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SERUM ELECTROLYTE LEVELS IN PREECLAMPTIC WOMEN: A COMPARATIVE STUDY**MAGNA MANJAREEKA*¹ AND SITIKANTHA NANDA²**

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ABSTRACT

One of the most complicating factors during pregnancy is preeclampsia, a hypertensive disorder leading to a variety of problems. Serum electrolyte levels and anion gap, mean weights, SBP/DBP of preeclamptic age-matched women (devoid of diabetes, UTI, renal and liver disorders) in their third trimester, as compared to their normotensive counterparts, have been measured, analysed and compared with results of earlier studies. The preeclamptic group exhibits significant lowering of serum Ca^{2+} (-22.6 %) or K^+ (-3.85 %) and significant enhancement of each of serum Na^+ (+6.93 %), Cl^- (+7.25 %), HCO_3^- (+8.74 %) and an insignificant and small increase in anion gap (+1.5 %). The observed results do not show any region-specific changes. Most plausible explanations are offered for the observed results.

KEY WORDS

Preeclampsia, Hypertension, Serum Electrolyte Levels, Anion Gap

INTRODUCTION

Preeclampsia and eclampsia are the most common hypertensive disorders which complicate pregnancy and lead to pre-term labour/ delivery, considerably low birth weight infants and deaths up to 17.6% among pregnant women. Generally, the incidence of preeclampsia is in the range of 4 – 8 % of all pregnancies¹.

Numerous studies are available in literature describing complex dependence of electrolyte concentrations in respect of normotensive and preeclamptic pregnant women. Results of some of the important studies are confusing and often contradictory. Studies on comparative accounts of electrolyte levels of normotensive and preeclamptic pregnant women of different regions, as also those on inter-comparisons of serum electrolyte levels of preeclamptic women of different regions, appear to be severely restricted.

For example, several important reports are available linking preeclampsia with serum calcium; many studies showed that low dietary calcium intake significantly increased the risk of developing hypertension during pregnancy. While a majority of studies observed a significant lowering of serum calcium in preeclamptic group as compared to the normal pregnant group²⁻¹¹, several other studies did not find any significant difference in the serum calcium levels in the mentioned groups¹²⁻¹⁴, presenting a confusing picture.

In a study of normal pregnant Malay women, no significant difference in the levels of each of Na^+ and K^+ was noticed in the three different trimester monitored¹⁵. In two earlier studies^{16, 17}, no noticeable difference in the electrolyte levels of Na^+ or of K^+ was noticed in normotensive pregnant and preeclamptic groups. Serum sodium level and the anion gap were lower in preeclamptic women than in the normotensive women, while the Cl^- and the

HCO_3^- levels were not very much different^{18,19}. Nearly inconsequential change in each of the levels of Na^+ , K^+ and Cl^- in the normal pregnant and preeclamptic groups was noted in yet another study¹³. It was observed by Kashyap et al that the concentration level of serum Na^+ , Cl^- or HCO_3^- had definitely higher values in the preeclamptics; the anion gap was higher for the former than for the normotensive group²⁰.

A recent work¹¹, much after our work was completed, stated that the serum Na^+ concentration was much lower in the preeclamptics than in the normotensive group. Thus complex results have been reported on the influence of these electrolyte levels in preeclampsia of pregnant women. Moreover, a comparative analysis of such reports with reference to observation(s) in the context of Indian pregnant women appears quite desirable. We have recently made a preliminary report on the role of serum calcium levels in normotensive and preeclamptic pregnant women of South India²¹. The present report makes a detailed account of serum electrolyte levels and anion gap of normal pregnant and preeclamptic women of South India, and inter-comparison of the same with pregnant women of other regions wherever available.

MATERIALS AND METHODS

This hospital based cross-sectional study involved 50 normal pregnant and 55 preeclamptic women in their singleton pregnancy during December 2008 to July 2009, from the outpatients and inpatients wards of Department of Obstetrics and Gynaecology of Sri Ramachandra Medical College Hospital and Research Centre, Sri Rama Chandra University, Porur, Chennai. All were age-matched and in their third trimester.

