C-Reactive Protein and Preterm Labor, a Case-Control Study

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Abstract: About 75% of prenatal mortality and morbidity is related to preterm labor and infection is a leading cause of preterm labor. Fast, non invasive and simple assessments can predict intrauterine infections in women who have no symptoms. Previous studies have shown relations between serum CRP, MMP-9, IL-6 and preterm labor. However, few studies have been conducted to evaluate the relationship between these markers and preterm labor among pregnant women. The aim of this study was to evaluate the relationship between CRP levels and preterm labor. This case control study was conducted in 2012 in Shariati Hospital of Bandar Abbas. One hundred pregnant women with a gestational age below 37 weeks were enrolled in the case group and 100 pregnant women with term deliveries were enrolled in the control group. Patients with diabetes, hypertension, premature rupture of membrane, BMI above 30, and infections were excluded from the study. Blood samples were taken from all the participants to assess CRP levels. Demographic data were also collected. Data was analyzed by SPSS v. 16 using logistic regression, descriptive statistics and odd's ration. Among 200 participants, the mean age of the participants was 25.91 ± 6.308, and 26.93 ± 5.495 for the case and control group, respectively. The mean CRP level was 19.5082 ± 20.2566 and 6.1467 ± 5.2827 for the case and control group, respectively. This difference was significant ($P<0.0001$). The results of this study showed that CRP levels can predict preterm labor. However, more studies are necessary to confirm this result.

1. Introduction

Preterm labor is associated with infant's mortality and mortality (Sorokin, Romero et al. 2010). It affects 5 to 9 percent of pregnancies of developed countries. More than 60% of infant mortality occurs in gestational age below 32 weeks (Goldenberg, Culhane et al.). Also, women with preterm labor are at increased risk for cardiovascular diseases (Romero, Espinoza et al. 2006). The physiopathology of preterm labor is unknown. However, evidence shows the subclinical infections and chronic inflammations are responsible for 30 to 50 percent of all deliveries (Sorokin, Romero et al. 2010). It is also related to preeclampsia, intrauterine growth retardation and intrauterine infections (Epstein, Goldenberg et al. 2000, Romero, Espinoza et al. 2006, Sorokin, Romero et al. 2010).

Systemic infections increase the level of inflammatory cytokines which provokes prostaglandin production. This process may induct uterine contractions and increase preterm labors. C-reactive protein (CRP) is an acute phase protein that is produced in response to IL-6 and TNF-α in hepatic cells. It is a sensitive inflammatory marker which is related to intrauterine infections (Sorokin, Romero et al. 2010). CRP concentrations are nonspecific markers for inflammation and are related to preeclampsia, IUGR and low birth weight (Goldenberg, Culhane et al. , Yoon, Romero et al. 2003).

Preterm labor may impose many risks and costs to the mother and neonate and finding new ways of early diagnosis and prevention can improve the level of health of the society. Therefore, we aimed to evaluate the association between CRP levels and preterm labor.

2. Material and Methods

This was a prospective case control study that was conducted in 2012 in Shariati Hospital of Bandar Abbas, Iran. Shariati Hospital is the main hospital of Hormozgan province.

In this study, 200 women were enrolled; 100 patients who went into labor at gestational age below 37 weeks and 100 patients in the control group. Patients with diabetes, high blood pressure, premature rupture of membrane, body mass index above 30 and twin pregnancies were excluded from the study. All the patients who participated in this study provided informed, written consent.

Blood samples were acquired on admission and the samples were sent to the laboratory. The

gestational age was calculated by their last menstrual period and first trimester sonographies. The age, gravidity, history of abortion and history of cervical surgeries were matched.

The quantitative and qualitative CRP levels were measured by Roche kit and Qush Intgram device. Data was entered SPSS v.16 and was analyzed using descriptive statistics and chi square. The level of significance was p-value <0.05.

3. Results

In this study, 200 patients were enrolled. The mean age of the patients of the control and case group was 26.93 ± 5.495 and 25.91 ± 6.308, respectively. Table -1 compares the baseline characteristics of both groups.

Table -1: Baseline characteristics of participants of the two groups

	Preterm		Control		P-value
	Mean	SD	Mean	SD	
Age	25.91	6.308	26.93	5.495	0.245
Weight	65.04	8.736	64.51	9.93	0.993
Height	166.28	47.727	163.46	5.308	0.558
BMI	24.0897	2.6164	23.9551	2.61889	0.717
Number of pregnancies	1.93	1.191	2.25	1.215	0.092
History of abortion	0.25	0.609	0.34	0.688	0.064

The patients of the control group had no previous history of preterm labor while 24 (24%) patients of the case group had history of preterm labor.

As it can be seen in table 2, the body mass index (BMI) of patients of both groups was mostly normal (60% in the preterm groups compared with 61% among the control group). There difference of BMI of the two groups was not significant (P > 0.05).

Table -2: Comparison of Body Mass Index both groups

	Control		Case		`
	Number	Percent	Number	Percent	
Thin	1	1	2	2	
Normal	61	61	60	60	
Over weight	35	35	36	36	0.845
Obese	3	3	2	2	
Total	100	100	100	100	

The mean CRP level of the participants of the preterm group and control group was 19.5082 ± 20.2566 and 6.1467 ± 5.2827, respectively (P < 0.001).

4. Discussions

This study was conducted in 2012 in order to determine the difference of CRP of term and preterm labors. The findings of this study show that serum levels of CRP are higher among women with preterm labor. This result shows that inflammation can lead to a series of changes which ends with preterm labor.

A study conducted a study on 109 pregnant women and observed that 34 women entered labor at gestational ages below 35 weeks, 50 were still pregnant and 25 had term deliveries. They reported that a CRP level of 0.8 mg/dl could predict preterm labor within a week with a sensitivity of 85% and specificity of 81% (Dodds and Iams 1987).

Another study measured the level of CRP in gestational ages of 15 to 18 weeks and observed that women with high blood levels of CRP were more likely to experience preterm labor (Hyun Yoon, Romero et al. 2000). Torbe et al also reported that women who went into labor at 36 weeks of gestational age or less had higher levels of CRP (Torbe and Czajka 2004).

CRP plays a significant role in inflammatory responses. It can activate the classic complement pathway and induce the production of cytokines and tissue factors of monocytes (Cermak, Key et al. 1993, Janeway, Travers et al. 2001). However, the main activity of CRP is decreasing neutrophil migration to inflammatory site and their adhesion to endothelial cells (Burlingame, Volzer et al. 1996).

Many other factors can increase CRP such as obesity, smoking and cardiovascular diseases while alcohol intake and physical activity reduce CRP concentrations (Pearson, Mensah et al. 2003). Since obesity can play an effective role on CRP concentrations and can be known as a confounding variable (Ramsay, Ferrell et al. 2002), the participants of both groups were matched in our study.

One of the strengths of this study was that more confounding variables were matched compared to other studies. Another limitation of this study was that we could not exclude patients with diseases such as chorioamnionitis which mamy lead to preterm labor. Also, CRP levels were not measured before the study.

We suggest other investigators to design more studies in order to determine a threshold for CRP that shows the risk of preterm labor..

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