

Evaluation the Levels of Serum Hormones (Progesterone, Estradiol, and hCG) in Preeclamptic Iraqi Pregnancies

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Received 1, March, 2010

Accepted 28, November, 2010

Abstract:

This study aimed to evaluate serum levels of steroid hormones and human chorionic gonadotropin (hCG) hormone in preeclamptic Iraqi pregnancies compared to those of healthy pregnancies.

This study enrolled 120 pregnant women, divided into four groups:

1. 30 healthy pregnant women.
2. 37 pregnant women with mild preeclampsia
3. 53 pregnant women with severe preeclampsia
4. 90 pregnant women with preeclampsia

Preeclamptic women and their severe cases but not mild cases had significantly ($P<0.01$) increased levels of serum hCG as compared with healthy pregnancies. By contrast, sera levels of estradiol were significantly ($P<0.01$) decreased in total preeclamptic groups and their severe cases but not in mild group as compared to healthy pregnant women (controls), while there were no significant differences in the levels of serum progesterone in all preeclamptic groups as compared with controls.

This study that concludes Preeclampsia is associated with increased levels of hCG hormone and decreased levels of estradiol hormone and these support the suggestion of the role of hormones in preeclampsia.

Key words: preeclampsia, maternal serum, progesterone, estradiol, HCG

Introduction:

Preeclampsia is a multisystemic disorder involving the placenta, liver, kidneys, blood, and the neurological and cardiovascular systems [1]. The symptoms of this multisystemic disorder, which appear during the second and third trimester of pregnancy are caused by the increased vasoconstriction, which result in maternal hypertension, decreased uteroplacental blood flow, edema, proteinuria, abnormal clotting, liver and renal dysfunctions[2,3]. A generalized dysfunction of maternal cells may underlie most of the clinical

symptoms such as hypertension, fluid retention, and clotting abnormalities. Hormonal changes contribute to the physiological maternal adaptation during human gestation. Fluid balance, blood pressure, digestion, respiration, fuel and mineral metabolism, immune response, and sexual behavioral functions are reprogrammed during pregnancy and occur under modulation of hormonal changes from very early gestation to fetal delivery and beyond [4]. These hormonal changes are different in pathological pregnancies and may be monitored for diagnosis or

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risk prediction of gestational diseases, taking into account both hormonal levels and the preexisting maternal risk factors [5]. Intrauterine tissues (placenta, amnion, chorion, deciduas) express hormones that play a decisive role in maternal physiological interactions, in the reprogramming of the maternal endocrine system, and in the signaling mechanisms that determine the timing of parturition [5,6].

The excessive or deficient release of some placental hormones in association with gestational diseases may be of an adaptive response of the placenta and fetal membranes to adverse environmental conditions such as hypertension, hypoxia, and infection, or to malformations of the fetus and placenta [7].

The high concentrations of these placental hormones in maternal peripheral blood, in fetal (cord) blood, and in the amniotic fluid are clinically accessible signs of increased placental hormone synthesis [5]. The secretion of several placental hormones is augmented in preeclamptic patients such as hCG, estrogen, activin A, and inhibin A [8].

Materials and Methods:

This study was carried out at the Obstetric Department of Baghdad Teaching hospital and in the immunology department of the Teaching laboratories of medical city from May 2008 to May 2009. Thirty apparently healthy pregnant women as control (group 1) with mean age 27.07 ± 1.12 years. The patients were classified into three groups; 37 mild preeclampsia (group 2) with mean age 30.03 ± 1.14 years, 53 severe preeclampsia (group 3) with mean age 28.85 ± 0.98 years and 90 total preeclampsia (group 4) with mean age 29.33 ± 0.74 years. The diagnosis of preeclampsia was established in

accordance with the American College of Obstetrics and Gynecology definition [9]. The healthy pregnancy was diagnosed on the basis of clinical, biochemical, and ultrasound findings and none of the patients had pre-existing hypertensive disorders or any renal, hepatic, or hematological diseases, and had received no medication.

