Estimation of Serum Aldosterone and Electrolytes in Pregnancy Induced Hypertension

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Abstract

Pregnancy Induced Hypertension(PIH) is one of the most frequent complications of pregnancy , however little is known about its etiology. The renin angiotensin aldosterone system(RAAS) has been implicated in the pathogenesis of PIH. The study of serum electrolytes is gaining ground in the pathophysiology of hypertension. The study sample consist of 50 normal non pregnant women, 50 normotensive pregnant women, and 50 preeclamptic pregnant women in their third trimester in Mosul city. The aim of this study was designed to evaluate the role of serum aldosterone and the serum electrolytes in pathogenesis of PIH. The results of this study showed that there was a highly significant reduction ($P<0.000$) in serum sodium, calcium, and aldosterone levels in preeclamptic pregnant women in comparison with normotensive pregnant women & the control group. While there is a highly significant elevation ($P<0.000$) in the serum level of potassium in preeclamptic women in comparison with normotensive pregnant women & the control group. The serum chloride level showed a highly significant reduction ($P<0.006$) in preeclamptic women in comparison with the normotensive pregnant women. The serum aldosterone has a positive and negative correlation with serum sodium and potassium respectively in preeclamptic pregnant women.

تقدير مستوى الالدستيرون والشوارد في مصل الدم في ارتفاع ضغط الدم المحرض بالحمل

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الملخص

يعتبر ضغط الدم المحرض بالحمل من اكثر مضاعفات الحمل شيوعا وعلى اية حال القليل عرف عن سببه0 ان دراسة شوارد مصل الدم اكتسب مكانة في تفسير اسباب ضغط الدم 0 جهاز الرينين الانجيوتينسين الالدستيرون له دور في ضغط الدم المرض بـالحمل 0عينة الدراسة شملت خمسين امراة سليمة وغير حامل 0خمسين امراة حامل لديها ضغط دم طبيعي وخمسين امراة مصابة بقبل التشنج الحملي في خلال الاشهر الثلاثة الاخيرة من الحمل في مدينة الموصل 0 الهدف من الدراسة هو تقييم دور شوارد مصل الدم و الالدستيرون في تسبيب ضغط الدم المحرض بالحمل 0 اظهرت نتائج الدراسة انخفاض معنوي شديد في مستوى الصوديوم والكالسيوم والالدستيرون في مصل الدم لدى النساء الحوامل المصابات بقبل التشنج الحملي بالمقارنة مع النساء الحوامل بالحمل الطبيعي 0 بينما كان هناك ارتفاع معنوي شديد في مستوى البوتاسيوم في مصل الدم لدى النساء الحوامل المصابات بقبل التشنج الحملي بالمقارنة مع النساء الحوامل بالحمل الطبيعي والنساء الغيرحوامل 0مستوى الكلور في مصل الدم اظهر ارتفاع معنوي شديد لدى النساء الحوامل المصابات بقبل التشنج الحملي بالمقارنة مع

النساء الحوامل دوات الحمل الطبيعي0 اظهر الالدوستيرون علاقة موجبة مع الصوديوم وعلاقة عكسية مع البوتاسيوم بالتعاقب.

