

Research Report

Relation between C-Reactive Protein Level and Intrauterine Infection in Pregnant Women with Premature Rupture of Membrane (PROM)*Hubungan antara Kadar C-Reactive Protein dengan Infeksi Intra Uterin pada Penderita Ketuban Pecah Dini*

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Abstract

Objective: To know the relationship between C-Reactive protein level in the blood of pregnant women with premature rupture of membrane (PROM) less than 12 hours and the incidence of intrauterine.

Method: This study was case series in 55 pregnant women with PROM less than 12 hours at Department of Obstetrics and Gynecology Medical Faculty, University of Sriwijaya Dr. Mohammad Hoesin Hospital, Palembang from July 1, 2009 until January 1, 2010. Data analysis was performed using Pearson Correlation test.

Result: The mean levels of C-reactive protein in pregnant women with PROM less than 12 hours was 27.12 ± 15.58 mg/dl, in which 16.4% women had C-reactive protein level ≤ 10 mg/dl and 83.6% women had C-reactive protein level > 10 mg/dl. The mean rectal temperature of women was $37.41 \pm 19^\circ\text{C}$, in which 85.5% women had rectal temperature $< 38^\circ\text{C}$. The mean of leucocyte count in women was $10586 \pm 2835/\text{mm}^3$, in which 69.1% women had leucocyte count $< 15000/\text{mm}^3$. The correlation value between C-reactive protein level with rectal temperature was $R=0.218$ with $p=0.110$ and the correlation value between C-reactive protein level with leucocyte count was $R=0.236$ with $p=0.082$.

Conclusion: C-reactive protein can not be used as a single predictor of intrauterine infection.

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Keywords: C-reactive protein, intrauterine infection, premature rupture of membrane (PROM)

Abstrak

Tujuan: Untuk mengetahui hubungan kadar C-reactive protein dalam darah ibu hamil dengan Ketuban Pecah Dini (KPD) kurang dari 12 jam dengan terjadinya infeksi intrauterin.

Metode: Penelitian ini merupakan penelitian serial kasus yang dilakukan pada 55 perempuan hamil yang mengalami ketuban pecah dini < 12 jam di Bagian Obstetri dan Ginekologi Rumah Sakit. Dr. Moh. Hoesin, Fakultas Kedokteran Universitas Sriwijaya Palembang, dari 1 Juli 2009-1 Januari 2010. Analisis data dilakukan dengan Pearson Correlation test.

Hasil: Rerata kadar C-reactive protein ibu dengan KPD ≤ 12 jam adalah $27,12 \pm 15,58$ mg/dl, di mana 16,4% ibu memiliki kadar C-reactive protein ≤ 10 mg/dl dan 83,6% memiliki kadar C-reactive protein > 10 mg/dl. Rerata pengukuran suhu rektal ibu adalah $37,41 \pm 19^\circ\text{C}$ di mana 85,5% ibu mempunyai suhu rektal $< 38^\circ\text{C}$. Rerata pengukuran jumlah leukosit ibu adalah $10586 \pm 2835/\text{mm}^3$ di mana 69,1% ibu memiliki jumlah leukosit $< 15000/\text{mm}^3$. Hubungan kadar C-reactive protein dengan suhu rektal diperoleh $R=0,218$ dan $p=0,110$ dan hubungan kadar C-reactive protein dengan jumlah leukosit diperoleh $R=0,236$ dan $p=0,082$.

Kesimpulan: C-reactive protein tidak dapat digunakan sebagai prediktor tunggal infeksi intrauterin.

