Predictive Value of Early 3rd Trimesteric Maternal Serum C-Reactive Protein Level in Pre-eclampsia

Thesis

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By

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Introduction

Pregnancy induced hypertension (PIH) is the most frequent complication in pregnancy after the 20th week of gestation. This form of hypertension is classified as preeclampsia (PE) and gestational hypertension (GH). The latter is defined as the acute development of hypertension in a woman whose blood pressure (BP) was normal in the early stages of pregnancy and who subsequently developed persistent elevation of BP to at least 140/90 mmHg. Both GH and concomitant 24 hours Proteinuria (0.3 gm/L or more) in the absence of urinary tract infection is defined as PE ***(Ronald et al., 2007)***.

The condition of PE is the main cause of maternal and perinatal mortality, low birth weight, and intrauterine growth restriction, whereas GH has been associated with increased rates of preterm delivery and small for gestational age infants ***(Buchbinder et al., 2002)***.

Preeclampsia develops in 4–5% of human pregnancies. It is characterized by an elevated blood pressure and Proteinuria and develops after 20 weeks of gestational age. PE can result in eclampsia when convulsions develop or manifest as the hemolysis, elevated liver enzymes and low platelet count (HELLP) syndrome. Both eclampsia and HELLP syndrome are

known to be associated with severe complications such as cerebral hemorrhage, lung edema, renal insufficiency, and liver hemorrhage ***(Van Wijk et al., 2000)***.

Several etiologies have been implicated in the development of preeclampsia. Some of them include abnormal trophoblast invasion of uterine blood vessels, immunological intolerance between fetoplacental and maternal tissues, maladaptation to the cardiovascular changes or dietary deficiencies and genetic abnormalities ***(Sibai, 2003)***. Endothelial dysfunction or inappropriate endothelial cell activation are the most common clinical manifestations in preeclampsia, including enhanced endothelial-cell permeability and platelet aggregation ***(Wang et al., 2004)***.

Endothelial dysfunction is accompanied by elevated levels of inflammatory markers such as CRP ***(Teran et al., 2001)***. C-reactive protein (CRP) is an objective and sensitive index of overall inflammatory activity in the body ***(Kluft and Maat, 2002)***. There had been a growing interest in the role of inflammation as a key factor of endothelial dysfunction. A generalized activation of circulating leukocytes, characteristic of inflammation, has been found during preeclampsia ***(Redman et al., 1999)***.

C-reactive protein (CRP) was identified in the 1930s as a plasma protein associated with acute inflammatory responses ***(Tillet, 1930).***

In the past decade, elevations in serum CRP have been associated with risk of cardiovascular disease ***(Pai et al., 2004).***

Raising interest in the relationship of CRP with preeclampsia as a predictor of the syndrome and possible contributor to its pathogenesis. CRP concentrations are elevated in women with clinically evident preeclampsia ***(Wolf et al., 2001; Deveci et al., 2009).***

However, the utility of CRP in the pre-clinical prediction of preeclampsia has been less consistent ***(Tjoa et al., 2003).***

Our objective was to assess the relationship between CRP in early pregnancy and the change in CRP during pregnancy with the subsequent development of preeclampsia in a population of women at high-risk for the syndrome.

Aim of the Work

To determine the predictive value of maternal serum level of C-reactive protein (CRP) for pre-eclampsia and its severity

1^{ry} outcome : The first goal of this study is to investigate the relation between CRP and development of mild and/or severe pre-eclamptic Egyptian women between 24 and 40 weeks of gestation.

2^{ry} outcome : The second goal was to determine a reliable CRP cut-off level and to evaluate its association with severity and adverse feto-maternal outcomes of pre-eclampsia at third trimester.

