# MODE OF DELIVERY DOES NOT EFFECT C - REACTIVE PROTEIN AND FERRITIN LEVELS

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**ABSTRACT**

***Objective**: C-reactive protein (CRP), a marker of systemic inflammation, increases rapidly in ischemia or traumatic injury. Ferritin, an acute phase reactant, has been found to be elevated in many chronic inflammation-related diseases. The aim of the present prospective study was to investigate and compare serum CRP and ferritin levels after vaginal birth and cesarean section.*

***Methods**: One hundred sixty pregnant women who gave birth in our hospital were included in the study. Vaginal birth (n=80) and cesarean section (n=80) groups were matched for age and gestational age. In all subjects, CRP and plasma levels of ferritin were determined.*

***Results**: Maternal age, gestational age and body mass index were not significantly different between the groups. Ferritin levels were similar in vaginal birth and cesarean section subjects. There were also no significant differences in serum concentrations of CRP between the two groups. Serum CRP was 5.8 ± 3.7 mg/L in vaginal birth group and 7.0 ± 6.8 mg/L in cesarean section group (p=0.190).*

***Conclusion**: In conclusion, our findings reveal that mode of delivery has no effect on the acute-phase proteins namely, ferritin and CRP.*

***Key words**: C-reactive protein, ferritin, delivery.*

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## Introduction

C-reactive protein (CRP), a marker of systemic inflammation, is associated with increased risk of cardiovascular disease[1]. CRP levels are <1.0 mg/dl in 98% of healthy subjects. Even when relatively increased within this "normal" range, CRP has been revealed to be predictive of a first cardiovascular event in previously healthy women[2]. It also increases rapidly in infection, inflammation, ischemia or traumatic injury[3,4].

Ferritin, an iron binding protein and an acute phase reactant, has been found to be elevated in many chronic inflammation-related diseases[5]. The increased levels of ferritin are due to inflammation rather to increased iron concentration.

Although some studies determined the concentration of cytokines in maternal blood and their correlation with cervical dilatation[6], and mode of delivery(7), none of these studies tried to correlate cytokines with the acute-phase protein ferritin.

The aim of the present prospective study was to investigate and compare serum CRP and ferritin levels after vaginal birth and cesarean section.

## Material and methods

One hundred sixty pregnant women who gave birth in our hospital were included in the study. The study was carried out at the main maternity Hospital in Ankara. Our Hospital as a tertiary center in Turkey has approximately 20000 deliveries per year. This study was approved by the local ethical committee-and the procedures followed were in accordance with the institutional guidelines. Informed consent was obtained from all patients before participation in the

study. Power analyses were performed for the primary objective. The sample size was calculated using G* Power software version 3.17 for sample size calculation (*Heinrich Heine Universität; Düsseldorf; Germany)[8], setting the primary outcome as CRP levels, the α-error probability at 0.05, power (1-β error probability) at 0.95 %, and effective sample size (w) at 0.25. The number of participants needed to produce a statistically acceptable scene was 63 patients in each study group.

The study population consisted of 2 groups: Group 1 consisted of 80 women, who gave birth after spontaneous onset of labor. No operative deliveries were included. Women who needed induction by amniotomy and intravenous (IV) oxytocin were excluded. Any patients who had pre-labor membrane rupture or those who needed emergency surgical intervention in labor were also excluded.

Group 2 consisted of 80 women who underwent planned cesarean section. We only included patients with an indication of previous cesarean section. Patients with a history of systemic disease were excluded from the study. All subjects were nonsmokers. None of the participants were receiving any medications. Patients who suffered any adverse birth outcome were also excluded from the study. The patients participating in the study were recruited consecutively. Vaginal birth and cesarean section groups were matched for age and gestational age. The gestational age was calculated on the basis of the weeks of gestation since the last menstrual period and confirmed by ultrasound. Their height (m) and weight (kg) measurements were recorded and used to calculate the body mass index (BMI, kg/m$^2$).