Introduction

Pregnancy Induced Hypertension (PIH) is one of the most common complications of pregnancy and it contributes significantly to the maternal mortality, premature birth, intra uterine growth retardation and perinatal mortality.(1).Several pathophysiological mechanisms have been implicated in the development of preeclampsia, these include the renin-angiotensin aldosterone system(RAAS). (2),low calcium intake. (3),endothelial dysfunction (4), and oxidative stress (5). The RAAS may be one of the mechanisms underlying the deficiency of uteroplacental perfusion. Recent investigations of the RAAS in PIH have highlighted a need for a comprehensive review of this subject. PIH may present with variable manifestations of the multiple systems involved but is most consistently associated with renal involvement. There is broad agreement that the component of the rennin Angiotensin Aldosterone system are markedly reduced in women with preeclamsia, which could contribute to the reduced plasma volume in preeclampsia.(6). Serum sodium and potassium contribute significantly in the functioning of the vascular smooth muscles.(1). Pregnancy induced hypertension may be an early sign of abnormality in the transport of sodium and potassium across the vascular smooth muscle cell membrane, which is responsible for regulation of blood pressure.(6). An abnormal low rate of net sodium extrusion by the Na/K transport was observed in the PIH patients. In PIH the sodium pump activity is decreased and there is also increase in circulating concentration of a sodium pump inhibitor.(7), which altered sodium transport across the cell membrane & leads to the accumulation of sodium in the extravascular spaces & a decrease in the plasma sodium level.(1).The serum sodium levels tend to decline in cases of preeclampsia as the disorder increase in severity. Disturbances in potassium homeostasis may also occur, (8). The study of Jantarasaengaram *et al.*, 2002 showed that no much difference in serum chloride level between the preeclamptic pregnant and the control, (9). Calcium play a critical role in the function of the cardiac & vascular smooth muscles. The low serum calcium increase the membrane permeability to sodium entry toward the interior of the smooth muscle which lead to depolarization and contraction of vascular smooth muscle.(10).

Subjects and Methods

This study represents a case control study, and it was conducted during the period from March 2011 to March 2012 in al-Batool and al-Khansaa teaching hospitals. The subjects involved in this study were divided into three groups: Group(1) which served as a control group included 50 apparently healthy, non-pregnant, normotensive women, their ages ranged from (16-35) years. Group (2) which composed of 50 normotensive apparantly healthy pregnant women in their third trimester, their ages ranged from (16-36) years and having the following inclusion criteria:(1). Pregnant female with a singleton pregnancy (2). Primigravida & multiparas, (3). Gestational ages were at 28-40 weeks calculated according to the date of last menstrual cycle

,clinical examination & by ultrasound findings. The exclusion criteria include the following: (1).Previous history of hypertension, diabetes mellitus, thyroid disease, blood disease, renal & hepatic disease. (2). Any associated disorders like urinary tract infection. (3). Multiple pregnancy. Group (3) **:**This group consisted of 50 preeclamptic pregnant women, in their third trimester, with the same previous inclusion & exclusion criteria. They were diagnosed to have preeclampsia according to the diagnostic criteria of this complication & were taking anti-hypertensive treatment at time of sampling. Their ages ranged from (19-39)years. All cases were selected by taking a detailed medical history and by physical examination. The Ethical and Research Committee of the Medical College and Hospital approved the study protocol and a verbal consent was obtained from the controls and the patients before the collection of the blood samples. About 5ml of fasting venous blood samples were obtained for the measurement of the biochemical parameters from all subjects included in this study by anticubital venepuncture and using disposable plastic syringe, without using elastic band tourniquet. The blood was allowed to clot and the serum was obtained by centrifugation at 3000rpm for 10 minutes. The serum was used to measure serum electrolytes including sodium(Na), potassium (K) , and chloride (Cl) by Ion Selective Electrode(ISE) ,the serum total calcium(Ca) was measured by a colorimetric method (Ginder and king, 1972) using a Biomerieux kit of calcium(11). Serum aldosterone concentration was determined by enzyme immunoassay (EIA), by using a kit supplied from (Enzo life science).

Statistical Analysis

The SPSS statistical package(version 19) was used for the statistic analysis of the data. The comparison between the studied groups were done by ANOVA(one way analysis of variance) followed by Duncan's multiple range test (DMRT). Pearson correlation was used to find the relation between the studied parameters.The statistical test results were considered highly significant at $P \leq 0.001$, significant at $p \leq 0.05$, and not significant at $p \leq 0.05$.

