Study the correlation between Human Chorionic Gonadotropin Hormone and Some Biochemical Parameters in Iraqi Women with Pregnancy-Induced Hypertension

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Abstract

Pregnancy-induced hypertension (PIH) is a major pregnancy complication that causes pregnant women mortality. Here, we had scrutinized the correlation between serum levels of □-hCG and biochemical parameters in PIH. Serum samples were collected from eighty Iraqi women (forty women with pregnancy-induced hypertension as patients group, twenty normotensive pregnant women as a positive control, and twenty normotensive non-pregnant women as a negative control) all groups were diagnosed clinically. All □-hCG hormone level was measured for all studied groups, also serum uric acid, albumin, and total protein levels were measured as biochemical parameters. Data analysis showed that serum level of □-hCG hormone was significant increase ($p \leq 0.05$) in PIH in compared to control groups. Also Uric acid level was increased significantly in PIH group in compared with control groups. While Albumin show there was no significant difference in PIH group. Total serum protein level was measured by Bradford total Protein assay all results was in normal value and showed a significant difference in PIH group in comparison to control groups. Our study shows that there is correlation between β-hCG with uric acid and albumin levels in PIH. Serial estimation of serum β-hCG, uric acid, and albumin can be important to use as a marker of disease and also can be used in better early management of established cases that lead to preeclampsia and eclampsia.

Keywords: PIH, □-hCG, uric acid, albumin, total protein, Iraq.

دراسة العلاقة بين هرمون موجهة الغدد التناسلية المشيمائية البشرية وبعض الدلائل الكيموحيوية في النساء العراقيات المصابات بارتفاع ضغط الدم الحملي

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الخلاصة

يعد ارتفاع ضغط الدم الحملي (PIH) هو أحد مضاعفات الحمل الرئيسية التي تؤدي إلى وفاة الأم. تم التقصي عن العلاقة بين هرمون موجهة الغدد التناسلية المشيمائية البشرية و الدلائل الكيموحيوية في النساء

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العراقيات المصابات بارتفاع ضغط الدم الحملي. جمعت عينات مصل الدم من 80 امرأة عراقية (أربعون إمرأة مصابة بارتفاع ضغط الدم الحملي كمجموعة المرضى قيد الدراسة وعشرون من النساء الحوامل الطبيعيات باعتبارها مجموعة سيطرة إيجابية ، وعشرون من النساء غير الحوامل باعتبارها مجموعة سيطرة سلبية) وكل المجاميع شخصت سريريا. كما تم قياس مستويات كل من مستوى هرمون موجهة الغدد التناسلية المشيمائية البشرية (hCG-β) لكل المجاميع و حامض اليوريك ، البروتين الكلي والألبومين كعوامل كيموحيوية. اظهرت النتائج ارتفاع معنوي عال (p<0.01) لهرمون hCG-β و حامض اليوريك في النساء اللاتي تعاني من ارتفاع ضغط الدم الحملي بالمقارنة مع مجموعتي السيطرة ، في حين كانت نسبة البروتين الكلي ضمن الحدود الطبيعية ولم تظهر اختلاف معنوي (p<0.05) وأظهرت انخفاضاً في النساء الحوامل الطبيعية مقارنة مع المجاميع الاخرى كما ان نتائج الالبومين لم تظهر اختلاف معنوي (p≥0.05) بين النساء اللاتي تعاني من ارتفاع ضغط الدم الحملي مقارنة مع مجموعة الحوامل الطبيعية بينما لوحظ زيادة في مجموعة النساء غير الحوامل. دراستنا ايضا كشفت عن وجود علاقة بين هرمون موجهة الغدد التناسلية المشيمائية البشرية و حامض اليوريك والألبومين. ان تحديد مستوى هرمون hCG-β وحامض اليوريك والالبومين يعتبر مهم ويمكن استخدامه كدلالة على المرض وايضا يمكن استخدامه للسيطرة المبكرة للحالات المشخصة التي ممكن ان تتحول الى تسمم حمل او الإرتجاع.

