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RESEARCH

Differences in Blood Plasma Levels of Vitamin C in Term Pregnancy With Premature Rupture Of Membranes and Blood Plasma Levels of Vitamin C in Term Pregnancy Without Premature Rupture Of Membranes

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Abstract

Premature rupture of membranes is the most common complication of pregnancy. The incidence of premature rupture of membranes in pregnancy ranged from 6% to 10%, and 20% of these cases occur before 37 weeks gestation. The incidence of premature rupture of membranes in Indonesia ranges from 4.5% to 7.6% of all pregnancies. This research was conducted to determine the cross-sectional differences in the blood plasma levels of vitamin C in term pregnancy premature rupture of membranes with blood plasma levels of vitamin C in term pregnancy without premature rupture of membranes in M. Jam- il Padang hospital, Achmad Muchtar Bukittinggi hospital, and Pariaman Hospital. There are significant differences in vitamin C blood plasma levels in term pregnancy with premature rupture of membranes and term pregnancy without premature rupture of membranes ($P < 0.05$). Mean levels of vitamin C in blood plasma at term pregnancy with premature rupture of membranes lower than in the blood plasma levels of vitamin C in term pregnancy without premature rupture of membranes.

Keywords: *Premature rupture of membrane in aterm, blood plasma levels of vitamin C*

INTRODUCTION

Premature rupture of membranes is one of the most common pregnancy complications. The incidence of premature rupture of membranes in pregnancy ranges from 6% to 10%, and 20% of these cases occur before 37 weeks' gestation. The incidence of premature rupture of membranes in Indonesia ranges from 4.5% to 7.6% of all pregnancies.[1]

Premature rupture of membranes causes an increase in complications in pregnancy, both at term and preterm gestation. The risk of infection after the rupture of the membranes affects the mother, fetus, or neonate. The incidence of neonatal infection after premature rupture of membranes for more than 24 hours is about 1% and if there is clinical chorioamnionitis the risk increases to 3% to 5%.[2]

Chorioamnion is a multiple and complex layer consisting of epithelial and supporting tissue elements where each component has an important role in metabolism, which is

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important for physiological integrity for pregnancy development. Amnion gets its strength through collagen. How exogenous and endogenous mechanisms can weaken the fetal membrane is still under active investigation. Endogenous factors such as local variations in the membrane or collagen depletion and exogenous factors such as effects caused by microbial metabolism, hosts or due to nicotine which reduces antiprotease activity also cause local membrane disturbances.[3]

The strength and integrity of the chorioamnion are maintained by a balance of intrinsic factors that regulate the synthesis and degradation of connective tissue. Matrix metalloproteinases control collagen degradation in chorioamnions. Tissue inhibitors of metalloproteinases or TIMPS.3 regulate the release of matrix metalloproteinases

The unstable molecules produced continuously in the body known as reactive oxygen species (ROS) are said to produce tissue damage that causes premature rupture of membrane (PROM) / premature rupture of membranes. Chorioamnion exposure with ROS is said to increase matrix metalloproteinase, causing premature rupture of membranes. There is normally a balance between production and elimination from ROS. Oxidative stress occurs when prooxidants outnumber antioxidants. [4]

Vitamin C (ascorbic acid) is a water-soluble vitamin that is not synthesized by humans. Therefore, this essential vitamin must be obtained from food. As we know, vitamin C is an antioxidant. The body uses a variety of antioxidants to limit tissue damage caused by free radicals. Ascorbic acid directly stimulates collagen synthesis. Ascorbic acid also functions as a reducing agent by sending a hydrogen atom with its single electron to the ROS. Ascorbic acid makes collagen strong and stable. [5]

Oxidative stress occurs when prooxidants exceed antioxidants so that it can cause premature rupture of the membranes and one of the roles of vitamin C is to send hydrogen atoms with their single electrons to the ROS to make collagen stronger and more stable, therefore researchers want to compare the vitamin C levels of pregnant blood plasma at term in ruptured membranes. Premature pregnancy without premature rupture of membranes in several hospitals in West Sumatra, namely Dr.M. Djamil Padang Hospital, Achmad Mochtar Bukittinggi Hospital, Pariaman Hospital.

METHOD

This study was conducted using a cross-sectional method to determine the differences in blood plasma vitamin C levels in term pregnancy with premature rupture of membranes and blood plasma vitamin C levels in term pregnancy without premature rupture of membranes in RS.Dr.M. Djamil Padang, RSU Achmad Mochtar Bukittinggi, Pariaman Hospital.