Results

The results of the data analysis are presented according to the grouping of the subjects **:**

Group (1): This group was considered as a control group for the comparison with other groups during pregnancy. Their number were 50 subjects. their systolic BP was (112.10 ± 8.98mmHg) & their diastolic BP was (69.30 ± 10.35 mmHg) Their age ranged from (16-35) years with a mean of (24.40 ± 5.12), they also had a BMI of(22.66 ± 2.04) kg/m^2, mean +SD with a range of (17.7-28.7) $kg/m^{2.}$

Group (2): This group consist 50 of normotensive pregnant women, their systolic BP was (107.52 ± 8.00) mmHg, with a range of (85-121) mmHg & their diastolic BP was (64.50 ± 7.75) mmHg, with a range of (50-80)mmHg. Their age ranged from(16-36) years with (25.24 ± 4.11) year, mean +SD, they also had a BMI of(27. 21 ± 2.42) kg/m^2, mean ± SD , with a range of (19.3-30.8) kg/m^2, with a gestational age of (34.90 ± 3.10) week, mean ± SD , with a range of(28-40) weeks.

Group(3): This group consist of 50 preeclamptic pregnant women. They were hypertensive according to the American Heart Association criteria: >140mmHg for systolic BP & 90>

mmHg for diastolic BP. (Hedesson & Ferrara, 2008), their systolic BP was (15.20 ± 11.99)mmHg with a range of (140-190) mmHg & their diastolic BP was (101.40 ± 7.65) mmHg with a range (90-120)mmHg, their BMI was(32.68 ± 3.9) Kg/m^2 , with a gestational age of(35.48 ± 2.54) week , mean ± SD, with a range of (19.3-36.8) kg/m^2, with a gestational age of (35.48 ± 2.54) week , mean ± SD, with a range of (28-39) week. Their age ranged from (16-35) years with a mean of (24.40 ± 5.12), they also had a BMI of(22.66 ± 2.04) kg/m^2, mean +SD with a range of (17.7-28.7) $kg/m^{2.}$. The demographic characteristics of the studied groups were presented in table (1)

Table (1):- Demographic characteristic of the studied groups

Parameters	**Groups**	**No.**	**Mean**	**SD**	**Min.**	**Max.**	**95% C.I.**	
							Lower	**Upper**
Age(year)	G1	50	24.40	5.12	16	35	22.94	25.86
	G2	50	25.24	4.11	16	36	24.07	26.41
	G3	50	28.90	4.69	19	39	27.57	30.23
Weight(kg)	G1	50	56.54	6.16	47	71	54.79	58.29
	G2	50	67.30	6.35	50	83	65.49	69.11
	G3	50	83.96	10.99	50	100	80.83	87.09
Height(cm)	G1	50	157.86	4.35	149	169	156.62	159.10
	G2	50	157.35	4.50	150	170	156.04	158.60
	G3	50	160.24	4.58	149	172	158.94	161.54
BMI(kg/m2)	G1	50	22.66	2.04	17.7	28.7	22.08	23.24
	G2	50	27.21	2.42	19.3	30.8	21.52	27.90
	G3	50	32.68	3.95	19.3	36.8	31.55	33.80
SBP(mmHg)	G1	50	112.10	8.98	90	130	109.55	114.65
	G2	50	107.52	8.00	85	121	105.25	109.79
	G3	50	155.20	11.99	140	190	151.79	158.61
DBP(mmHg)	G1	50	69.30	10.35	50	80	66.36	72.24
	G2	50	64.50	7.75	50	80	62.35	66.65
	G3	50	101.40	7.65	90	120	99.25	103.55
Gestational	G1	50	-	-	-	-	-	-

age(week)	G2	50	34.90	3.10	28	40	34.02	35.78
	G3	50	35.48	2.54	28	39	34.76	36.20

Table (2):- Descriptive statistics of the serum electrolytes, and serum aldosterone levels among the studied groups.