In all subjects, blood was drawn 6 hours after birth and CRP and plasma levels of ferritin were determined. Nephelometric assay (Behring BN2-Germany) for CRP was performed using a commercial kit (Dade Behring- N High Sensitivity CRP reagent kit). The assay has a detection limit of 0.1 mg/L. The day-to-day imprecision coefficient of variation (CV), at CRP concentrations of 0.16, 2.2 and 18 mg/L was 5.8 %, 4.6 % and 3.9 % respectively.

Ferritin levels were assessed by Roche E-170 Modular System Electro Chemiluminecance.

Statistical analysis of the data was performed with the software package SPSS for windows 11.0 (Statistical package for social sciences; SPSS Inc. Chicago, IL). Kolmogorov-Smirnov analyses were used to test if the results were normally distributed. The data were reported as mean ± standard deviation (for normally distributed data) or as median and range (for non-normally distributed data). Statistical differences between the study groups were estimated using non-parametric tests (Kruskal–Wallis and Mann-Whitney U tests). A Pearson correlation coefficient evaluated the relation between CRP and ferritin. $P < 0.05$ was considered to indicate a statistically significant difference.

## Results

Table 1 shows the demographic data of the two groups. Maternal age, gestational age and body mass index were not significantly different between the groups. The mean age of the cesarean section group was 26.8 ± 4.7 years.

Mean serum ferritin and CRP levels after vaginal birth and cesarean section are presented in Table 1. Ferritin levels were similar in vaginal birth and cesarean section subjects. There were also no significant differences in serum concentrations of CRP between the two groups. Serum CRP was 5.8 ± 3.7 mg/L in vaginal birth group and 7.0 ± 6.8 mg/L in cesarean section group (p=0.190). Serum CRP had a significant correlation with ferritin (r=0.248, p=0.002).

| | Vaginal birth (n=80) | Cesarean section (n=80) | P |
|---|---|---|---|
| Age* | 25.9 ± 4.2 | 26.8 ± 4.7 | 0.207 |
| Gravidity** | 2 (1-4) | 2 (1-4) | 0.051 |
| Parity** | 1 (0-3) | 1 (0-3) | 0.077 |
| Gestational age at birth** | 275.2 ± 8.6 | 273.3 ± 5.5 | 0.119 |
| Body mass index (kg/m2) | 28.8 ± 4.1 | 30.0 ± 3.7 | 0.058 |
| C-reactive protein (mg/L)* | 5.8 ± 3.7 | 7.0 ± 6.8 | 0.190 |
| Ferritin* | 16.9 ± 14.1 | 16.5 ± 13.3 | 0.859 |
| Hemoglobin* | 12.1± 1.2 | 12.1 ± 0.9 | 0.030 |
| Birth weight (g)* | 3350.2 ± 411.0 | 3337.5 ± 405 | 0.845 |

**Table 1**: Maternal characteristics.
**Values are mean ±standard deviation.*

## Discussion

Many studies have shown alterations of CRP during pregnancy, labor and postpartum in normal conditions and disease[9,10]. The present study showed

that serum CRP was 5.8 ± 3.7 mg/L in vaginal birth group and 7.0 ± 6.8 mg/L in cesarean section group. No significant difference was observed in CRP levels between the two groups.

Cicarelli et al[7] revealed that the CRP values after delivery increased 10-to 20-fold when compared with those recorded upon admission, which were similar to the clinical reference value (lower than 0.5 mg/dL).

Changing CRP levels after different types of surgery have been studied by several authors[11]. Study of Stahl et al[12] on abdominal surgery reported a correlation between the magnitude of the CRP increase and the amount of tissue damaged by surgery. It is known that the type of anesthesia given, the amount of blood loss or blood transfusion, use of antibiotics or anti-inflammatory drugs, operative time, and patient age and gender have no impact on CRP levels[13].