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Kata kunci: C-reactive protein, infeksi intrauterin, ketuban pecah dini

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INTRODUCTION

Premature Rupture of Membrane (PROM) is rupture of amniotic membrane before onset of labour. PROM is one of most common obstetrics problem faced by obstetrician, which requires accurate assesment, since by its time it will increase risk of infection on mother and baby. Cox et al stated that perinatal morbidity was 20% among mothers suffering from PROM.^{1,2}

Causes of PROM are multifactorial, in which infection being the most frequent. In defining diagnosis of PROM, anamnesis and physical examination alone are not enough to determine whether PROM definitely happened. Moreover there is no single test can accurately diagnose PROM, so we need integration of anamnesis, physical examination, and additional examination to complete the diagnosis.²⁻⁴

C-reactive protein (CRP) is an abnormal serum produced by hepatocyt cell during acute inflammation, which production is regulated by interleukin 1b (IL-1b), interleukin 6 (IL-6) and tumor necrosing factor α (TNF α). CRP level measurement has been well developed during the last three decade. Because CRP can fastly be removed when infection resolved, detection of CRP level is significant to determine the inflammatory or infection process on mother with PROM.^{5,6}

C-reactive protein concentration in serum of PROM mother has been known to increase, but to what extent is not surely established. Data about CRP level and its relation with neonatal outcome are also still contradiction, so emerge question about how the relation between CRP level in mother with PROM, the risk for chorioamnionitis, and neonatal outcome.⁷⁻⁹

C-reactive protein is an acute phase protein which concentration raise just few hours after infection happens and tissue destruction occurs, and reach peak level after 2-6 hours. Its serum level depends on severity of infection process. Since it is synthesized rapidly and its half time is relatively short (6-12 hours), CRP can be used to detect inflammation/infection early.¹⁰⁻¹²

Remembering the number of PROM cases, it is considered important to do study in order to do effort in preventing infection during pregnancy and labour. One of potential way to detect such infection is by assesment of CRP level in maternal serum.^{11,12}

METHODS

This study was designed as case series to see the relation between CRP serum level and the risk of intrapartum infection on mother with PROM ≤ 12 hours, conducted in delivery room in Dr. Mohammad Hoesin Hospital Palembang from July 1, 2009 - January 1, 2010. Sample were chosen with consecutive sampling method. 139 pregnant women with PROM entering delivery room Dr. Mohammad Hoesin Hospital Palembang, with inclusion criteria aterm, life baby, age 20-35 years. Pregnancy with obstetrical complication like severe preeclampsia and medical complication like diabetes mellitus, being on certain antibiotics medication, or neonates with congenital anomaly were excluded from this study. Some variables such as body temperature, leucocyte count, mothers CRP level and neonates APGAR score were then measured. Mothers temperature was measured by accessing rectal mucose with digital termometer microlife MT 200. Blood sample for leucocyte and CRP sample were drawn from mothers vena mediana cubiti account for 3 cc leucocyte count for $\geq 15000/\text{mm}^3$ was considered abnormal. CRP serum was quantitatively measured by latex serology method with Avitex[®] (Omega Diagnostic), C-reactive protein was abnormal if > 10 mg/dl. Neonatal outcome was then measured by APGAR score.

Patient data were recorded in an available form, then arranged as a data base.

Tabulation was then made according to simple linear regression and analyzed by SPSS stastic 15.0th version.

RESULTS

From July 1, 2009 - January 1, 2010 55 subjects for the study that matched inclusion criteria were obtained. Most subjects were between 26-30 years old, which were distributed mostly in urban area, and subject parity 56.4% were nullipara. Subjects education level were quite good (mostly from high school) and 78.2% were housewives. It was found that average level of CRP ≤ 12 hours PROM mother were 27.12 ± 15.58 mg/dl with all of the PROM mother both ≤ 12 and ≤ 6 hours were CRP (+). This showed that infection or inflammation happened to all of mothers with PROM, this statement goes along with study by Menon et al, in which PROM as one of complex pathological process was caused by inflammation. 83.6% mother with ≤ 12 hours PROM whose CRP level > 10 mg/dl was also found in this study. Results from rectal temperature measurement and leucocyte count can be seen in Table 1 and 2.