From each subject included in the study, 3 ml blood were taken by venous puncture and collected in test tubes without anticoagulant. The serum obtained by centrifugation was divided into triplicates and stored in 600 μ l freezing tubes at a temperature of -20C, until testing. The concentrations of hormones were measured using VIDUS kit according to manufacturer's instructions. All immunoassay kits were purchased from Biosource Europe S.A Systems. The albuminuria was measured by dipstick test.

Results are expressed as mean \pm Standard Error ($X \pm SE$). The significance of the difference between the values from different groups is determined using one way analysis of variance (ANOVA) (F-test). A level of $P < 0.05$ is defined as statistically significant [10].

Results:

The Demographic and obstetric features of the groups maternal age, gestational week and mean systolic and diastolic blood pressure at the time of sample collection are shown in Table 1. All the preeclamptic patients have albumin in urine $\geq +1$, while no one of the control group have albuminuria.

There was no significant ($P > 0.05$) difference in maternal age, gestational week between the groups. There were a significant ($P < 0.001$) increase in mean systolic and diastolic blood pressure, 142 ± 0.71 & 91.89 ± 0.53 mmHg in group 2, and 167.74 ± 1.63

& 112.45 ± 1.40 mmHg in group 3 , and 157.44±1.64 & 104.00±1.37 mmHg in group 4 as compared with controls, . The mean ± SE serum levels of progesterone (ng/ml), estradiol (pg/ml), hCG (mIU/ml) in total preeclamptic group were 167.62±9.66, 8022.08±611.05 and 43659.01±3611.85 respectively, while the mean ± SE serum levels of progesterone (ng/ml), estradiol (pg /ml) and hCG (mIU/ml) in severe preeclamptic group were 162.26±13.02, 6962.09±747.73 and 49478.53±3950.35 respectively , the mean ±SE serum levels of progesterone (ng/ml), estradiol (pg/ml), hCG (mIU/ml) in mild preeclampsia group were 175.29±14.43, 9540.43±989.82 and

35322.92 ± 4974.22 respectively, and the mean ± SE plasma levels of progesterone (ng/ml), estradiol (pg/ml) and hCG (mIU/ml) in control group were 190.69± 13.26, 11024±1161.83 and 17588.03± 2869.01 respectively (Table 2). Statistical analysis shows there was significant positive correlation between hCG hormone and the severity of disease (diastolic blood pressure) in preeclamptic women (Figure.1), also there was significant negative correlation between estradiol levels and diastolic blood pressure in preeclamptic women (Figure 2), while there was no significant correlation between progesterone levels and the severity of the disease.

Table 1. Demographic and clinical characteristics of patients with preeclamptic and healthy normotensive pregnant women (Mean ± SE).

Characteristics	(1)Control(N=30)	(2)MPE(N=37)	(3)SPE(N=53)	(4)TPE(N=90)
Maternal age (years)	27.07 ± 1.12	30.03 ± 1.14 *	28.85 ± 0.98 *	29.33±0.74 *
Gestational age (weeks)	33.63± 1.00	34.43 ±0.68 *	35.72 ±0.60 *	35.19±0.45 *
Systolic blood pressure (mmHg)	108.00±1.99	142.70±0.71 **	167.74 ±1.63 **	157.44±1.64 **
Diastolic blood pressure (mmHg)	74.50 ±1.05	91.89 ±0.53 **	112.45 ±1.40 **	104.00±1.37 **
Albumin in urine	-----	1+	2+ 4+	1+ 4+

MPE =Mild preeclampsia; SPE = Severe preeclampsia; TPE = Total preeclampsia
 * = Non Significant ; ** = Significant at the level P< 0.01

Table 2. Serum hormonal levels (progesterone, estradiol, and hCG) among the studied groups (mean ±SE).

