Serum C-reactive protein in pregnancy-induced hypertension

Jenny V. Garmendia[a], Zoraida Regalado De Rios[b], N.E. Bianco[b] and Juan B. De Sanctis[b]

[a]*Internal Medicine Department, Maternidad Concepción Palacios Hospital, Caracas,* [b]*Instituto de Immunología, Faculty of Medicine, Universidad Central de Venezuela, Caracus, Venezuela*

Requests for reprints to Dr Juan B De Sanctis, Instituto de Immunología, Faculty of Medicine, Universidad Central de Venezuela, Aerocav care of 1216, PO Box 02-5304, Miami FL 33102-5304, USA

Received 4 February 1999; revised 26 April 1999; accepted 28 April 1999

Abstract: We have determined the serum levels of C-reactive protein in 20 non-pregnant women and 66 pregnant women- 20 normal subjects (NP), 16 with mild preeclampsia (MPE), 17 with severe preeclampsia (SPE), six with chronic hypertension plus preeclampsia (CHT+PE) and seven with chronic hypertension (CHT). There were no significant differences between the non-pregnant women and the NP group. The levels of CRP in MPE, SPE and CHT + PE patients were significantly higher ($P < 0.05$) as compared to normal pregnancies (NP). There was no significant elevation in the CHT group as compared to NP. We conclude that CRP levels may be important in the pathophysiology of pregnancy-induced hypertension.

Keywords: C-reactive, chronic hypertension, hypertension, preeclampsia, pregnancy, protein

Introduction: Pregnancy induced hypertension (PIH) is a clinical event that occurs during gestation and reverts after the women has given birth. It is one of the main causes of death during pregnancy [1–3]. Patients with PIH may develop HELLP, which is a syndrome characterized by haemolysis, an increase in the activity of hepatic enzymes and thrombocytopenia [1–4]. Those with chronic hypertension may develop preeclampsia (PE) during pregnancy [1–4].

C-reactive protein (CRP) is an acute phase protein secreted by the liver following various types of stimuli [5–7]. Increases in the level of this protein in serum have been correlated with different inflammatory events and diseases [5–7]. There are contradictory reports regarding an elevation in CRP in normal human pregnancy [7]. However, most authors have reported only a mild increase [8].

The aim of our investigation was to assess the possible importance of CRP levels in PIH and the relationship; between CRP and the severity of PIH.

Patients and methods: The patients were among those admitted to the Maternity Hospital (Maternidad Concepción Palacios) of Caracas. The study was accepted by the Ethical Committee of the hospital.

We studied 66 pregnant women: 20 normal (NP), 16 with mild preeclampsia (MPE), 17 with severe preeclampsia (SPE), six with chronic hypertension plus preeclampsia (CHT+PE) and seven with chronic hypertension (CHT). Upon written consent, a single blood sample was taken during pregnancy. In addition, 20 normal non-pregnant women (laboratory personnel) were used as controls.

We use the classification of the hypertensive disorders of pregnancy adopted by the American College of Obstetricians and Gynecologists [9, 10].

Blood pressure was measured by the first and fifth Kortkoff sound with patients in the left lateral decubitus position. This was done on admission, before and after starting anti-hypertensive treatment (patients with preeclampsia) and immediately before blood collection.

All patients had more than 20 weeks of pregnancy. Mild preeclampsia was defined by the following: recent hypertension, persistently ≥ 140 mmHg systolic or ≥ 90 mmHg diastolic; mild proteinuria or oedema.

Patients with severe preeclampsia had one or more of the following: recent systolic blood pressure persistently ≥ 160 mmHg; diastolic blood pressure persistently ≥ 110 mmHg; proteinuria > 2,000 mg/24 h (or > 3+ in semi-quantitative tests), raised serum creatinine levels (> 177 μmol/l–2 mg/dl) or oliguria (< 500 ml/24 h), platelet count $< 1 \times 10^9$ l or evidence of microangiopathic haemolytic anaemia (schistocytes, increase in indirect bilirubin levels, or increased in serum free haemoglobin levels),

Table 1. Blood pressure, serum uric acid, bilirubin and creatinine levels, ALT and AST activities and platelet counts in the five groups (means ± SD)