From Table 1 shows 85.5% subjects temperature $< 38^\circ\text{C}$ with mean $37.41 \pm .19^\circ\text{C}$. Steward et al. take definition of chorioamnionitis is if rectal temperature $> 37.5^\circ\text{C}$ on two times measurement with 1 hour interval or if temperature $> 38^\circ\text{C}$ on one time measurement. Our standard operating procedure in Dr. Moh. Hoesin Hospital, Palembang took rectal temperature $> 38^\circ\text{C}$.³

Table 2 shows 69.1% of subject had leucocyte count $< 15.000/\text{mm}^3$ with average $10586 \pm 2835/\text{mm}^3$. Menon's definition of chorioamnionitis is if leucocyte count > 15000 cell/ mm^3 while Hartman et al. stated that leucocytosis more than 15000 - 30000 are still considered normal, while based on standard operating procedure in Dr. Moh. Hoesin Hospital Palembang, it is called infection if leucocyte count $> 15000/\text{mm}^3$.

Relation between increase of CRP level and increase in rectal temperature and leucocyte count was searched (Figure 1) and the result was $R=0.218$ and $p=0.110$, in which there was slightly association between CRP in mothers serum and increase of rectal temperature and leucocyte count.

Although can not be counted methodologically, there was less APGAR score in group CRP > 10 mg/dl.

Table 1. Rectal temperature on mother with PROM.

Subject	Rectal temperature							
	$< 38^\circ\text{C}$				$\geq 38^\circ\text{C}$			
	N	%	Mean	SD	N	%	Mean	SD
PROM ≤ 12 hr	47	85.5	37.415	.1919	8	14.5	38.263	.1061

Table 2. Leucocyte count on mother with PROM.

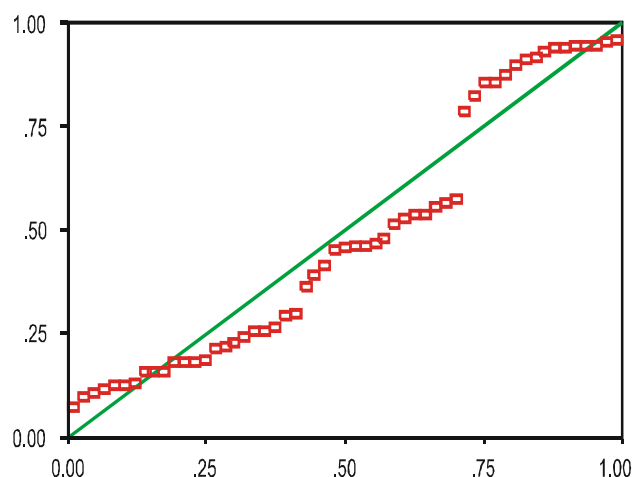
Subject	Leucocyte count							
	< 15.000/mm ³				≥ 15.000/mm ³			
	N	%	Mean	SD	N	%	Mean	SD
PROM ≤ 12hr	38	69.1	10586	2835	17	30.9	19629	3910

DISCUSSION

There was a slight association between CRP increase and rectal temperature and leucocyte count found in this study. Also there was a relation between CRP level in mother serum and leucocyte count found in this study. Also there was a relation between CRP level in mother serum and leucocyte count.

CONCLUSION

In this study, relation between CRP and leucocyte count and rectal temperature in mother with PROM ≤ 12 hours was slightly associated C-reactive protein cannot be the only factor to predict intrauterine infection. We need further study with bigger sample size to get better result for relationship between CRP and the risk for intrauterine infection for mother with PROM.

**Figure 1.** Relation between C-reactive protein with leucocyte count and rectal temperature.

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Yoon et al. measured leucocyte count contained in amniotic fluid with the result that leucocyte count measurement in amniotic fluid was a better tool to identify intrauterine infection/chorioamnionitis because it could describe better identification of pathogen role in amniotic fluid. Some researchers agreed that amniotic fluid culture is gold standard for detection amniotic infection.

This result was according to meta-analysis by Laar et al. which concluded that not single study clearly support the evidence on the use of C-reactive protein as a diagnostic tool for histologic chorioamnionitis, and systematic review conducted by Trochez-Martinez et al. claimed histologic chorioamnionitis as gold standard. It was regretted that any study by Laar et al or Trochez et al did not support accuracy of CRP as single predictor for clinical chorioamnionitis, including this study.

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