Introduction

Pregnancy-induced hypertension (PIH), is the Elevation of systolic blood pressure (SBP) level of more or equal to 140 mmHg and/or diastolic blood pressure (DBP) level of more or equal 90 mmHg. PIH is one of the primary causes of maternal death [1]. The onset of disease typically occurs in 20 weeks gestation [2]. Multiple organs dysfunction can occur, which may be a risking factor for mother and fetus life [3]. A tissue that is affected by pregnancies problematical like hypertension is the placenta, this may be considered that early placental vascular damage in preeclamptic pregnancies and cause a decreasing of and cause a decreasing of oxygen amount. So, the result is increasing of human chorionic gonadotropin (hCG) hormone production by hyperplastic syncytiotrophoblastic cells. Previous researches had shown a link between β-hCG raising levels and the progress of hypertension [4]. Protein in serum have a central role in sustain blood balance, so total protein may be raised or reduced because of some physiological and pathological modifications in human body during pregnancy period. The blood serum contain many proteins that differ in origin and functions. The main functions are responding to cases of inflammation, controlling disease, carry out transport, control extracellular fluid distribution and a source of nutrition of the tissues. The two major type of blood proteins are albumin and globulins [5]. Albumin helps to keep the blood from leaking out of blood vessels. It also helps carry medicines & important substances through the blood. While globulins are made in the liver and immune system. Some globulin has several function such as transportation of metals through the circulatory system others serve for fighting infections [6]. Previous researches in biochemistry proved that serum albumin has a role as an antioxidant scavenging carbon-centered free radicals. However, the correlation between levels of human serum albumin, oxidative stress, and endothelial function in pregnant women especially those with PIH, remains unknown [7].

Uric acid (UA) has been considered as the inactive end product in the catabolism of purine. Purine metabolism by xanthine oxidase couples the production of uric acid with the generation of superoxide anion (O_2^-) and hydrogen peroxide (H_2O_2) [8]. The excess of UA in the human body causes a chronic hyperuricemia. This accumulation could lead to a progress of hypertension, as well as chronic kidney disease, cardiovascular diseases, and metabolic syndrome. Hyperuricemia is a common outcome in pregnancies that suffer from PIH [9].

The aim of current study is to determine correlation between serum levels of □-hCG and some biochemical parameters in Iraqi women with pregnancy-induced hypertension in compression to normal pregnant and non-pregnant woman.

Materials and Methods
Participants

Eighty participants women involved in this study during their attendance at Fatima al-Zahraa hospital in Baghdad through the period from October 2017 to January 2018. The selection of women

were as follows: forty women with pregnancy-induced hypertension as a patient group, twenty normal pregnant women as a positive control, and twenty non-pregnant women as a negative control.

Samples Collection

Five milliliters (ml) of venous blood had been collected from pregnancy-induced hypertension, normotensive pregnant, and non-pregnant women using a clean plain tube and allowable to clot at 37°C for 10 minutes. Then it has been centrifuged for 5 minutes at 2500 rpm until serum separated. Serum was reserved at -20°C until used.

- **Determination the levels of □-hCG in serum**

By using an Electrochemiluminescence immunoassay (ECLIA) kit cobas®e411, serum levels of □-hCG were measured in women with PIH in addition to normotensive pregnant and non-pregnant women, following the manufacturer's instructions. Ten μL of the sample was incubated with both a biotinylated, monoclonal hCG-specific antibody and a ruthenylated, monoclonal hCG-specific antibody to form a sandwich complex. Streptavidin-coated microparticles were added to the reaction mixture and the complex binds to the solid phase via biotin–streptavidin interactions. The reaction mixture was transferred to a measuring cell and the microparticles are magnetically captured onto the surface of an electrode; unbound sample was washed away before a chemiluminescent reaction was induced by applying a voltage to the electrode. Chemiluminescence was measured by a photomultiplier and the concentration of β-hCG within the sample is calculated using a calibration curve (Roche, Germany).