Chapter (1):

Preeclampsia

Hypertensive disorders are the most frequent medical complication during pregnancy. These disorders are usually categorized into those that preexist pregnancy (underlying microvascular disease) and those that develop for the first time after 20 weeks of gestation (gestational hypertension or pre-eclampsia) ***(Sibai et al., 2005)***. In addition, preeclampsia can develop in women who are thought initially to have gestational hypertension ***(Barton et al., 2001)***.

Classification:

According to the American college of Obstetricians and Gynecologists:

1-Prenancy Induced:

- Hypertension without Proteinuria or pathological oedema.
- Preeclampsia with Proteinuria and/or pathological oedema.
- Eclampsia with convulsions.

2-Pregnancy Aggravated:

- Superimposed preeclampsia.
- Superimposed eclampsia.

3-Coincidal Hypertension.

Definition:

The American College of Obstetricians and Gynecologists (ACOG) guidelines defined preeclampsia as sustained pregnancy induced hypertension with Proteinuria. Hypertension was defined as sustained two or more blood pressure (BP) readings of ≥140/90 mm Hg (with readings taking place ≥ 6 h apart) or a sustained 15 mm Hg diastolic rise or in systolic BP of 30 mm Hg above first trimester BP values. The ACOG defined Proteinuria as urine protein concentrations of ≥300 mg/L in 24 hours (or +1 on a urine dipstick) on two or more random specimens collected ≥ 4 hours apart ***(Yusuf et al., 2005)***.

Types of preeclampsia:

According to **Working Group of the *National High Blood Pressure Education Program (NHBPEP, 2000),***

Preeclampsia is classified into:

1- Preeclampsia:

Preeclampsia refers to the new onset of hypertension and Proteinuria after 20 weeks of gestation in a previously normotensive woman.

2- Preeclampsia superimposed upon chronic hypertension:

The superimposed preeclampsia is diagnosed when woman with chronic hypertension develops new onset Proteinuria after 20 weeks of gestation. Women with chronic hypertension on preexisting Proteinuria (before 20 weeks) are considered preeclamptic if there is an exacerbation of blood pressure to the severe range (systolic 160 mmHg and diastolic 110 mmHg) in the latter part of pregnancy especially if accompanied by symptoms or a sudden increase in Proteinuria.

3- Eclampsia:

Eclampsia refers to the development of seizures (grand mal) in a woman with preeclampsia. These seizures should not be attributed to another cause.

Incidence:

Frequency of preeclampsia ranges between 2% and 7% in healthy nulliparous women ***(Vatten and Skjaerven, 2004)***. In these women, the disease is mostly mild, the onset mostly near term or intrapartum (75% of cases), and only conveys a negligible increased risk for adverse pregnancy outcome ***(Sibai, 2003)***, By contrast, frequency and severity of the disease are substantially higher in women with previous pre-eclampsia

(Hnat et al., 2002), pregestational diabetes mellitus, and pre-existing thrombophilias ***(Alfirevic et al., 2002)*.**

Risk factors for preeclampsia:

1) **Age:** Preeclampsia is more common below age 17 and above 35 years. This may be due to poor immune capacity at that age ***(Khaliq et al., 1999).*** Pre eclampsia in the older women is more likely to be pregnancy-aggravated hypertension ***(Zhang, 2007).***

2) **Parity:** Preeclampsia is essentially a disease of the first pregnancy and even if occurring in subsequent pregnancies, it will be much less severe ***(Khalia et al., 1999).*** It is indeed a disease of first pregnancies, but at the level of a couple (primipaternity) rather than only the mother's side (primigravidity). Therefore, multigravidae share the risk with primigravidae in case of conception with a new partner ***(Robillard et al, 1998)*.**

3) **Previous preeclampsia:** Compared to nulliparous women, women with preeclampsia in the previous pregnancy had significantly higher rates of preeclampsia and adverse perinatal outcomes associated with preterm delivery as a result of preeclampsia ***(Hnat et al., 2002).***

4) **Gestational age:** A peak of gestational age incidence is seen after 20 week gestation. Rarely, preeclampsia develops