Research Article

# High Sensitivity C-Reactive Protein (hs-CRP) Level on Premature Rupture of Membrane (PROM) at Term Pregnancy

## Kadar High Sensitivity C Reactive Protein (hs-CRP) pada Ketuban Pecah Dini dengan Kehamilan Aterm

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## Abstract

**Objective**: To compare the level of high sensitivity C-Reactive Protein (hs-CRP) on patients with premature rupture of membranes (PROM) at term pregnancy.

**Methods**: The study was cross-sectional design. The data collection included age, parity, gestational age, birth weight, and APGAR score on 28 pregnant women at term pregnancy consisting of 14 subjects of Premature Rupture of Membrane (PROM) less than 12 hours and the remaining one was equal or more than 12 hours. We took blood samples from the subjects for the examination of hs-CRP level. Data were analyzed using non-parametric statistical test and processed using Statistical Package for Social Sciences (SPSS) version 20.

**Results**: The mean hs-CRP level on PROM <12-hour and ≥12-hour group was 12.9 and 17.8 mg/l. There was not significant difference on hs-CRP level between both of group at term pregnancy (p=0.734).

**Conclusion**: The level of hs-CRP does not have association with the incidence of PROM.

[Indones J Obstet Gynecol 2017; 5-1: 12-15]

**Keywords**: high sensitivity C-Reactive Protein, premature ruptures of membranes, term pregnancy

## Abstrak

**Tujuan**: *Untuk membandingkan kadar high sensitivity C-Reactive Protein (hs-CRP) pada pasien ketuban pecah dini (KPD) dengan kehamilan aterm.*

**Metode**: *Penelitian ini merupakan studi dengan desain potong lintang. Pengumpulan data dilakukan pada 28 wanita hamil dengan kehamilan aterm yang meliputi usia, paritas, usia kehamilan, berat lahir, dan nilai APGAR. Subjek terbagi dalam 2 kelompok yaitu dengan KPD <12 jam dan ≥12 jam. Data dianalisis dengan menggunakan tes statistik non parametrik dan diproses melalui SPSS versi 20.*

**Hasil**: *Rerata nilai hs-CRP pada KPD <12 jam ialah 12,9 mg/l dan 17,8 pada kelompok KPD ≥12 jam. Tidak terdapat perbedaan bermakna pada kadar hs-CRP antara kedua kelompok pada kehamilan aterm. (p=0,734).*

**Kesimpulan**: *Kadar hs-CRP tidak berhubungan dengan kejadian KPD.*

[Maj Obstet Ginekol Indones 2017; 5-1: 12-15]

**Kata kunci**: *hamil aterm, high sensitivity C-Reactive Protein, ketuban pecah dini*

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## INTRODUCTION

Premature rupture of membrane (PROM) at term pregnancy occurs before the onset of labor at term gestational age (between $37^{+0}$ and $41^{+6}$ weeks). Patients with PROM usually complain of vaginal bleeding, pelvic pressure, vaginal discharge, water going out of birth canal without uterine contraction.[1,2] The incident of PROM happened approximately 12% of all pregnancies; however, it was varied from 2 to 18% of pregnancies. About 70% PROM cases occur at term pregnancy. Recent studies showed that the incident of PROM was between 14 and 17% of all pregnancies. At term pregnancy, the incidence rate was approximately 5-18%. This breakage of amniotic sac was probably influenced by several factors, such as cervico-vaginitis, incompetent cervix, maternal smoking, prenatal diagnostic procedures (amniocentesis, chorionic villus sampling), coitus, also mineral and vitamins deficiency.[3-5]

In term pregnancy, PROM is the beginning from 8 to 10% of all pregnancies and it will be followed by the onset of labor and birth. A random study found half of women with PROM delivered within 5 hours and 95% of them delivered in 28 hours after the rupture of membrane.[6-8]

Most PROM women would continue to deliver on the second or third day; therefore, patients and their fetal had to be fully observed. The expectative management for PROM can be considered on

patient at the first 12-24 hours. However, the risk of intrauterine infection increases during PROM. Some studies stated that the risk of chorio-amnionitis increased up to 24% after the occurrence of prolonged PROM.[8,9]

C-Reactive Protein is an inflammation marker produced and released by the liver under the stimulation of cytokines interleukin 6 (IL-6), interleukin 1 (IL-1), and tumor necrosis factor $\alpha$ (TNF- $\alpha$).[4,10] High sensitive C-Reactive Protein (hs-CRP) is an acute phase reactant that is synthesized primarily in the liver cells as a response to pro-inflammatory cytokines. Further-more, hs-CRP will stimulate the release of matrix metalloproteinase (MMP-1). The role of MMP plays in the process of remodeling/degradation of extracellular matrix causing rupture of membranes.[4,5,10]

A lot of studies has conducted to determine the impact of CRP on normal pregnancy, preeclampsia, premature labor. Some studies reported an elevation on the level of CRP in maternal serum above normal level which was common seen in non-pregnant women. It was also reported that high level of CRP in maternal serum at the beginning of delivery process would increase risk of fetal intrauterine infection. Wiser, et al. through their study reported increasing CRP to the level of more than 10 mg/l is indication of an infection.[8,10,11] Therefore, our study aims to compare the level of hs-CRP on patients with PROM at term pregnancy, whereas we differ into two-time limit for the PROM.