Biochemical parameters determination in serum

- **Serum uric acid determination**

The mixture of sample and reagent was incubated at 37C for 5 min. The strength of the red color formed was relational to the uric acid concentration in the sample, and the colored complex had been measured at 520nm by spectrophotometry (Spinreact, Spain).

- **Serum albumin determination**

Sample and reagent were mixed and left for 1 min at room temperature then the absorbance of colored complex that formed when Albumin in the sample reacts with bromocresol green in acid medium determined at 630nm by spectrophotometry (BioSystems, Spain).

- **Serum total protein determination (Bradford assay)**

The Bradford assay is a favorite colorimetric assay for measuring protein it based on an absorbance shift of the dye Coomassie Brilliant Blue [10].

Statistical Analysis

The program of Statistical Analysis System (SAS) was used to analysis the different factors in study parameters. The least significant difference LSD test (ANOVA) was used for significant compare between means and Estimatation of the correlation coefficient between parameters in this study (SAS. 2012).

Results

The analysis of data showed a highly significant difference (P<0.01) between PIH group and other positive control and negative control groups in uric acid concentration, the mean of uric acid was (6.41 ± 0.20, 4.12 ± 0.28 and 4.10 ± 0.26 respectively) and it was shown in (Table-1).

Total serum protein level was measured by Bradford total Protein assay all results was in normal value there was significant different between groups the Mean ± SE (5.76±0.12) in PIH group in comparison to normal pregnant and non-pregnant women (5.13 ± 0.13,and 5.93 ± 0.19) respectively as shown in (Table-1).

Other finding in this study showed that there was no significant differences of albumin in pregnant women with PIH and normal positive control (3.33 ± 0.05 and 3.17 ± 0.10), respectively. Whereas the negative control group showed significant differences comparing to other groups (3.90 ± 0.08) as shown in Table-1

Table 1-Compare between PIH and control groups in the serum uric acid, albumin and total protein in the Iraq women.

Group / Parameters	Mean ± SE		
	Uric acid (mg/dl)	total Protein (mg)	Albumin (g/dl)
PIH	6.41 ± 0.20 a	5.76 ± 0.12 a	3.33 ± 0.05 b
Control +ve	4.12 ± 0.28 b	5.13 ± 0.13 b	3.17 ± 0.10 b
Control -ve	4.10 ± 0.26 b	5.93 ± 0.19 a	3.90 ± 0.08 a
LSD value	0.722 **	0.433 **	0.209 **
P-value	0.0001	0.0001	0.0023
** (P<0.01): Means having with the different letters in same column differed significantly.			

Uric acid is a simple supportive parameter used to confirm the diagnosis of preeclampsia to one in which we appreciate its independent link with adverse outcomes [11]. Bahediya proved that there was no significant change in serum uric acid of normal pregnant women, compared to non-pregnant women, Boyle also support this proof [12, 13]. The endothelial dysfunction and vasospasm in PIH may eventually leads to widespread ischemic injury and oxidative stress, consequently promoting a uric acid production. Hyperuricemia may then have partial effects on placental and maternal vascular dysfunction [14]. Hyperuricemia is a communal result in PIH women. Disease severity and perinatal mortality had described to correlate with Hyperuricemia [8]. Recently, augmented oxidative stress and the formation of reactive oxygen species have been proposed as other sources of the elevated serum acid levels seen in preeclampsia and cause the toxemic cases [15].

Total Proteins are normally stopped from transitory into urine by both the tubules and the glomeruli. In non-pregnant women The abnormal excretion of total protein is more than 150 mg daily [16]. In normal pregnancy, increasing urinary protein excretion is detected due to a mixture of amplified permeability of the glomerular basement membrane and increased glomerular filtration rate. Also, in PIH highly molecular weight protein was lost due to endothelial dysfunction and vasospasm [17].