Hormones	(1)Control(N=30)	(2)MPE(N=37)	(3)SPE(N=53)	(4)TPE(N=90)
Progesterone (pg/ml)	190.69±13.26	175.29±14.43 *	162.26±13.02 *	167.62±9.66 *
Estradiol (pg/ml)	11024.60±1161.83	9540.43±989.82 *	6962.09±747.73 **	8022.08±611.05 **
hCG (mIU/ml)	17588.03±2869.01	35322.92±4974.22 **	49478.53±3950.35 **	43659.01±3166.84 **

* = Non Significant
 ** =Significant at the level P< 0.01

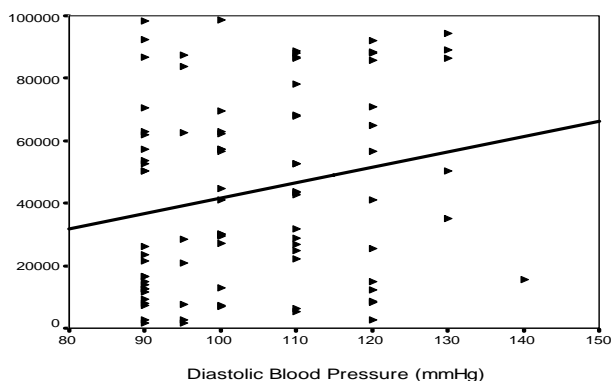


Fig.1: Scatter diagram with fitted regression line showing the positive linear correlation between diastolic blood pressure and serum hCG concentration in preeclamptic women.

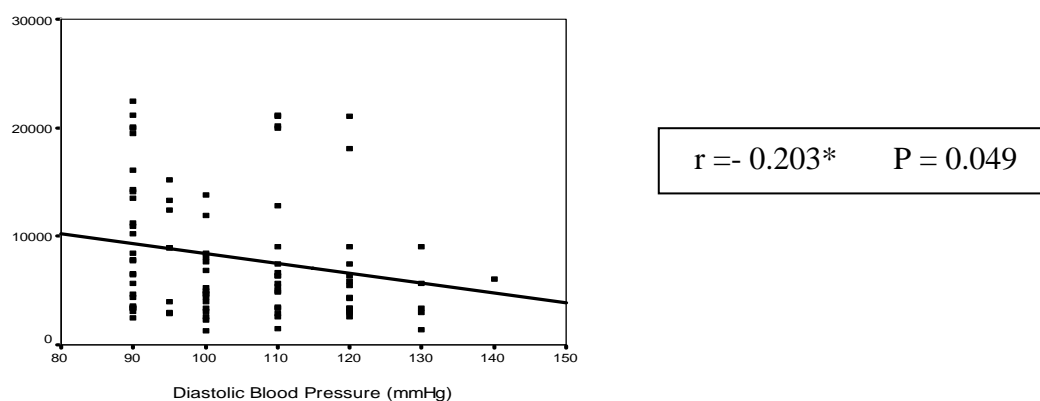


Fig. 2: Scatter diagram with fitted regression line showing the negative linear correlation between diastolic blood pressure and serum estradiol concentration in preeclamptic women

Discussion:

The placenta is the main source of pregnancy hormones, and pregnancy hypertension and preeclampsia are associated with placental malfunction, including altered levels of hormones such as sex hormones and hCG [11]. Preeclampsia is characterized by a disturbance in the fundamental balance between steroids and other pregnancy hormones during pregnancy [12].

Jirecek *et al* [13] showed that alteration of steroid hormones profile has been suggested to be involved in the pathophysiology of preeclampsia.

In this study, levels of progesterone were found to be lower but not significant in all groups of preeclampsia. This was consistent with the results of Zeisler *et al* [14] who found that the serum levels of progesterone in preeclamptic women and controls were not significantly different, and this indicates that the absence of altered levels of progesterone may not reflect the potential role of this hormone in preeclampsia.

Luisi *et al* [15] reached a conclusion that the maternal serum progesterone levels displayed a high variability between subjects, without reaching any statistical difference in comparison with healthy pregnant women. However the results of progesterone

levels in preeclamptic pregnancies are not consistent across studies. Lou *et al* [16] reported that the levels of progesterone was significantly lower in preeclamptic cases than control women with similar age, gestational age, and body mass index (BMI), this difference indicates a role of progesterone in the pathogenesis of PE. Salas *et al* [17] found high levels of progesterone in women with preeclampsia; therefore it's tempting to speculate that higher progesterone concentration might have a causal role in both vasospasm and in the imbalance between thromboxan and prostocyclin described in preeclampsia.

