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Status of serum electrolytes in preeclamptic pregnant women of Riyadh, Saudi Arabia.

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Abstract

Preeclampsia is characterized by new-onset hypertension, proteinuria and is responsible for substantial maternal and fetal morbidity. The electrolytes like sodium, potassium and chloride contribute significantly in the functioning of the vascular smooth muscles and may play an important role in the aetiopathogenesis of hypertension. The present study was undertaken to evaluate the role of serum ionized sodium, potassium and chloride levels as a predisposing factor in the genesis of preeclampsia and to find out the association of these elements with blood pressure in preeclamptic pregnant women living in Riyadh, Saudi Arabia. One hundred and twenty subjects were enrolled in this case-controlled study and divided into three groups; control, high-risk of preeclampsia (HR) and preeclampsia (PET) of 40 each. Blood samples were obtained from all the patients and the serum levels of sodium, potassium and chloride were determined. Statistical analysis was performed by one way ANOVA and Pearson's correlation coefficient. In preeclamptic group, the mean values of Na^+, K^+ and Cl^- were 138.27±2.99, 3.56 ± 0.38 and 104.2 ± 3.86 mEq/L respectively in comparison to control (135.44 ± 2.24, 4.11 ± 0.42 and 100.4± 2.43 mEq/L respectively). Raised levels of Na^+ and Cl^- in preeclamptic patients was significant at $p<0.001$ level of significance. There was significant positive correlation between raised sodium levels and systolic blood pressure ($P<0.05$), while K^+ showed a significant negative association with increased diastolic blood pressure. On the other hand, chloride exhibited insignificant correlation with blood pressure. In conclusion, our study suggests that hypernatremia and hypokalemia observed in preeclamptic patients bring about altered homeostatis of these elements in serum and therefore may act as predisposing factors in pathogenesis of preeclampsia.

Keywords: Electrolytes, Preeclampsia, Hypernatremia, Hypokalemia

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Introduction

Preeclampsia is the most common medical complication of pregnancy. It is also known as pregnancy-induced hypertension (PIH) or toxemia and is one of the leading causes of maternal and perinatal mortality throughout the world [1]. 790 maternal deaths per 100,000 live births have been reported due to preeclampsia [2]. In Saudi Arabia, the incidence of preeclampsia is extrapolated to 13,876 out of a population of 25,795,938 [3]. Preeclampsia is characterized by development of high blood pressure (hypertension) and proteinuria after 20 weeks of gestation and affects about 5-8% of all pregnancies [4]. Numerous studies have described the complex dependence of electrolyte concentrations in normotensive and preeclamptic pregnant women. Results of some of the important studies are contradictory. The electrolytes like sodium and potassium contribute significantly in the functioning of the vascular smooth muscles and may play an important role in the aetiopathogenesis of hypertension which is evident from the use of dietary sodium restriction as one of the prime treatments of high blood pressure.

Hypertension results primarily from the interplay of internal derangements (primarily in the kidney) and the external environment. Sodium, the main extracellular cation, has long been considered the pivotal environmental factor in the disorder. Numerous studies show an adverse effect of a surfeit of sodium on arterial pressure [5, 6]. By contrast, potassium, the main intracellular cation, has usually been viewed as a minor factor in the pathogenesis of hypertension. However, abundant evidences indicates that potassium deficit has a critical role in hypertension and its cardiovascular sequelae [7,8]. In a clinical study, a diet

low in potassium (10 to 16 mmol per day) coupled with the participants' usual sodium intake (120 to 200 mmol per day) caused sodium retention and an elevation of blood pressure; on average, systolic pressure increased by 6 mm Hg and diastolic pressure by 4 mm Hg in normotensive subjects, and systolic pressure increased by 7 mm Hg and diastolic pressure by 6 mm Hg in hypertensive subjects [9]. Studies have shown that increasing the potassium intake of hypertensive rats that were fed on high sodium diets lowered blood pressure, reduced the incidence of stroke and stroke-related death and prevented cardiac hypertrophy, mesenteric vascular damage, and renal injury. In view of the above evidences, the present study was carried out to understand the role of these electrolytes (Na^+, K^+ and Cl^-) in the pathogenesis of preeclampsia.