In subjects who matched the inclusion and exclusion criteria, blood samples were taken as much as five cc, put into a 5 cc vacutainer tube and carried out a centrifuge then

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the serum was separated 2 cc into a microtube and sent to the regional health laboratory to check the level of vitamin C in blood plasma. Examination using a special ascorbic acid kit for serum type KT671-100 using the chromatography method. The results were recorded and then analyzed the data.

RESULTS

Research has been conducted to determine the comparison between blood plasma vitamin C levels of term pregnant with premature rupture of membranes and term pregnancy without premature rupture of membranes in several hospitals in West Sumatra. This research was conducted on pregnant women who came to the delivery room at Dr. M. Djamil Padang, Achmad Mochtar Hospital Bukittinggi, RSUD Pariaman and examinations were carried out at the Padang Health Laboratory in the period March 2014 - September 2014. The total number of women included in the statistical calculation after the inclusion and exclusion criteria were met was 144 people, divided into 2 groups, namely 72 people in the group pregnant at term with amniotic fluid. Premature rupture and 72 people in the term pregnant group without premature rupture of membranes.

Of the 144 samples that met the inclusion and exclusion criteria, it was found that the characteristics of the study sample were based on age, parity, smoking, and infection, as shown in Table 1.

Table 1. Characteristics of Samples

	Did not experienced RPOM (n-72)	Experienced PROM (n-72)	Total	P
Age	29,47±5,22 tahun	29,00±5,53 tahun		0,600
Parity	Nullipara 26 (36,1%)	29 (40,3%)	55 (38,19%)	0,153
	Multipara 48 (83,9%)	43 (59,7%)	89 (81,81%)	
Smoke	Yes 1 (1,4%)	4 (6,6%)	6 (3,47%)	0,174
	No 71 (98,6%)	68 (94,4%)	139 (96,53%)	
Infection	Yes 1 (1,4%)	7 (9,8%)	8 (5,55%)	0,002
	No 71 (98,6%)	65 (90,29%)	135 (94,45%)	

The results of statistical analysis are shown in Table 1 based on the age of the respondents. It was found that the mean age values were almost the same in pregnant women at term without PROM with aterm pregnancy in PROM. The results of further statistical analysis showed that the age difference between term pregnant women without ruptured membranes and term pregnant women with ruptured membranes did not significantly differ. This can be seen from the p-value of 0.600 (p> 0.05).

The number of term pregnant women without PROM nulliparous was smaller than that of pregnant women with PROM nullipara. In contrast, in multiparity parity, term pregnant

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women without PROM was higher than at term pregnant woman with PROM. The results of further statistical analysis, parity in pregnant women without rupture of membranes and pregnant women with ruptured membranes did not have a significant difference. This can be seen from the p-value of 0.153 (p> 0.05).

At term pregnant women who smoked with PROM were greater than at term pregnant women who smoked without PROM. In comparison, at pregnant women with PROM who did not smoke were lower than pregnant women without PROM who did not smoke. The t-test results showed that there was no significant difference between smoking in pregnant women without ruptured membranes and term pregnant women with ruptured membranes. This can be seen from the p-value of 0.174 (p> 0.05).

At term pregnant women without PROM infections were less than at term pregnant women with PROM. In contrast, in terms of pregnant women without PROM without infection, it was higher than at term pregnant women with PROM who were not infected. Further statistical results showed that there was a significant difference in infection (leucocyte levels) in pregnant women without rupture of membranes and pregnant women with ruptured membranes, which had a significant difference, this can be seen from the p-value of 0.002 (p <0.05).

Table 2. Comparison of blood plasma vitamin C levels between term pregnant and premature rupture of membranes with term pregnancy without premature rupture of membranes

	Did not experienced RPOM n = 72	**Experienced RPOM n = 72**	**P**
Minimum	0,35 nmol/mL	1,78nmol/mL	0.001
Maximum	306,43nmol/mL	210,71nmol/mL	
Mean Vitamin C levels	97,56 nmol/mL	60,07 nmol/L	
SD	78,28 nmol/mL	50,33 nmol/L	

Blood plasma vitamin C levels for term pregnant without premature rupture of membranes were higher than blood plasma levels for pregnant at term with premature rupture of membranes. Normality test conducted using Kolmogorov Smirnov normal distribution, this can be seen from the p-value on blood plasma vitamin C levels of pregnant women at term without PROM of 0.110 and the p-value on blood plasma vitamin C levels for pregnant women at term with PROM of 0.174 (p> 0.005) so that can be done t-test. The results of statistical analysis with a t-test showed a significant difference in the mean blood plasma vitamin C levels between the group pregnant at term without premature rupture of membranes and pregnant at term with premature rupture of membranes, this can be seen from the p-value of 0.001 (p <0.05).