## METHODS

This study was a cross-sectional design conducted from December 2015 to February 2016 in Department of Obstetrics and Gynecology, Faculty of Medicine Universitas Sam Ratulangi/Prof. dr. R.D. Kandou Hospital, Manado and Kasih Manado Hospital. We recruited 14 women as study subjects at term pregnancy with PROM less than 12 hours and 14 women at term pregnancy with PROM equal or more than 12 hours. We took the distributive characteristics including age, weight, height, body mass index (BMI), and the women were examined the blood samples for hs-CRP level. The level of hs-CRP was measured by turbidimetry methods using Li heparin serum and ethylenediaminetetraacetic acid (EDTA).

We reviewed the medical records and then all patients who would be enrolled on the study got the counseling explanation about the purpose, benefit, and study procedures, as well as the risk could occur. If they agreed to be included in this study, they had to signed the informed consent. The collected data were analyzed using non-parametric statistical tests in SPSS.

## RESULTS

Table 1 showed that the most pregnant women with PROM were between 20 and 35 years old which the average of it was 29.4 years old. The gestational age on either PROM <12-hour or $\geq$12-hour group was less than 40 weeks, with an average of 38.4 weeks of gestation. According to parity, most of them had not ever delivered; there-fore, the average parity was only 0.7. Furthermore, the baby's birth weight on the PROM <12-hour and PROM $\geq$12-hour group mostly had less than 3500 grams and the mean of it was 3103.6 grams. Meanwhile, APGAR score on PROM <12 hour and PROM $\geq$12-hour group at first and fifth minute was >7 and >7; whereas, the average of 7.1 at minute 1 and 9.1 at minute 5.

The lowest and highest hs-CRP level on PROM <12 hour was 0.8 and 70.7 mg/l, with mean (standard of deviation/SD) of 12.9 (19.2) mg/l. While on PROM $\geq$12-hour group, the lowest, highest, mean, and SD were 1.0, 158.1, 17.8, 40.7 mg/l; respectively.

Based on the data obtained, we conducted a normality test using Shapiro-Wilk test due to small sample size. The result on BMI, length of PROM, and hs-CRP pointed out that the p less than 0.05 so that it meant that the data distribution was not normal and we continued to non-parametric statistical test.

The Mann-Whitney non-parametric statistical test resulted that there was no significant difference in BMI between PROM <12-hour and PROM $\geq$12-hour group (p=0.306). It defined that the BMI did not have association with the incidence of PROM. Meanwhile, there was a significant difference on PROM length between groups (p<0.001). The analysis of hs-CRP level described that there was not statistically different between groups (p=0.734).

**Table 1.** Patient Characteristics on Premature Rupture of Membrane (PROM) group

| Characteristics | PROM <12 hours (n=14) | PROM ≥12 hours (n=14) | Mean | SD |
|---|---|---|---|---|
| Age (years old) | | | | |
| <20 | 0 | 1 | | |
| 20-35 | 12 | 9 | 29.4 | 6.4 |
| >35 | 2 | 4 | | |
| Parity | | | | |
| 0 | 8 | 6 | | |
| 1 | 4 | 5 | | |
| 2 | 1 | 1 | 0.7 | 1.0 |
| 3 | 1 | 2 | | |
| >4 | 0 | 0 | | |
| Gestational Age (weeks) | | | | |
| 37-<40 | 13 | 11 | | |
| ≥40-<41 | 1 | 3 | 38.4 | 1.0 |
| 41-<42 | 0 | 0 | | |
| Birth Weight (grams) | | | | |
| 2500-<3000 | 4 | 7 | | |
| 3000-<3500 | 8 | 4 | 3103.6 | 303.2 |
| 3500-<4000 | 2 | 3 | | |
| APGAR Score | | | | |
| Minute 1 | | | | |
| 4-6 | 3 | 2 | | |
| 7-10 | 11 | 12 | 7.1 | |
| Minute 5 | | | | 0.8 |
| 4-6 | 0 | 0 | 9.1 | |
| 7-10 | 14 | 14 | | |

**Table 2.** hs-CRP Level on Premature Rupture of Membranes (PROM)

| PROM Group | hs-CRP Level | | Mean | SD |
|---|---|---|---|---|
| | Lowest (mg/l) | Highest (mg/l) | | |
| PROM <12 hours (N=14) | 0.8 | 70.7 | 12.9 | 19.3 |
| PROM ≥12 hours (N=14) | 1.00 | 158.1 | 17.8 | 40.7 |

## DISCUSSION

A review held by Martinez, et al. in 2007 stated that there were eight main studies consisting of 610 cases that fulfilled the criteria; whereas, three of the studies concluded that hs-CRP was a diagnostic instrument for chorioamnionitis occurrence on PROM cases; although, one study suggested higher level of hs-CRP had more diagnostic value. Meanwhile, the other five studies concluded that the hs-CRP as single indicator to diagnose chorioamnionitis incidence on PROM still lacked of power; therefore, it needed further study on that indicator.[12] Another study by Serkan Kahyaoglu, et al. on 86 patients concluded that hs-CRP as an inflammation marker, revealed less specific and sensitive to predict the labor with PROM.[13]

This study showed that the measurement of hs-CRP level on patients with PROM at term pregnancy was not a single indicator to predict the success of labor induction. The limitation of study included small sample size so that it would be difficult to be applied in general. We suggested to conduct another study covered bigger population in Indonesia to determine the use of hs-CRP on PROM at term pregnancy.

## CONCLUSION

The level of hs-CRP does not have association with the incidence of PROM.

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