Materials and Methods

Study Population

The study was carried out at College of Applied Medical Sciences, and the subjects were recruited from King Saud Medical City Hospital, Riyadh from September 2012 to June 2014. A total of 120 pregnant women were enrolled in this study and divided into three groups of 40 each- healthy normotensive pregnant women (Control group), pregnant women at high risk of preeclampsia (HR group) and women with preeclampia (PET group). All study subjects were attending antenatal OPD or labor room in their third trimester of pregnancy. The study was approved by hospital's ethics committee. Informed consent was obtained from patients before blood sampling.

Inclusion criteria

Control- pregnant women with normal BP, absence of proteinuria and without any other systemic or endocrine disorder and age-matched with the cases. All subjects included were in their third trimester (gestational age of ≥24 weeks).

High-Risk group- Women in high risk group were included based on the following criteria: pregnant women with body mass index (BMI) of 35 or more, with mild hypertension or those with preeclampsia, gestational diabetes, IUGR (intrauterine growth restriction) or pre-term delivery in previous pregnancies and those with family history of preeclampsia.

PET group- Selection and the diagnosis of preeclamptic group were based on the definition of American College of Obstetrics and Gynecologists [10].

Exclusion criteria

Patients with congestive heart failure, kidney disease, thyroid and parathyroid disorders, cirrhosis of the liver and alcoholics were excluded from the study.

Analysis of serum electrolytes

Serum analysis for Na^+, $K^+$and Cl^- was determined in COBAS INTEGRA Autoanalyzer 800 using I.S.E direct potentiometric method. Serum samples were filtered prior to analysis. 300 µl of serum was appropriately diluted with 1% HNO_3 and 0.01% Triton X 100 (HPLC grade, Sigma Aldrich) as diluents. All measurements were conducted in duplicate. The concentrations of trace elements analyzed were expressed in mEq/L.

Statistical analysis

The results were expressed as Mean ± S.D. Statistical analyses were performed using SPSS software. Comparison between the groups was performed by one way ANOVA followed by Holm-Sidak test. Pearson's correlation was performed to determine the effect of electrolytes (Na^+, $K^+$and Cl^-) on gestational age, BMI, systolic and diastolic blood pressure (SBP and DBP respectively).

Results

In the present study, total of 120 patients were included. Table 1& 2 reveals the characteristics studied between the three groups. Mean values of Na^+, K^+ and Cl^- were 135.44 ± 2.24, 4.11 ± 0.42 and 100.4± 2.43 mEq/L respectively, in control and 135.23 ± 2.22, 4.00 ± 0.40 & 102.24± 2.61mEq/L respectively in HR group. In preeclamptic group, the mean values of Na^+, K^+ and Cl^- were 138.27±2.99, 3.56±0.38 & 104.2±3.86 mEq/L respectively. The levels of Na^+ were found to increase significantly in HR and preeclamptic group compared to control ($p<0.001$). Like Na^+, Cl^- levels were found to increase significantly ($p<0.001$) in PET group compared to control and $p<0.05$ was observed between HR and PET group. Unlike Na^+ and Cl^-, serum levels of K^+ decreased significantly ($p<0.001$) in PET group compared to control. In HR group also, K^+ levels were found to decrease significantly ($p<0.001$) when compared with PET. One way ANOVA showed overall significance of $p<0.001$ for difference in levels of Na^+, K^+ and Cl^- among the control and cases. The data was further analyzed by Pearson's correlation in order to determine the effect of maternal age, gestational age, BMI, systolic and diastolic blood pressure on serum trace elements in preeclamptic group (Table 3).

There was positive significant correlation between increased sodium levels and SBP ($r=0.37, P<0.05$), Cl^- showed an insignificant positive association with SBP and DBP; while K^+ showed a significant negative association with increased DBP. The correlation of Na^+, K^+ and Cl^- with SBP and DBP in preeclamptic group is shown in Figure 1 &2.

