

C-reactive protein levels at the onset of labour and at day 3 post-partum in normal pregnancy

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Summary

Objectives: To record maternal serum C-reactive protein levels during normal onset of labour and normal puerperium and to evaluate if inflammation or infection could be predicted during these two periods when serum C-reactive protein is increased.

Methods: Eighty-five pregnant women were enrolled in a longitudinal prospective study and had a blood sample to assess serum C-reactive protein levels on admission to the labour ward for normal onset of labour and at day three post-partum. Inclusion criteria were no previous history, a normal single pregnancy, normal vaginal delivery and an uneventful post-partum course. Twelve non-pregnant women of the same age constituted a control group. An automatic Behring Nephelometer® was used to measure serum C-reactive protein concentrations. The Student's t-test (significance $p < 0.05$) was used for statistical analysis.

Findings: C-reactive protein was significantly increased during the onset of labour (4.10 ± 2.79 mg/L) and reached very high levels during the post-partum period (24.07 ± 18.28 mg/L) compared to the standard normal serum C-reactive protein level in a population of non-pregnant women of the same age (2.39 ± 0.07 mg/L).

Interpretation: Increased serum C-reactive protein has been reported to be a marker for subclinical infection during pregnancy in various situations including premature labour and premature rupture of membranes and for complications occurring during puerperium such as thrombophlebitis, thromboembolism or endometritis. This interpretation depends on which upper limit is considered as abnormal. Because serum C-reactive protein was raised during the onset of labour, values of less than 10 mg/L could not be considered as a marker for infection during this period. Elevated serum concentrations of estrogen, progesterone and prostaglandins during labour might be one explanation for those physiological changes. Normal vaginal delivery could be compared to a surgical procedure and tissue injury consecutive to vaginal birth as reflected by a dramatic increase in C-reactive protein. More studies using nephelometry are needed to determine normal and upper values of C-reactive protein during pregnancy.

Key words: C-reactive protein; Labour; Puerperium.

Introduction

C-reactive protein (CRP) is an acute-phase serum reactant which is produced in the liver. Tissue trauma, necrosis, inflammation and infection can produce a rapid elevation of CRP serum concentrations up to 1000-fold. Management of premature rupture of membranes and of premature labour are very much dependant on infection screening results and many authors have tried to find out the usefulness of CRP as a marker for infection in such situations [1-8].

Serum CRP concentrations are difficult to interpret since the normal values during pregnancy are not well documented and no reference technique has been chosen so far [9-13]. Our purpose was to establish normal serum CRP concentration values during the beginning of labour and at day three post-partum.

Methods

Between 01-10-1994 and 30-11-95, 100 women gave informed consent and were enrolled in a longitudinal prospective study with

the following selection criteria: age between 18 to 35 years, weight before pregnancy between 40 to 70 Kg and weight gain of less than 15 Kg during pregnancy, a normal pregnancy on clinical and biological standard investigations, a negative screening for toxoplasmosis, a normal vaginal term delivery and an uneventful post-partum course. Exclusion criteria were: previous obstetrical history (more than two miscarriages, preeclampsia, intrauterine growth retardation, in utero fetal death and abruptio placenta), multiple pregnancy, chronic disease including collagenosis, chronic hypertension, nephropathy, liver dysfunction, anemia, pharmacological treatment (except iron supplementation), alcohol and toxic abuse, premature rupture of membranes, positive urine dipstick test, fever $>38^\circ$ Celsius during labour and/or during the post-partum period, stained amniotic fluid, cesarean section and forceps delivery.

The first sample was taken on admission to the labour ward for spontaneous onset of labour and a second sample was taken at day three during the post-partum period. An automatic Behring® Nephelometer was used to measure serum CRP concentrations. The study was approved by the ethics committee at our institution. Fifteen patients were excluded from the study: 10 had a forceps delivery, one a cesarean section, one a fever $>38^\circ$ Celsius during labour and three experienced fetal tachycardia >160 beats per minute on continuous monitoring during labour.

A total of 85 women fulfilled the inclusion criteria and had a serum CRP concentration measured at the onset of labour and at day three post-partum.

A control group of 12 non-pregnant women was constituted by

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the following criteria: age between 18 and 35 years old, no pregnancy for 6 months, no hormonal treatment (including contraceptive treatment), no previous abnormal pregnancy, no chronic disease including collagenosis, chronic hypertension, nephropathy, liver dysfunction, anemia and no alcohol or toxic abuse.

The Student's t-test (significance $p < 0.05$) was used for statistical analysis.

Results

Control group: The mean age in the control group was 27.25 ± 5.56 years old versus 28.32 ± 4.37 in the study group (not significant).