The preeclamptic subjects were diagnosed to have preeclampsia based on the development of hypertension in the third trimester for the first time and proteinuria with or without edema. After obtaining informed written consent, personal information of each subject was collected in a supplied questionnaire. Diabetics and patients with history of UTI, renal disorders and liver disorders were excluded from the study.

Blood pressure measurements using a sphygmomanometer and proteinuria analysis were performed using standard procedures. For each experiment, 3 ml of venous blood sample was collected and immediately centrifuged; serum was separated for estimation of individual electrolyte concentration. Na^+ , K^+ and Cl^- levels were monitored by Integrated Multisensor Technique, while HCO_3^- was estimated at 405 nm and 700 nm, and Ca^{2+} was estimated at 577 nm spectrophotometrically, adopting improved procedures²². Data were statistically

analysed using SPSS software (Statistical Package for Social Sciences); statistical significance was found using paired t – test, chi-square test.

RESULTS

The present results of Table-1 can be briefed as follows.

- The mean age in years and the mean gestational period in weeks were not statistically different in normotensives and preeclamptics, as the same were nearly matched in both the groups.
- The mean weight in kilograms was statistically different in these two groups, being higher for the preeclamptics.
- The systolic blood pressure (SBP) was significantly higher for the preeclamptic group than for the normal pregnant group. Similar results were noticed in diastolic blood pressure (DBP).

Table -1
Group Statistics

Characteristics	Groups	Mean Value	Standard Deviation	P Value	% Change
Age in Years	Normal	24.76	3.497	0.689	
	Preeclamptic	25.04	3.554		
Weight in Kilograms	Normal	55.40	8.958	0.000	+24.9
	Preeclamptic	69.20	5.091		
Gestational Age in Weeks	Normal	34w 2 d	3.0280	0.305	
	Preeclamptic	34 w 4d	2.9885		
Systolic BP in mm of Hg	Normal	114.56	6.664	0.000	+44.4
	Preeclamptic	165.42	7.569		
Diastolic BP in mm of Hg	Normal	73.44	6.273	0.000	+39.9
	Preeclamptic	102.76	5.894		
Serum Calcium (mg/dL)	Normal	9.524	0.4475	0.000	-22.6
	Preeclamptic	7.371	0.5138		
Serum Sodium (mEq/L)	Normal	131.2	2.6	0.000	+6.93
	Preeclamptic	140.3	3.1		
Serum Potassium (mEq/L)	Normal	4.133	0.37	0.041	-3.85
	Preeclamptic	3.974	0.41		
Serum Chloride (mEq/L)	Normal	99.02	2.5	0.000	+7.25
	Preeclamptic	106.2	2.1		
Serum Bicarbonate (mEq/L)	Normal	21.42	1.6	0.000	+8.54
	Preeclamptic	23.25	1.5		
Anion Gap	Normal	10.68	2.2	0.676	+1.5
	Preeclamptic	10.84	1.6		

- d. Serum calcium level in the preeclamptic group was significantly lower (-22.6%) than the normal pregnant group. It was further observed that hypertensive women in the later part of the third trimester (34 – 40w) showed further decline in serum calcium level (- 24.2 %), with a mean value of 7.221 mg / dL, when compared to women in the early third trimester (28 -33w) who had a mean serum calcium level of 7.595 mg / dL (-20.2 %); the additional decrease was statistically significant with a p value of < 0.05.
- e. Serum potassium level for the preeclamptic group was lower (- 3.85%) than for the normal pregnant group.
- f. Serum sodium level for the former group was significantly higher (+6.93%) than for the latter group.
- g. The preeclamptic group registered a significant increase of serum chloride (+7.25%) or serum bicarbonate (+8.74%) compared to the normotensive group.
- h. Anion gap (AG) in the preeclamptic group was slightly higher (+1.5%), but was not statistically very significant.

regnant women, as mentioned earlier, the observed results, on the influence of serum electrolyte levels on preeclampsia of pregnant women in most published works, are often contradictory and confusing; this can be seen from Table – 2 listing representative works. It appears there is no clear-cut and precise change (as to its nature and extent), and the possible reasons thereof.