Inter-element correlations in preeclamptic group

Inter-element correlation for the analyzed elements in preeclamptic group was performed using pearsons correlation and represented in Table 4. Inter-element analysis

reflected a negative correlation between Na^+ and K^+ and between K^+ and Cl^- whereas positive correlation between Na^+ and Cl^- in preeclamptic women. However, the correlation was not statistically significant.

Table 1. *Levels of serum electrolytes among the groups*

	Control group (n=40)	**High risk (HR) group** (n=40)	**Preeclamptic group** (n=40)
SBP (mmHg)	113.56 ±13.93	124.7 ±16.21	167. 0 ±24.43
DBP (mmHg)	67.66 ±9.38	74.45 ±19.14	98.51 ±11.16
Serum Sodium (mEq/L)	135.44 ± 2.24	135.23 ± 2.22	138.27±2.99
Serum Potassium (mEq/L)	4.11 ± 0.42	4.00 ± 0.40	3.56 ± 0.38
Serum Chloride (mEq/L)	100.4± 2.43	102.24± 2.61	104.2 ± 3.86
Serum Osmolality (Mosm/kg)	265.8±4.32	268.87±3.6	272±2.5

Values are expressed as mean ±SD

Table 2*. Comparison of the clinical characteristics between the groups by ANOVA*

	Control with high risk group		**High risk group with Preeclampsia**		**Control group with Preeclampsia**	
	t	**p**	**t**	**P**	**t**	**P**
SBP (mmHg)	2.63	0.01**	10.07	< 0.001*	12.64	< 0.001*
DBP (mmHg)	2.16	0.033**	7.66	< 0.001*	9.762	< 0.001*
Serum Sodium (mEq/L)	0.39	0.69	5.63	< 0.001*	5.23	< 0.001*
Serum Potassium(mEq/L)	1.42	0.15	5.79	< 0.001*	7.21	< 0.001*
Serum chloride (mEq/L)	2.79	0.007**	3.03	0.007**	5.82	< 0.001*
Serum Osmolality (Mosm/kg)	4.83	< 0.001*	5.98	< 0.001*	10.82	<0.001*

**p < 0.001 and **p < 0.05*

Table 3. *Correlation of Gestational age, BMI, Systolic and Diastolic blood pressure with electrolytes in preeclamptic group*

	Sodium	**Potassium**	**Chloride**
	r (p value)	r (p value)	r (p value)
Age(years)	0.10(0.52)	-0.11 (0.46)	-0.29(0.06)
Gestational age(weeks)	0.11(0.49)	0.07 (0.63)	0.24(0.13)
BMI(kg/m^2)	0.18(0.24)	0.30 (0.05)	-0.10(0.50)
SBP(mmHg)	0.37(0.018)**	-0.06 (0.69)	0.28 (0.07)
DBP(mmHg)	0.15(0.34)	-0.006 (0.96)**	0.25(0.11)

*(-) negative correlation;**p < 0.05*

Table 4. *Interrelationship between trace elements in preeclamptic group.*

Correlation parameters	**Control group**		**PET group**	
	r	**p value**	**r**	**p value**
Na^+ and K^+	-0.19	0.23	-0.2	0.21
Na^+ and Cl^-	0.17	0.27	0.06	0.68
Cl^- and K^+	-0.05	0.72	-0.05	0.75