Serum albumin was slightly elevated in PIH than normal pregnant and this is in accordance with the finding of previous study done by Ephraim, et al., 2018 who recorded a high urinary protein level and decreased serum albumin concentration among preeclamptic women compared to the healthy pregnant women. This could be due to the dangerous effect of human albumin serum levels on vascular oxidative stress in some diseases of human[18].

Determination of serum levels of ▢-hCG

The obtained result showed that maternal serum level of β-hCG in PIH women was significantly higher (P<0.05), (9601.43 ± 78.71 miu/ml) than positive and negative control groups (4344.50 ± 423.93 miu/ml and 8.83 ± 4.64 miu/ml respectively) as shown in Table-2.

Table 2-Compare between PIH and control groups in the serum β-hCG hormone concentration.

Group	Mean ± SE of β-hCG (miu/ml)
PIH	9601.43 ± 78.71 a
Control +ve	4344.50 ± 423.93 b
Control -ve	8.83 ± 4.64 c
LSD value	578.49 **
P-value	0.0001
** (P<0.01). Means having with the different letters in same column differed significantly.	

Many studies also has been demonstrated that maternal serum concentrations of beta human chorionic gonadotropin (β-hCG) were significantly rising in the PIH women [19-21]. Although the regulation mechanism of gestational hCG remains largely unknown, it is mostly established that syncytiotrophoblast is secreted β-hCG. Also, β-hCG manufacture has been shown to rise when normal placental villi in organ culture were maintained under hypoxic condition [22].

It is well recognized that hCG can act straight on arterial vascular tension and on trophoblast function including syncytiotrophoblast differentiation and secretion and spiral arteries invasion and transformation [23]. Increasing of hCG secretion is supposed to reflect early endothelial dysfunction and/or placental damage [24]. Using hCG as an indicator of cytotrophoblast differentiation, this results are reliable with the results of Gurbuz et al., which showed that serum levels of hCG increased according to the severity of preeclampsia [25].

Correlation coefficient between β-hCG and biochemical parameters

Statistical analysis showed that there was a significant positive correlation between β-hCG hormone with Uric acid r=0.60 as well as a significant negative correlation between β-hCG hormone with Albumin r=0.40. While total protein showed no correlation with β-hCG hormone r=-0.01, (Table 3).

Table 3-Correlation coefficient between β-hCG and biochemical parameters

Parameters	r	p-value
Uric acid	0.60 **	0.0002
Albumin	-0.40 **	0.0001
Total protein	-0.01 NS	0.832
** (P<0.01), NS: Non-Significant		

Analysis of the data of this work also found a positive correlation between β-hCG and uric acid as shown in (Table-3). Uric acid mechanism can mediated maternal vasculature damage which cause unsuccessful placental bed formation because of interference in trophoblast invasion. This consequently leads to ischemia-reperfusion injury to the placenta and oxidative stress which lead to increase secretion of β-hCG [26]. Uric acid and β-hCG levels in pregnancy help in early recognition and better organization of patients who are at risk of pregnancy-induced hypertension [27].

The result also showed a negative correlation between β-hCG and albumin, as shown in Table-3. Human serum albumin corresponds inversely to oxidative stress. Human serum albumin seems to decrease superoxide levels via NADPH oxidase and superoxide scavenging inhibition independently in the human. This explain that when human serum albumin increase it work as an antioxidant in the endothelial function. This antioxidant effect on oxidative stress has a negative correlation which lead to decrease the secretions of β-hCG in PIH women [7].

Conclusion

Our study showed that there is correlation between β-hCG with uric acid and albumin levels in PIH. Serial estimation of serum β-hCG uric acid and albumin can be important to use as markers of disease and also can be used in better early management of established cases that lead to preeclampsia and eclampsia.

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