Parameters	**Groups**	**No.**	**Mean**	**SD**	**Min.**	**Max.**	**95% C.I.**	
							L.B.	**U.B.**
S. Sodium (mmol/L)	G1	50	144.42	1.33	140	147	144.04	144.80
	G2	50	141.46	0.92	1.39	143	141.20	141.72
	G3	50	134.17	2.10	129	140	133.57	134.77
S. Potassium (mmol/L)	G1	50	4.12	0.04	4.00	5.00	4.06	4.17
	G2	50	3.86	0.17	3.00	4.00	3.81	3.91
	G3	50	4.45	0.29	4.00	5.00	4.36	4.53
S.Chloride (mmol/L)	G1	50	102.31	2.13	97	106	101.66	102.97
	G2	50	103.59	1.87	100	108	103.06	104.13
	G3	50	102.81	1.71	101	111	102.32	103.30
S.Calcium (mmol/L)	G1	50	2.12	0.23	2.00	3.00	2.05	2.18
	G2	50	1.95	0.11	1.00	2.00	1.91	1.98
	G3	50	1.73	0.15	1.00	2.00	1.69	1.77
Aldosterone (pg/ml)	G1	50	11.46	3.03	6.40	17.70	10.60	12.32
	G2	50	28.65	11.69	13.70	55.40	25.33	31.98
	G3	50	4.38	2.36	1.00	8.30	3.71	5.06

The results of the measured biochemical parameters in the studied groups were presented in table (2), and (3).There was a highly significant reduction (P<0.000) in the level of serum sodium in preeclamptic women (134.17 mmol/L) in comparison with normotensive pregnant women (141.46 mmol/ L) & the control group (144.42 mmol/L). There is a highly significant elevation (P<0.000) in the serum level of potassium in preeclamptic women (4.45mmol/L) in comparison with normotensive pregnant women (3.86 mmol/L) & the control group (4.12 mmol/L). The serum chloride level showed no any difference in preeclamptic women in (102.81 mmol/L) in comparison with the control group (102.31 mmol/L). The serum total calcium showed a highly significant reduction (P<0.000) in preeclamptic pregnant women (1.73 mmol/L) in comparison with normotensive pregnant women (1.95 mmol/L) & the control (2.12 mmol/L). There is a highly significant reduction (P<0.000) in the serum level of serum aldosterone in the preeclamptic pregnant women (4.83pg/ml) in comparison with normotensive pregnant (28.65pg/ml) & the control group (11.46pg/ml).

Table (3):- Comparison of serum electrolytes, and serum aldosterone levels between the control, normotensive, and preeclamptic pregnant women.

Parameters	**Groups**	**No**	**Mean**	**SD**	**P≤ value**
S.Sodium (mmol/L)	G1	50	144.42 c	1.33	0.000
	G2	50	141.46 b	0.92	
	G3	50	134.17 a	2.10	
S.Potassium (mmol/L)	G1	50	4.12 b	0.04	0.000
	G2	50	3.86 a	0.17	
	G3	50	4.45 c	0.29	
S.Chloride (mmol/L)	G1	50	102.31 a	2.13	0.006
	G2	50	103.59 b	1.87	
	G3	50	102.81 a	1.71	
S.Calcium (mmol/L)	G1	50	2.12 c	0.23	0.000
	G2	50	1.95 b	0.11	
	G3	50	1.73 a	0.15	

S.Aldosterone(pg/ml)	G1	50	11.46 b	3.30	0.000
	G2	50	28.65 c	11.69	
	G3	50	4.38 a	2.36	

Correlation of serum aldosterone with maternal demographic characteristics of preeclamptic pregnant women.

Using pearson correlation test, the correlation between serum aldosterone & maternal demographic characteristic of preeclamptic pregnant women, table (4) revealed the following: The serum aldosterone has a positive correlation with gestation age (r=0.070), (P=0.627), SBP (r=0.035), (P=0.809), DBP (r=0.056) , (P=0.697), & with body mass index (r=0.056),(p=o.697). while aldosterone has a negative correlation with maternal age (r= -0.008), (P=0.955).