(-) negative correlation

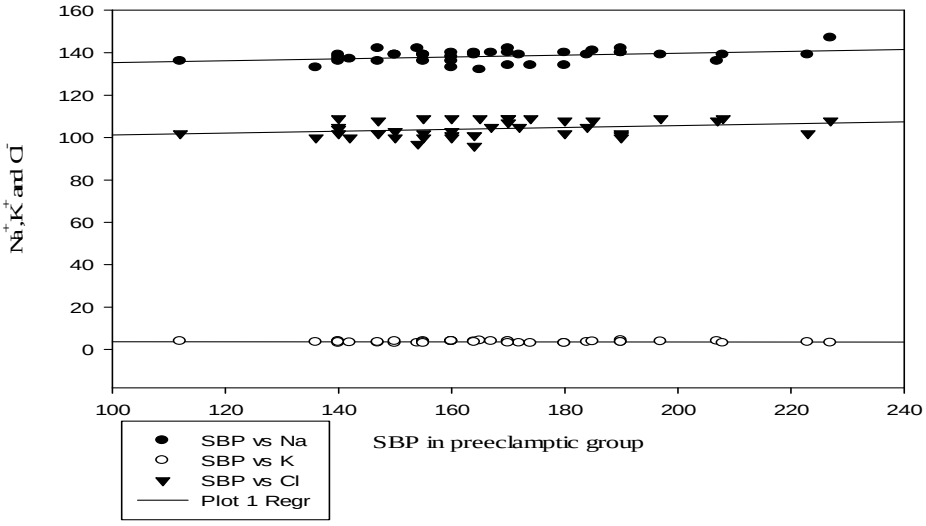

Figure1. *Regression graph showing correlation of Na^+, K^+ and Cl^- with SBP in preeclamptic group.*

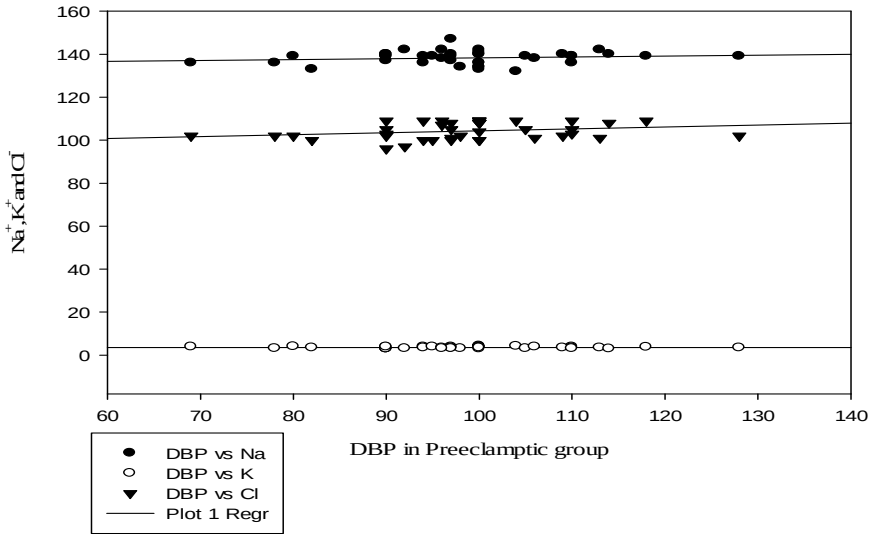

Figure 2. *Regression graph showing correlation of Na^+, K^+ and Cl^- with DBP in preeclamptic group.*

Discussion

Preeclampsia has been termed the "disease of theories" because of the multiple hypotheses that have been proposed to explain its occurrence [11].The etiology of preeclampsia is yet to be fully elucidated despite of numerous studies that have done. Preeclampsia is accompanied by amplification of the sodium retention and substantial alterations in intracellular water and electrolyte concentration. These changes are related to changes in cell membranes, which appears to be responsible for some pathological changes in preeclampsia. Some of the best documented alterations involve changes in handling of sodium ion both on the systemic and intracellular levels [12].

Of the total body content of potassium in humans, 90% is sequestered inside the cell and sodium is predominantly located extracellularly. This preferable location of sodium and potassium depends on the active transport of the Na+/K+ ATPase or sodium pump. 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 [13].