	NP	MPE	SPE	CHT+PE	CHT
n	20	16	17	6	7
Age (yr)	26 ± 6	22 ± 7	23 ± 6	34 ± 3*	31 ± 8*
Systolic pressure	120 ± 5	138 ± 11**	164 ± 14***	176 ± 28***	157 ± 15***
Diastolic pressure	72 ± 7	92 ± 6***	111 ± 5***	118 ± 20***	101 ± 12***
Uric acid (mg/dl)	3.2 ± 0.6	5.0 ± 1.6**	5.9 ± 2.7****	6.0 ± 2.4***	5.2 ± 1.2*
Total bilirubin (mg/dl)	0.4 ± 0.2	0.45 ± 0.25	0.49 ± 0.38	0.5 ± 0.23	0.6 ± 0.19
ALT activity (U/l)	17.3 ± 9	16.5 ± 2.6	22 ± 15	26.1 ± 23	21.2 ± 12
AST activity (U/l)	27.3 ± 4	20 ± 4.4	38 ± 27	86.8 ± 119***	27.3 ± 3
Creatinine (mg/%)	0.6 ± 0.2	0.66 ± 0.13	0.81 ± 0.19***	0.83 ± 0.12**	0.73 ± 0.1
Platelet/(mm^3)	242,000 ± 6,0000	256,000 ± 7,9140	232,000 ± 8,8640	200,000 ± 53,398	290,000 ± 67,509
Weeks of gestation	38 ± 3	37 ± 2	36 ± 3	31 ± 5	33 ± 2

The weeks of gestation refers to the time of blood sample collection.
As compared with NP, *P < 0.05, **P < 0.01, ***P < 0.005, ****P < 0.0001 *(ANOVA)*

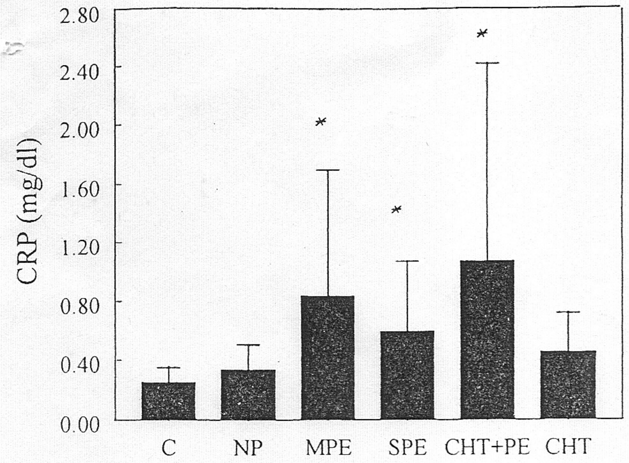

*Figure 1. Serum CRP levels in non-pregnant women (C), normal pregnancy (NP), mild preeclampsia (MPE), severe preeclampsia (SPE), chronic hypertension (CHT), chronic hypertension plus preeclampsia (CHT+PE) (means ±SD). *As compared to NP, P < 0.05 (Student's t-test).*

upper abdominal pain, headache, visual disturbances or other cerebral signs.

Women with chronic hypertension were diagnosed as having essential hypertension before pregnancy. Patients with a previous history of chronic hypertension who developed proteinuria, abnormal oedema or any signs of severe preeclampsia were classified as chronic hypertension with superimposed pregnancy-induced hypertension.

We excluded any patient with fever, infection or other chronic disease (such as diabetes, renal disorders and cardiopathies) and those whose syndromes were not clearly defined by the described earlier criteria. A complete medical record of each patient was kept from admission to discharge.

Hypertensive patients were treated with α methyldopa (Merck Sharp & Dohme, Caracas, Venezuela), hydralazine (Novartis, Caracas, Venezuela) or nifedipine (Bayer, Caracas, Venezuela), alone or in combination. The doses varied depending on the response.

CRP was quantified using nephelometry and the conditions of the assay were as described in the Kallested QM 300 Kit (Sanofi Pasteur Diagnostics, Chaska, Minnesota, USA) and according to the instructions accompanying the Kallested QM 300 nephelometer.