Table (4):- Correlation of serum aldosterone with maternal demographic characteristics of preeclamptic pregnant women.

Characteristic	**aldosterone**	
	r	**p**
Maternal age (year)	-0.008	0.955
Gestational age (week)	0.070	0.627
SBP (mmHg)	0.035	0.809
DBP (mmHg)	0.094	0.516
BMI (Kg/m^2)	0.056	0.697

Correlation of serum aldosterone with serum sodium & potassium in preeclamptic pregnant women.

By using Pearson correlation test we found the following: The serum aldosterone has a positive correlation with serum sodium (r=0.066), (P= 0.647). while serum aldosterone has a negative correlation with serum potassium (r = - 0.74), (P=0.610), as shown in table(5).

Table (5):- Pearson correlation coefficient of serum aldosterone with serum sodium & potassium in preeclamptic pregnant women.

	Serum aldosterone	
	r	**P**
Serum sodium	0.066	0.647
Serum potassium	-0.074	0.610

Discussion

The RAAS has been implicated in the pathogensis of preeclampsia.(2). Steven et al., 2007 showed that the RAAS is markedly depressed in preeclampsia compared with uncomplicated pregnancy.(12).The present study showed that the serum aldosterone level was significantly reduced in preeclamptic pregnant women as compared with the control group at $p \leq 0.000$.This reduction in serum aldosterone level in preeclamptic pregnant women may be due to genetic mutations that primarily lead to a decrease in aldosterone synthase activity (CYP 11 B2), resulting in inefficient volume expansion & poor placental perfusion in early pregnancy which believed to be the initiating event of preeclampsia.(13). The intravascular volume depletion would reduce placental perfusion with subsequent placental ischemia and a systemic maternal hypertensive response, leading to the clinical phenotype of preeclampsia. The hypothesis that reduced aldosterone synthesis account for preeclampsia at least in some patients is supported by a repeatedly reported diminished aldosterone productions in preeclampsia. So far, it is unknown whether these reduced Aldosterone secretion rates are the cause or the consequence of preeclampsia.(14). The present study showed that there was a significant reduction in the serum sodium level in preeclamptic women as compared to the control group at $p \leq 0.000$. This decrease may be due to low aldosterone level which accompany the preeclampsia, the dilutional effect of pregnancy and salt restriction may play a role. Our findings are in accordance with those reported by other authors.(1). There was a significant elevation in the serum level of potassium in the preeclamptic pregnant women as compared to the control group at $P<0.000$.This elevation may be due to low aldosterone in preeclampsia. Our results are in the same line with the result of the study of Handwerker et al., 1995 which revealed a highly significant elevation ($P <.001$) in the mean K level in the preeclamptic patients. Thus, it appears that disturbances in potassium homeostasis may occur in preeclampsia.(8). There was no significant difference in the mean value of serum chloride level between the preeclamptic pregnant and the control group. Our findings are in accordance with those reported by other authors.(7). The mean value of serum total calcium was significantly reduced in preeclamptic

women as compared to the control group at $p \leq 0.000$. Abnormalities in calcium homeostasis may contribute to the increased vascular sensitivity which is documented in preeclampsia.(10). The effect of serum calcium on changes in blood pressure could be explained by the level of intracellular concentration of calcium. The increase of intracellular concentration of calcium when serum calcium went lower lead to constriction of smooth muscles in blood vessels & increase of vascular resistance.(15). Indumati et al.,2011 found that there was a significant decrease in serum total calcium in preeclampsia as compared with normal pregnancy cases. Which indicate an association between calcium deficiency & preeclampsia.(1). Many previous studies like Idogun et al., 2007, Golmohammad ., et al 2008, and Chanvitya et al.,2008, all observed that serum calcium level were significantly lower in preeclamptic pregnant women compared to the control and normotensive pregnant women.(16,17,18).All the above results, supports the idea that calcium deficiency plays an important role in the pathogenesis of preeclampsia

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