleeding and severe abdominal pain. The second one is threatened abortion. Threatened abortion is the most common complication in the first half of pregnancy and have incidence about 20-25%. Less than 30% of the women who experience threatened abortion will end in spontaneous abortion[1].

There are many factors that associated with abortion, so it is hard to determine the exact mechanism. In spite of many possibilities, there is now a clear evidence that abortion is associated with placental oxidative stress. The abnormal placentation will lead to placental oxidative stress with resultant destructive effects on the syncytiotrophoblast. The theory has been proposed as a mechanism involved in the etiopathogenesis of abortion[2].

The body has many antioxidant systems to defend the excessive Reactive Oxygen Species (ROS) production[3]. In a healthy body, ROS and antioxidant remain in balance. When the body has an excessive amount of ROS, Oxidative Stress (OS) then occurs. An increase in the expression of oxidative stress marker in the trophoblast was detected in abortion and this was speculated to be a cause of early pregnancy loss[4].

Antioxidant system divided into enzymatic and nonenzymatic group. Catalase (CAT) is one of enzymatic antioxidant that can remove hydrogen peroxide (H_2O_2), prevents lipid peroxidation in the cell membrane and works as free radicals binding[5]. The CAT role in pregnancy is very important, in early pregnancy CAT plays a role for implantation by protecting the blastocysts from superoxide radicals in the endometrium. The CAT is also important for embryonic development and the maintenance of early pregnancy. The CAT level was found increased during pregnancy and low CAT activity in plasma or placenta found in cases of spontaneous abortion[6]. Another study also suggests that low antioxidant level increases the risk of spontaneous abortion[7].

Free radicals are thus highly unstable molecules that have electrons available to react with a various organic substrate such as lipids, proteins and DNA[8]. Accumulation of lipid peroxides may cause not only tissue damage but also some biological events to accelerate the termination of pregnancy. It has been reported that ROS or lipid peroxide stimulate synthesis of PGF2α that causes uterine contraction[6]. Oxidative stress has been variably determined by many ways. The most reliable assessment of free radicals synthesis is using assays directly to detect the superoxide or other free radical. However, this technique is difficult and require specialized document. In another side, measurement of the products of oxidative modification product provides the most direct and possible assessment of oxidative stress. Malondialdehyde (MDA) is a metabolite of lipid peroxides that detectable in plasma and was used as an indicator of lipid peroxidation[9]. This study was carried out to estimate the mean difference of CAT and MDA in normal pregnancy, threatened abortion and incomplete abortion.

MATERIALS AND METHODS

This was an observational study with cross-sectional design on February-December, 2014. The population was all pregnant women before 20 weeks gestations were enrolled in the maternity ward of Dr. M. Djamil Hospital and Dr. Reksodiwiryo Hospital, Padang, Indonesia. Subjects were taken by consecutive sampling method. Cases were those diagnosed with threatened and incomplete abortion by a specialist doctor. Meanwhile, controls were normal pregnant women without any other comorbid.

Exclusion criteria were a mother with hydatidiform mole, uterus disorder, myoma, history of provocating and recurrent abortion. After providing informed, written consent, subject's blood was taken from antecubital vein for analyzed the CAT activity and MDA concentration with spectrophotometry method in Biomedical Laboratory of Medical Faculty of Andalas University.

The significant difference among the three groups was analyzed with ANOVA test. If $p<0.05$ was found, then the analysis continued with *post hoc* multiple comparison test to determined the differences between two group. Statistical analysis was conducted using a computer program.

RESULTS

During the study period, 42 blood samples were collected, consisting of 14 subjects with threatened abortion, 14 subjects with incomplete abortion and 14 subjects with normal pregnancy before 20 weeks gestations. Table 1 shows the activity of CAT enzyme in incomplete abortion group was 51.10±12.20 IU mg^{-1}, the threatened abortion group was 66.46±9.11 IU mg^{-1}, whereas normal pregnancy group was 78.26±8.88 IU mg^{-1}. The analysis with statistical tests ANOVA found that $p<0.001$. To saw the specific difference between two subjects, the analysis continued by *post hoc* multiple comparisons test. As presented in Table 2, there were significant differences of CAT activity between incomplete abortion group and threatened abortion ($p<0.001$), incomplete abortion and normal pregnancy ($p<0.001$), threatened abortion and normal pregnancy ($p = 0.01$).

Table 1: Difference of catalase activity in incomplete abortion, threatened abortion and normal pregnancy

Parameters	Catalase activity Mean±SD (IU mg^{-1})	95% CI	p-value*
Incomplete abortion	51.10±12.20	44.06-58.15	<0.001
Threatened abortion	66.46±9.11	61.20-71.72	
Normal pregnancy	78.26±8.88	73.13-83.38	

*p-values are obtained by ANOVA test, SD: Standard deviation, CI: Confidence interval

Table 2: *Post hoc* test for the difference of the mean level of catalase activity in incomplete abortion, threatened abortion and normal pregnancy

Parameters	Incomplete abortion	Threatened abortion	Normal pregnancy
Incomplete abortion	-	<0.001*	<0.001*
Threatened abortion	<0.001*	-	0.01*
Normal pregnancy	<0.001*	0.01*	-