The results provided no indication that the maternal circulating levels of progesterone have a role in the pathogenesis of PE, this may be due to many factors, such as gestational age, maternal age and BMI, and all these factors may have adverse effect on reliability of the results.

Also, many studies measuring estrogen levels in blood from preeclamptic women have been inconsistent with some studies showing lower estrogen values in preeclamptic women [17,18], while others showed either no differences [19,20], or higher concentration [21].

This study confirms the findings of other studies that observed decreased

levels of serum estradiol in preeclamptic women as compared to normotensive [22,23].

The results showed highly significant lowered levels of serum estradiol in total preeclampsia and severe groups but not in mild preeclamptic group as compared to controls, this may be due to the severity of the disease with abnormalities in fetal and placental development, reduced maternal estradiol levels may reflect a decrease in fetoplacental estrogen production.

Zeisler *et al* [24] observed that the estradiol and estriol levels was different in those with late onset severe preeclampsia, when they measured the concentration of these hormones in women with mild and severe preeclampsia compared to normotensive pregnant women.

In this study, results showed that the mean level of hCG tends to be significantly higher in preeclamptic women and their two sub groups (mild & severe) than those of controls. Also the mean levels of this hormone were significantly higher in severe preeclampsia as compared with mild group. Elevated maternal serum hCG in severely preeclamptic women might reflect a significantly pathologic changes and abnormal secretory function.

Several studies have reported an association between unexplained elevation of maternal second trimester serum hCG levels and the development of preeclampsia.

A study done on Iraqi preeclamptic pregnant women by Mohammed [25] demonstrated an increased risk of preeclampsia with increased second trimester hCG levels and suggested that a second trimester screening program might be useful to anticipate those at risk for pregnancy induced hypertension. Akbari *et al* [26] compared β -hCG levels in women

suffering from mild preeclampsia, severe preeclampsia with normotensive pregnant women during the third trimester of their pregnancy..

The statistical analysis findings indicate a correlation between the severity of the disease process and the levels of these mediators.

Preeclampsia and the severity of the disease appear to originate and correlate with the severity of the pathologic processes at the interface of the fetal and maternal circulation.

Conclusion:

It has been found that increased levels of hCG hormone and decreased levels of estradiol in the serum of women with severe preeclampsia. These findings suggest that severe preeclamptic women have higher hormonal changes than mild preeclampsia, and this reflect the abnormal placentation in these patients.

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تقييم مستوى الهرمونات في مصل النساء العراقيات ذوات مقدمة الارتجاج

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الخلاصة:

تضمنت هذه الدراسة تقييم مستويات كل من الهرمونات الستيرويدية البروجستيرون والاستراديل وهرمون hCG في امصال النساء العراقيات المصابات بمقدمة الارتجاج (تسم الحمل)، شملت هذه الدراسة 120 امرأة حامل قسمت الى اربعة مجاميع:

- المجموعة الاولى : مجموعة النساء السليمات كسيطرة (30)
المجموعة الثانية : مجموعة النساء ذوات مقدمة الارتجاج المعتدل (37)
المجموعة الثالثة : مجموعة النساء ذوات مقدمة الارتجاج الشديد (53)
المجموعة الرابعة : مجموعة النساء ذوات مقدمة الارتجاج الكلي (90)

اظهرت نتائج الدراسة الحالية ارتفاع معنوي ($P < 0.01$) في مستوى هرمون hCG في امصال النساء ذوات مقدمة الارتجاج الشديدة منها مقارنة بالحالات المعتدلة ومجموعة السيطرة وكذلك انخفضت معنويا ($P < 0.01$) مستوى هرمون الاستراديول في امصال النساء ذوات مقدمة الارتجاج وخاصة الحالات الشديدة مقارنة بالحالات المعتدلة ومجموعة السيطرة ، في حين لم يكن هنالك اي فرق معنوي في مستوى هرمون البروجستيرون في كافة مجامي المرضى ومجموعة السيطرة . نستنتج من هذه الدراسة ان مقدمة الارتجاج له علاقة بزيادة مستويات هرمون hCG وانخفاض في مستويات هرمون estradiol وهذه تساند الاقتراح في دور الهرمونات في مقدمة الارتجاج (preeclampsia).