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The highest blood plasma vitamin C levels for pregnant at term without PROM were in the range between 80-90 nmol / mL. In comparison, the levels of vitamin C for blood plasma at term pregnant with PROM ranged between 10-20 nmol / mL.

DISCUSSION

Data analysis of sample characteristics in this study showed that the incidence of premature rupture of membranes in pregnant women who smoked was more frequent than in pregnant women without premature rupture of membranes. However, this result was not statistically significant (p> 0.05). This is probably because there are not as many women who smoke in eastern countries like Indonesia. The data obtained here are passive smokers, so to assess whether smoking is associated with the incidence of premature rupture of membranes should be with larger sample size. The risk of premature rupture of membranes at the preterm is doubled in women who smoke during pregnancy. Mothers who smoke are associated with an increased incidence of premature rupture of membranes. Results from a large case-control study showed that the increased risk of premature rupture of membranes associated with smoking (OR = 2.2, 95% CI, 1.4- 3.5) could be reduced by quitting smoking before conception (OR = 1.4, 95% CI, 0.9-2.0) and in the first trimester (OR = 1.6, 95% CI, 0.8-2.9).[6]

Gosselink et al did not find an association of smoking (> 10 cigarettes per day) with premature rupture of membranes (OR = 0.94, 95% CI, 0.48-1.8). The pathophysiological mechanisms by which smoking causes premature rupture of the membranes are nicotine and the main metabolites of cotinine and carbon monoxide, hydrogen cyanide, nitrogen oxides, and other tobacco smoke components distributed to tissues and fluids throughout the body. Smoking increases the risk of premature rupture of the membranes with disruption of the cytokine system, decreased leukocyte function, changes in essential nutritional factors, and impaired function and normal development of the placenta. Smoking may also impair the immune function of the systemic and local reproductive tracts. Nicotine and cotinine concentrated in cervical mucus compared to serum and cigarette smoke constituents also interfere with endogenous antibacterial activity. They may interfere with the macrophage approach to microbes.

The data analysis results of sample characteristics in this study were found in patients with infection (blood leucocyte levels> 16,900 / mm3) the incidence of term pregnant women with premature rupture of membranes was more common than at term pregnant women without premature rupture of membranes. There is one pregnant woman at term without premature rupture of membranes with infection, namely sample number 45 (appendix 6) with blood plasma vitamin C levels 13.21 nmol / L. In contrast, in term pregnant women with premature rupture of membranes there are seven people with sample numbers

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83, 87, 105, 106, 107, 124 and 142 with blood plasma vitamin C levels of 3.21 nmol / mL, 159.28 nmol / mL, 22.5 nmol / mL, 13.92 nmol / mL, 35.35, respectively. nmol / mL, 46.07 nmol / mL and 57.14 nmol / mL.

Infection is said to reduce vitamin C levels. In this study, sample number 45, namely term pregnancy without premature rupture of membranes with infection, found vitamin C levels were quite low, namely 13.21 nmol / mL and in term pregnancy with premature rupture of membranes with infection the levels were obtained. Blood plasma vitamin C with a range of <60 nmol / mL but in sample no.87 (at term pregnant with premature rupture of membranes with infection) the blood plasma vitamin C level was 159.28 nmol / mL, therefore to assess whether the infection lowers plasma vitamin C levels more blood samples needed because in this study only 5.55% of cases had an infection. The infection causes an inexplicable decrease in vitamin C levels. Mac Flax (1977) says this is the effect of the migration of vitamin C-rich polymorphonuclear to the site of infection with the consequence of replacement with immature leukocytes having relatively low concentrations of vitamin C levels. In sample no. 124 (infection and smoking), the blood plasma vitamin C level was 46.07 nmol / mL.