*p-value obtained by Tukey's test to determine the difference between two groups

Table 3: Difference of malondialdehyde level in incomplete abortion, threatened abortion and normal pregnancy

Parameters	Malondialdehyde level Mean±SD (nmol mL^{-1})	95% CI	p-value*
Incomplete abortion	4.02±0.36	3.81-4.23	<0.001
Threatened abortion	3.46±0.39	3.24-3.68	
Normal pregnancy	2.83±0.21	2.71-2.96	

*p-values are obtained by ANOVA test, SD: Standard deviation, CI: Confidence interval

Table 4: *Post hoc* Test for the difference of the mean level of malondialdehyde in incomplete abortion, threatened abortion and normal pregnancy

Parameters	Incomplete abortion	Threatened abortion	Normal pregnancy
Incomplete abortion	-	<0.001*	<0.001*
Threatened abortion	<0.001*	-	<0.001*
Normal pregnancy	<0.001*	<0.001*	-

*p-value obtained by Tukey's test to determine the difference between two groups

As presented in Table 3, the mean level of MDA in incomplete abortion group was 4.02±0.36 nmol mL^{-1}, the threatened abortion group was 3.46±0.39 nmol mL^{-1}, whereas in normal pregnancy group was 2.83±0.21 nmol mL^{-1} with p = 0.00 by ANOVA test. To saw the difference between two group analysis continued with *post hoc* test. According to the Table 4, it was found that there were significant differences of MDA level between incomplete abortion with threatened abortion ($p<0.001$), incomplete abortion and normal pregnancy group ($p<0.001$), threatened abortion and normal pregnancy ($p<0.001$).

DISCUSSION

In this study, it was found that the mean of MDA level of incomplete abortion was higher than threatened abortion and normal pregnancy ($p<0.05$). Meanwhile, the mean level of CAT activity was lower in incomplete abortion than threatened abortion and normal pregnancy ($p<0.05$).

This study was accordance with a study conducted by Abdul-Barry *et al.*[8] that found the serum MDA level was significantly higher in patients with a history of recurrent spontaneous abortion than women with a healthy pregnancy. Ozkaya *et al.*[10] also reported that the spontaneous abortion before 8 weeks gestation was associated with higher serum of MDA than healthy pregnancy (66.4±13.7 vs. 40.3±16.1, $p<0.01$). Because MDA is a side product of lipid peroxidation, the increase in MDA level may reflect an overproduction of lipid peroxides and alter antioxidant defend mechanism. Jauniaux *et al.*[11] suggested the theory of how the free radical is higher in abortion than in normal pregnancy. They found that the intervillous O_2 flow appeared much earlier in the abortion group so it can lead to excessive free radicals production that can cause abortion[11].

The oxidative stress during pregnancy occurs in response to the fetoplacental energy demand. How the oxidative stress cause an abortion have been studied by other study. Many mechanisms have been proposed as the theory. Zhu *et al.*[12], suggested three factors that has an impact on the pathogenesis of abortion. First, the ROS can cause the lipid peroxidation injury in the embryo. Second, the increasing free radicals can change oxygen partial pressure in embryonic cells. And the last, increased of free radicals can lead to ischemia-reperfusion injury in the fetus[12].

Actually, increased of antioxidants activity also found in early healthy pregnancy. These indicate that the oxidative stress actually also occurs in normal pregnancy but the sufficient antioxidants are defended the free radicals and prevented the damage[6,13,14]. In this study, the mean activity of CAT enzyme of incomplete abortion was lower than normal pregnancy and threatened abortion ($p<0.05$). It means that there were differences between the CAT enzyme activity in incomplete abortion, threatened abortion and normal pregnancy. It was suggested that the excess of free radicals and the decreased of antioxidants in this study were associated with the abortion.

Sugino *et al.*[6] found that CAT total activity was decrease and prostaglandin F2α synthesis was increase in decidua in cases of spontaneous abortion with vaginal bleeding. They proposed that the termination of pregnancy was caused by decreasing activity of CAT which stimulates the synthesis of prostaglandins[6]. This study was accordance with the study by Yigenoglu *et al.*[15] that found the total antioxidant capacity is lower in pregnant women with history of spontaneous abortion than healthy pregnant women. It also accordance with a study conducted by Biri *et al.*[16] that found the CAT activity was higher in abortion group than in control group (87.62±8.19 vs 44.47±3.79 IU mg^{-1}).

CONCLUSION

Abortion group had lower antioxidant concentration and higher free radicals than normal pregnancy. There was an imbalance of free radical and antioxidant concentration in abortion.

SIGNIFICANT STATEMENT

The imbalance of free radical and antioxidant has been proposed to one of many theories that can cause abortion. This study tried to determine the comparison of antioxidant and free radical level by analyzed the catalase activity and malondialdehyde concentration in normal pregnancy and

abortion. Malondialdehyde (MDA) is a metabolite of lipid peroxides that used as an indicator of lipid peroxidation as a free radical. Meanwhile, catalase is one of antioxidant that works as free radicals binding by preventing lipid peroxidation in the cell membrane. The result of this study will determine the imbalance of free radicals and antioxidants in abortion and will help the medical field to develop the prevention of abortion.

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