Onset of labour: Eighty-five women with a mean gestational age of 39.25 ± 56 weeks, had a blood sample taken on admission to the labour ward. Mean CRP concentration was significantly increased compared to the normal value in non-pregnant women (4.10 ± 2.79 versus 2.39 ± 0.07 g/L, $p < 10^{-6}$).

Day three post-partum: The same women had a second sample taken at day three post-partum. Mean CRP concentration was significantly increased compared to the previous sample and to the normal value in non-pregnant women (24.07 ± 18.28 versus 4.10 ± 2.79 and 2.39 ± 0.07 g/L, $p < 10^{-6}$). These results are summarized in Table 1.

Discussion

Many authors studying serum CRP concentration have used various measurement methods with a low sensitivity. For five years nephelometry seems to have been the method of reference to measure this protein concentration and the normal values previously found during pregnancy could not be compared to ours. Although our methods and selection criteria were different from those in the literature, we found CRP to be raised during pregnancy when compared to CRP values in non-pregnant women. Considering normal serum CRP values, Ridker [14] studying 543 healthy men found a mean CRP serum concentration of 1.13 mg/L. This normal value was 1.5 mg/L in our laboratory with a maximum normal limit < 5 mg/L. Surprisingly, our control group showed little increase in serum CRP values (2.39 mg/L) but which were much lower than those in our study group (4.10 and 24.07 mg/L). Haram [13] found serum CRP values in pregnant

women to be below the reference range of 5 mg/L in 13 out of 27 patients with most of the values not being detectable under the experimental condition used (Laser Nephelometer). Romem [11], studying 252 pregnant women at various gestational ages found serum CRP to be increased during pregnancy from 1.6 during the first trimester to 1.8 mg/dL during the third trimester (onset of labour) with a sensitivity of the assay of 0.2 mg/dL (nephelometric immunoassay); moreover a dramatic increase in serum CRP was found during the post-partum period with a maximum level of 5.98 mg/dL decreasing to 2.51 mg/dL, respectively, 24 and 48 hours after vaginal delivery. When expressed in mg/L these results are almost 10-fold higher compared to ours, which is probably due to the measurement technique used. Watts *et al.* [9] studying longitudinally 90 normal pregnant women from 22 weeks' gestation through delivery with a lower limit of CRP detection of 0.5 mg/dL and an usual normal upper value of 1.0 mg/dL (quantitative immuno-turbidimetric assay) found serum CRP to be increased during pregnancy and labour from 0.7 to 1.3 mg/dL and concluded that there were only minimal changes in CRP with gestational age beyond 20 weeks and an elevation of CRP among normal pregnant women in labour at term. Two more recent studies have confirmed these results [10, 12] and the general conclusion of all these studies could be summarized as follows: serum CRP increases during pregnancy, during labour and in post-partum but the normal standard values during normal pregnancy have not yet been established.

The reason why such physiological changes occur during labour remains unclear but elevated estrogen and prostaglandin serum concentrations could stimulate CRP synthesis in the liver which could explain those findings [9, 11]. Specific immunological changes during pregnancy and particularly those in cytokine balance could interfere as well with CRP synthesis.

Since vaginal delivery could be compared to a surgical procedure [10], serum CRP is dramatically increased during puerperium.

Because CRP increases during labour, it may be difficult to use it as a marker for infection in case of premature labour or premature rupture of the membranes [1, 4, 7, 8] and this could explain the controversial results published in the literature [1-8]. Fisk [8] studying serial serum CRP values in 50 women with preterm premature rupture of membranes, found that consecutive serial values > 20 mg/L were highly predictive of infection. Serial measurement showing persistent or increasing high levels of serum CRP concentration may represent a way to screen for infection in such cases. Because serum C-reactive protein was found to be higher during the onset of labour, values of less than 10 mg/L could not be considered as a marker for infection during this period.

Considering puerperium, since CRP should decrease progressively over three to four days [10, 14], serial measurements could be used to diagnose complicated puerperium (endometritis, phlebitis, thromboembolism...).

More studies using nephelometry are needed to deter-

Table 1. — Serum C-reactive protein concentration (CRP) at the onset of labour and day three post-partum and in non-pregnant women

	Pregnant women N = 85	Non-pregnant women N = 12	Statistics Student's t-test
Age (Years \pm SD)	28.32 ± 4.37	27.25 ± 5.56	NS
CRP (mg/L \pm SD) onset of labour	$4.10 \pm 2.79^*$	2.39 ± 0.07	$p < 0.05$
CRP (mg/L \pm SD) post-partum	$24.07 \pm 18.28^*$	2.39 ± 0.07	$p < 0.001$

* student's t-test: $p < 0.001$

mine the normal value of CRP during pregnancy and a cut-off value to help in the diagnosis of infection in case of premature labour, premature rupture of the membranes or complicated puerperium.

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