The results of this study indicate that there is a difference in blood plasma vitamin C levels between term pregnant and premature rupture of membranes with term pregnancy without premature rupture of membranes where the blood plasma vitamin C levels for term pregnant with premature rupture of membranes are lower than the levels of vitamin C in blood plasma for term pregnant without premature rupture membranes. Not many studies have compared vitamin C levels in term pregnant blood plasma with premature rupture of membranes between term pregnancies without premature rupture of membranes, but the results of this study are in line with several previous studies seven but in several other studies show the opposite where it is blood plasma vitamin C levels for term pregnant with premature rupture of membranes are higher than levels of vitamin C in blood plasma for term pregnant without premature rupture of membranes.[7]

Research that shows a similar result is a study conducted by E. Casanueva (1998) wherein that study it was said that vitamin C levels <1.8 ug / 108 cells increased the risk of premature rupture of membranes, even said vitamin C levels <1.8 ug / 108 cells. At 28 weeks gestation showed high predictive value ($p < 0.05$). A study by Tejero et al. (2003) showed that vitamin C concentrations in women with premature rupture of membranes during term pregnancy were lower than those in pregnant women with the normal term (without premature rupture of membranes). In contrast to the study of Barret et al (1994), there was no relationship between low levels of vitamin C and the incidence of premature rupture of membranes, and in that study it was said that vitamin C supplementation could not prevent the incidence of premature rupture of membranes even though it was said that a larger

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sample size was needed. to assess whether vitamin C supplementation was associated with the incidence of premature rupture of membranes. Likewise, Rizka (2011) research resulted in the opposite, where the results obtained that vitamin C levels in term pregnant patients with premature rupture of membranes were higher than those in term pregnancies without premature rupture of membranes.

The literature says normal blood plasma vitamin C levels are 26.1-84.6 umol / L (> 0.6mg / dl,> 20 µg / 108 cells,> 114 nmol / 108 cells) and it is said to be deficient if <11 umol / L (0.2mg / dl, <10 µg / 108 cells, <57 nmol / 108 cells). From the results of this study, it was found that a fairly wide range, namely the blood plasma vitamin C levels of pregnant at term with premature rupture of membranes had a mean value of 60.07 ± 50.33 nmol / mL, with the smallest value 1.78 nmol / mL and the largest value 210.71 nmol / mL and vitamin C levels. Pregnant blood plasma without premature rupture of membranes has a mean value of 97.56 ± 78.28 nmol / mL, with the smallest value of 0.35 nmol / mL and the largest value 306.43 nmol / mL. However, if seen from appendix 7, 58.35% of blood plasma vitamin C levels pregnant women without premature rupture of membranes are <90 nmol / mL while 58.33% blood plasma vitamin C levels of pregnant women without premature rupture of membranes are <60 nmol / mL.

Vitamin C (ascorbic acid) is a water-soluble vitamin that is not synthesized by humans. Therefore, this essential vitamin must be obtained from food. As we know, vitamin C is an antioxidant. Ascorbic acid directly stimulates collagen synthesis. Ascorbic acid acts as a reducing agent by sending a hydrogen atom with a single electron to the ROS with a single unpaired electron in the outer ring. ROS now stabilizes the paired electrons in its outer ring. Ascorbic acid makes collagen strong and stable.6 Ascorbic acid also influences metalloproteinase 2 (MMP-2). In the analysis of the culture medium, there was a decrease in MMP-2 mRNA with ascorbic acid. In this experiment, there was an increase in collagen I production in response to ascorbic acid exposure. Besides, vitamin C's function is its involvement in the hydroxylation of proline and lysine in procollagen residues. This reaction is catalyzed by a prolihydroxylase, such as lysihydroxylase, which requires Fe and ascorbate. This step occurs in fibroblasts and has been observed in amniotic membrane cell cultures. It is said that ascorbate also plays a role in modulating mRNA expression in collagen synthesis, as well as expression of collagen genes, type I, III and X.[9]

CONCLUSION

The mean blood plasma vitamin C level in term pregnancy without premature rupture of membranes was 97.56 nmol / mL (± 78.28 nmol / mL) and premature rupture of membranes 60.07 nmol / mL (± 50.33 nmol / mL) . Mean blood plasma vitamin C levels in term pregnancy without premature rupture of membranes were higher than blood plasma vitamin C levels in

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term pregnancies with premature rupture of membranes in RS.DR.M. Djamil Padang, RSU Achmad Mochtar Bukittinggi and RSUD Pariaman.

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