The increase in CRP is known to be coincident with an increase in other acute phase proteins (fibrinogen, ceruloplasmin, von Willebrand factor originating from the liver and vessel walls)[14]. We studied another acute phase reactant, ferritin, but also found no significant differences between two modes of delivery. To our knowledge, this is the first study to show serum ferritin levels in vaginal birth and cesarean section patients. However, we were not able to study other markers of inflammation or level of proinflammatory cytokines like tumor necrosis factor alpha and interleukins in this study.

The concentration of CRP in the mother's serum after delivery is slightly higher than the basal level. The increase in acute-phase proteins observed in inflammatory conditions usually relates to the amount of tissue injury. In delivery, the intensity of stress in cesarean section may be higher than in vaginal birth. But neither CRP nor ferritin discriminated between these two conditions.

This research has endeavored to establish any links between ferritin and the acute phase response, using well established markers like CRP. In conclusion, our findings reveal that mode of delivery has no effect on the acute-phase proteins namely, ferritin and CRP.

**References**


1) Bassuk SS, Rifai N, Ridker PM. *High-sensitivity C-reactive protein*. Curr Probl Cardiol 2004; 29*: 439-493*.
2) Ridker PM, Hennekens CH, Buring JE, Rifai N. *C-reactive protein and other markers of inflammation in the prediction of cardiovascular disease in women*. N Engl J Med 2000; 342: *836–843*.
3) Kushner I, Gewurz H, Benson MD. *C-reactive protein and acute phase response*. J Lab Clin Med 1981; 97: *739*.
4) Pepys MB. *C-reactive protein, fifty years on*. Lancet 1981; 21*: 653*.
5) Chakraborty DS, Tewari DS, Sharma DR, Narula DS. *Effect of non-Surgical Periodontal Therapy on Serum Ferritin Levels: an Interventional Study.* J Periodontol. 2013 Jul 4. [Epub ahead of print]
6) Hebisch G, Grauaug AA, Neumaier-Wagner PM, Stallmach T, Huch A, Huch R. *The relationship between cervical dilatation, interleukin-6 and interleukin-8 during term labor.* Acta Obstet Gynecol Scand. 2001; 80: *840-848*.
7) Cicarelli LM, Perroni AG, Zugaib M, de Albuquerque PB, Campa A. *Maternal and cord blood levels of serum amyloid A, C-reactive protein, tumor necrosis factor-alpha, interleukin-1beta, and interleukin-8 during and after delivery.* Mediators Inflamm. 2005; 2005: *96-100*.
8) Faul F, Erdfelder E, Lang A, Buchner, A. *G*Power 3: A flexible statistical power analysis program for the social, behavioral, and biomedical sciences*. Behavior Research Methods, 2007; 39: *175-191*.
9) De Meeus JB, Pourrat O, Gombert J, Magnin G. *C reactive protein levels at the onset of labor and at day 3 postpartum in normal pregnancy.* Clin Exp Obstet Gynecol. 1998; 25: *9-11*.
10) de Villiers WJ, Louw JP, Strachan AF, Etsebeth SM, Shephard EG, de Beer FC. *C-reactive protein and serum amyloid A protein in pregnancy and labour.* Br J Obstet Gynaecol. 1990; 97: *725-730*.
11) Larsson S, Thelander U, Friberg S. *C-reactive protein levels after elective orthopaedic surgery*. Clin Orthop Relat Res 1992; 275: *237-42*.
12) Stahl WM. Acute phase protein response to tissue injury. Crit Care Med 1987; 15: *545*.
13) Niskanen RO, Korkala O, Pammo H. *Serum C-reactive protein levels after total hip and knee arthroplasty*. J Bone Joint Surg (Br) 1996; 78-B*: 431-3*.
14) Kluft C, Leuven JA, Helmerhorst FM and Krans HM. *Pro-inflammatory effects of oestrogens during use of oral contraceptives and hormone replacement treatment*. Vascul Pharmacol 2002; 39, *149-154*.


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