In the present study, there was significant increase in Na+ levels in preeclamptic patients compared to normal subjects. Hypernatraemia observed in this group could be due to sodium retention. Sodium retention, by means of the release of digitalis-like factor, and potassium deficit or hypokalemia inhibit the sodium pump of arterial and arteriolar vascular smooth-muscle cells, thereby increasing the sodium concentration and decreasing the potassium concentration in the intracellular fluid [14]. As a result,

hypokalemia inhibits potassium channels in the cell membrane and depolarizes the membrane. Because of its electrogenic nature, the inhibition of the sodium pump itself decreases the membrane potential. Membrane depolarization in the vascular smooth muscle cells promotes further rise in intracellular calcium by activating voltage-dependent calcium channels in the membrane, calcium channels in the sarcoplasmic reticulum, and the sodium-calcium exchanger [15]. The increased cytosolic calcium caused by these mechanisms triggers contraction of the vascular smooth muscles thereby raising blood pressure. The role of sodium in etiopathogenesis of preeclampsia therefore remains indeterminate. The mild hypernatraemia observed in preeclamptic pregnant women of this study may suggest that sodium may likely play a role in the etiopathogenesis of preeclampsia in this population of Riyadh region.

The statistically significant decrease in K^+ levels observed in preeclamptic group in this study is in accordance with reported by Anjum et al. [16]. Hypokalemic changes in normal pregnancy may be due to increased plasma levels of aldosterone and other mineralocorticoids (15). Potassium deficit in body is due to inadequate conservation of potassium by kidney and alimentary canal, fecal potassium losses can exceed even urinary losses [17].On contrary, Khan and Obeme et al. observed no significant difference in levels of these electrolytes in preeclamptic women [18,19]. Hypernatremia and hypokalemia observed in this study on preeclamptic pregnant women of Saudi Arabia is in accordance with that observed by Bera et al. and Yussif et al. on India and Iraqi populations respectively [17,20]. They reported significant difference in serum potassium levels between hypertensive pregnant women and normotensive pregnant women. Based on results obtained in our study and hypothesis given by Yussif et al. we assume that the raised sodium level and low potassium level in hypertensive pregnant women could be a causative agent of gestational hypertension. Therefore, the status of electrolytes in preeclampsia may vary in different population and environment.

When Na^+, K^+ and Cl^- levels were correlated with systolic and diastolic blood pressure, we found that there was positive correlation between Na^+ and blood pressure in preeclamptic group. This type of positive correlation was also observed by Ejike and Ugwuin on a population of non-urban dwelling Nigerians where significant correlation between urinary sodium and diastolic blood pressure was reported [21]. On the other hand, negative correlation was observed between K^+ levels and blood pressure in this study. In another population of Africans in the Diaspora in United States which included Jamaicans, Nigerians and Afro-Americans, Tayo et al. reported a strong correlation for sodium and potassium with blood pressure [22]. These studies reflect an association between sodium and blood pressure in this environment. Therefore, based on the results obtained in this study, it cannot be conclusively said that raised sodium levels has a definite role to play in the etiopathogenesis of preeclampsia, but the findings may be suggestive of a possible role, may be as a predisposing factor or as a risk factor in already predisposed individuals.

Fewer studies have performed to study the involvement of chloride in pathogenesis of preeclampsia. In the present study, there was significant increase in levels of serum Cl^- in preeclamptic group. Increased presence of serum Cl^- may result in increased osmolality leading to suppressed dilatation of vessels [23]. Role of chloride in hypertension is not clearly understood.

On inter-element analysis between the electrolytes studied in the present study, we observed that Na^+ was positively correlated with Cl^- and negatively with K^+. This association of Na^+ with K^+ could be due to K^+ depletion. Potassium depletion also decreases sodium excretion, apparently through changes in proximal or loop sodium reabsorption in kidney which results in elevation of blood pressure [24].

Conclusion

The present study concludes that in preeclamptic pregnant women of Riyadh region of Saudi Arabia, there is reduction in serum potassium and increase in sodium. Raised sodium and decreased potassium levels may have a possible role to play in the etiopathogenesis of preeclampsia. Sodium and potassium may act as predisposing factors or as risk factors especially in predisposed individuals, rather than major causative factors. Further studies still need to be carried out. On the basis of the results, pregnant women are advised to consume diet containing adequate amount of potassium and low sodium.

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