On the basis of experimental findings, no precise mechanism has been established relating serum calcium levels with preeclampsia. However, several theories have been advanced. One such possibility is that preeclamptic and normotensive pregnant women have equivalent levels of 25-hydroxyvitamin D, while preeclampsics have a significantly lower 1, 25 - dihydroxyvitamin D; the lower level of the latter may contribute to the suboptimal intestinal absorption of calcium during a time of increased calcium demand²³. Further, low calcium intake results in high parathyroid hormone levels and increased membrane permeability, resulting in increased intracellular calcium levels and decreased serum calcium levels. The former triggers vascular smooth muscle contraction and contributes to increased blood pressure³.

DISCUSSION

Although electrolyte levels play significant roles in the etiopathogenesis of hypertension in

Table – 2
Percentage change in mean serum electrolyte values of preeclampsics (with respect to normotensives) in some representative reports

Electrolyte	% Change	Reference No.	Electrolyte	% Change	Reference No.	
Ca²⁺	-	10.0	Cl⁻	+	0.6	
	-	7.2		+	3.0	
	-	3.2		No Change	18, 13	
	-	3.0		+	7.25	
	-	7.8				
	-	22.6		Present work		
Na⁺	+	5.8	HCO₃⁻	No Change	18	
	No Change	15, 17, 13		+	2.0	
	-	1.07		+	13.8	
	-	3.4		+	8.54	
	+	6.93		Present work		
K⁺	No Change	15, 18,13, 11	AG	-	20.8	
	-	3.85		Present work	+	36.2
				+	1.5	
					Present work	

+ Increase, - Decrease

One plausible reason that can be suggested for the effect of increased serum sodium is that it may lead to water retention, expansion of extracellular fluid and intravascular volumes, increased venous return and elevated cardiac output. As elevated blood flow to tissues continues, whole body auto regulation takes place with subsequent increase in total peripheral resistance and eventual development of hypertension²⁴. 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^+ ATPase²⁵. 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 pressure²⁶.

In an earlier study involving serum potassium on hypertensives it was conclusively established that an inverse relationship existed between serum potassium level and the extent of hypertension²⁷. The mechanism by which potassium enhancement might relate to hypertension regulation and vascular disease is not definitely known. Beneficial effect of potassium may be related to decreased

vascular responsiveness to vasopressors, such as nor - epinephrine²⁸. This effect may be mediated by enhanced release of NO by the endothelial cells²⁹. The latter induces vasodilatation and decreases platelet aggregation, which could both decrease blood pressure and protect against hypertension induced endothelial injury, all of which are responsible for pathogenesis of symptoms of preeclampsia³⁰. Potassium depletion also decreases sodium excretion, apparently through changes in proximal or loop sodium reabsorption in kidney; this results in elevation of blood pressure³¹.

None of the few studies reported on the effect of serum chloride or bicarbonate in

preeclampsia has been able to explain the change. One of the possible reasons for the increase in the serum HCO_3^- in preeclamptic group could be a decreased pCO_2 leading to suppression of vasodilatation. Increased presence of serum Cl^- in preeclamptics may bring about increased osmolality leading to suppressed dilatation of vessels³². There may be other reasons for these effects which are not known at present.

The anion gap (AG) is an apparent diagnostic quantity which is a difference between unmeasured anion concentrations and unmeasured cation concentrations in the plasma; that is calculated by: $\text{AG} = [\text{Na}^+] - [\text{HCO}_3^-] - [\text{Cl}^-]$. The anion gap rises as the concentration of unmeasured anions increases and/ or the concentration of unmeasured cations decreases³³. Since the concentrations of unmeasured cations (K^+ and Ca^{2+}) have decreased²¹, there may be a slight increase in anion gap, which is not statistically significant in the present study.

CONCLUSIONS

In this study, the preeclamptic women of South India exhibit significantly lower serum calcium or potassium levels, and each of higher serum sodium, chloride or bicarbonate levels than the normotensive pregnant group; similar results were also exhibited in a study conducted in the northern part of India²⁰. However, region-wise correlation of serum electrolyte levels with preeclampsia is not possible with the available data. Further detailed studies are needed to clinch unambiguous mechanisms.

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