Standard laboratory procedures were used to determine blood and serum parameters.

Results are expressed as means ± SD. ANOVA and Student's unpaired t-test were used for statistical analysis. P values < 0.05 were considered significant.

Results: Table 1 shows the general characteristics of the pregnant women. Patients with chronic hypertension (CHT or CHT+PE) were significantly older ($P < 0.05$) as compared with the other groups. The four different groups (MPE, SPE, CHT and CHT+PE) all showed significantly higher values of blood pressure and serum uric acid. Serum creatinine levels were significantly higher in the SPE and CHT+PE groups as compared with NP. Serum aspartate aminotransferase (AST) activities were significantly higher in the CHT+PE group as compared with NP. No significant differences were observed in serum alanine aminotransferase (ALT) or platelet counts. We did not find HELLP syndrome in these patients.

Figure 1 represents the quantitative serum CRP levels for the different types of hypertension. There were significant differences between the NP and MPE, SPE and CHT+P groups ($P < 0.05$ unpaired Student's t-test). However, ANOVA showed that only the values of MPE and CHT+PE groups were significantly higher ($P < 0.05$) as compared to NP.

There were no major differences in the CRP levels in NP at different weeks of gestation. The values were always < 1 mg/dl.

Discussion: Rise in circulating CRP may be a consequence of acute inflammatory responses or immune cell responses involving tissue damage [5–8]. We hypothesized that CRP levels may reflect PIH but not CHT-induced tissue damage.

In pregnancy, there are contradictory reports concerning serum CRP levels [6, 8]. A general consensus includes pregnancy as one of the physiological conditions in which these values are within the normal range or insignificantly elevated (< 1 mg/dl). Although the levels of CRP vary depending on gestational age, those observed in the serum of normal pregnant women in our study were < 1 mg/dl. On the other hand, several samples from the PIB patients showed values > 1 mg/dl.

We observed that the serum levels of CRP in NP and patients with chronic hypertension (CHT) were within the normal range. However, there were mild but significant elevations in the PE groups (MPE, SPE and CHT+PE) as compared with NP. These results leads us to postulate that serum CRP levels may be altered only in PIH and not in 'pure' CHT. Future studies should ascertain the importance of CRP levels in PIH and chronic hypertension.

Acknowledgements: The authors are indebted to all the patients and controls that collaborated with the present study as well as to the paramedical and medical personnel of the hospital, specially to Drs Freddy Bello, Abelardo Lopez, Nellys Avila, María E. Morantes and Isabel Iturria. This research was supported by the GENIC Program and Immunobiología AC (IBAC).

1. Sibai BM. Preeclampsia – eclampsia. *Probl Obstet Gynecol Fertil* 1990; **1**:9–40.
2. Cunningham FG, Lindheimer MD. Hypertension in pregnancy. *N Engl J Med* 1992; **326**:927–932.
3. Lockwood CJ. In: Cherry SY, Merkatz I (editors): *Medical, Surgical, Gynecological, Psychological and Perinatal Complications of Pregnancy*. 4th ed. Baltimore: Williams and Wilkins; 1991. pp. 477–494.
4. Lim KH, Friedman SA. Hypertension in pregnancy. *Curr Opin Obstet Gynecol* 1993; **5**:40–49.
5. Baumann H, Gauldie J. The acute phase response. *Immunol Today* 1994; **15**:74–80.
6. Ballou SP, Kushner I. C-Reactive protein and acute phase response. *Adv Inter Med* 1992; **37**:313–336.
7. Steel DM, Whitehead AS. The mayor acute phases reactants: C-reactive protein, serum amyloid P component and serum amyloid A protein. *Immunol Today* 1994; **15**:81–88.
8. Young B, Gleeson M, Cripps AW. C-reactive protein: a critical review. *Pathology* 1991; **23**:118–214.
9. Technical Bulletin. Washington DC. *American College of Obstetricians and Gynecologists* vol. 91: February 1986.
10. National High Blood Pressure Education Program Working Group Report on High Blood Pressure During Pregnancy. *Am J Obstet Gynecol* 1990; **163**:1689–1712.