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Original Article

Analysis of Serum Electrolytes Variation in Onset and Progression of Preeclampsia

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ABSTRACT

Preeclampsia is one of the most common, life-threatening complications of pregnancy that is related to maternal as well as perinatal morbidity or mortality. One of the significant causes of preeclampsia is elevated blood pressure which is directly linked with concentrations of electrolytes in the blood. **Objective:** To evaluate the possible variations of electrolytes in preeclamptic pregnant females. **Methods**: A total of 90 pregnant females of 20 to 45 years of age were divided into three groups (n=30 in each group) viz normotensive, hypertensive, and preeclamptic pregnant females. All anthropometric and biophysical variables were measured. Among biochemical parameters, serum sodium, potassium, chloride, and calcium levels were determined using colorimetric assays while bicarbonate levels were determined by an enzymatic test using phosphoenolpyruvate carboxylase and a stable nicotinamide dihydrogen phosphate analogue. A comparison of serum electrolytes among different groups was executed by one-way analysis of variance. **Results:** Preeclamptic females had significantly higher BMI, and systolic and diastolic blood pressure than hypertensive and normotensive pregnant females ($p<0.0001$). Serum concentrations of sodium and calcium were significantly lower in preeclamptic pregnant females compared to hypertensive pregnant and normotensive pregnant females ($p<0.0001$). **Conclusions:** Alteration in the electrolyte levels may contribute to the onset and progression of preeclampsia. Nutritional sodium restriction along with adjuvant supplementation of Ca^{++}, Na^{+}, K^{+}, and Cl^{-} may minimize the risk of preeclampsia. On the basis of outcomes, it is recommended that pregnant females should eat a balanced diet that contains appropriate amounts of minerals micronutrients, and vitamins.

INTRODUCTION

Preeclampsia is a condition categorized by hypertension in pregnancy (blood pressure rises above 160 mmHg), proteinuria (excretion of > 300 mg of urinary protein per day) and edema (Packer, 2005). Preeclampsia usually develops after 20 weeks of gestation and affects 3-8% of pregnancies globally. It is an important cause of perinatal and maternal morbidity or mortality. An elevated incidence of preeclampsia is 19% in a Pakistani women society [1]. Eclampsia isresponsible for 34% of maternal mortality in Pakistani tertiary care hospitals among women who are admitted for delivery [2]. Preeclampsia can trigger cardiovascular diseases, such as ischemic heart disease, chronic hypertension, and stroke in the mother, while infants born after preeclampsia are comparatively low at birth, have a higher danger of stroke, adult fracture syndrome and heart disease [3, 4]. The causes of preeclampsia are uncertain but have been related to poor nutrition, high body fat, lack of blood flow to the uterus, and/or genetic disposition [5]. Limited research has suggested a relationship between increased sodium intake and the development of preeclampsia. Chronic ingestion of excess sodium can lead to high blood pressure, heart disease, and stroke [6]. Many studies claimed low sodium as an uncommon but significant presentation of preeclampsia [7]. The sodium levels decrease considerably in pregnancy-induced hypertension cases. The intra-renal production of cyclic GMP, endothelin, and prostaglandin E2 are all decreased in preeclampsia, which can result in sodium retention, hypertension, intra-renal thrombosis, and preeclamptic pregnancy vasospasm [8].

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Pregnancy- induced hypertension (PIH) may be an initial sign of abnormality in the transportation of potassium and sodium through the vascular smooth muscle cell membrane that plays an important role in the maintenance of blood pressure. In erythrocytes, the Na/K pump and the Na/K co-transport perform the extrusion of the cellular sodium load. An abnormally small rate of Na/K co-transport net sodium extrusion was noted in patients with PIH [9, 10]. Chlorides are essential for hydration control, acid-base balance and osmotic pressure. Chloride overdose may result in the addition of hydrochloric acid in the bloodstream, leading to acidosis. The chloride toxicity is the result of chloride overproduction in the form of acid, or hydrogen chloride. Low chloride level results in a decrease in blood acid content. Malnutrition, excessive vomiting and low fluid intake, loss of acid base balance due to diarrhea may decrease the chloride during pregnancy [11, 12]. Calcium is a significant component in the functioning of cardiac and vascular smooth muscles. During pregnancy alternation in calcium metabolism contributes to increased vascular sensitivity. Low serum calcium increases intracellular calcium in the vascular smooth muscle by stimulating the release of parathyroid hormone and renin can cause high blood pressure. This causes vasoconstriction, increase resistance to the vascular smooth muscles, and a rise in blood pressure in preeclamptic females [13]. Epidemiological studies have shown that trace element deficiencies are linked with an increased risk of preeclampsia. However, prevention or management of PE randomized studies has failed to show a beneficial effect of supplementation. The study is stand on the hypothesis that serum electrolytes variations could be responsible for development of high blood pressure and ultimately preeclampsia in pregnant females. There is little information about the specific role so these trace elements are susceptibility to preeclampsia in early pregnancy.

METHODS

A case control study was planned to determine the electrolytes variation in onset and progression of preeclampsia. The study plan was placed before the Board of Studies of Zoology Department, Government College Women University, Faisalabad and approved. After the formal approval, the study was executed and multiple gynecological facilities of the Faisalabad district were surveyed to collect the data about the prevalence of hypertension and preeclampsia among pregnant females. Preliminary data suggested that public sector health care facilities had maximum number of female patients reporting with complications of pregnancies. On the basis of pilot survey, Allied Hospital, Faisalabad and District Head Quarter Hospital, Faisalabad was chosen for the study and formal approval of blood sample collection was seek by the head of theconcerned department. Pregnant females of second and third trimester with physician or clinical diagnosis of hypertension and preeclampsia were enrolled for the study. The age of study participants was 20 to 45years and they were in their second or third trimesters. The females who were in first trimester were excluded from the study as there were maximum chances of miscarriage due to hypertension that leads to unstable outcomes of the study. The study started in September 2019 and concluded in November 2020. After careful assessment, stratified random sampling technique was used to select thirty (30) hypertensive pregnant and thirty (30) preeclampsia pregnant females. Equal number (n=30) of age-matched normotensive pregnant females in the same phase of pregnancy were also registered as the control group for comparison. The sample size was computed through G power software (G*Power 3.1.9.7) by applying ANOVA: Fixed effect omnibus, one-way. The power analysis applied was Post hoc: compute achieved power, given α (0.05), sample size (90) and effect size (0.40). The power of analysis computed at described parameter was 0.92 that was statistically significant. The detailed purpose and procedure of the study was explained to the participants and informed consent was signed by them. It was made clear that they all will participate voluntarily and no financial/edible or health benefits were given. A comprehensive questionnaire was designed and filled out by patients as well as a control group to collect their detail about personal and demographic information. Anthropometric measurements like weight, height, and BMI and biophysical variables including blood pressure, pulse rate, body temperature, convulsion, edema, and blood sugar level were also noted. After taking written consent from all study participants, 5cc peripheral blood was withdrawn by using disposable plastic sterile syringes and dispensed into glass tubes. The blood was allowed to clot at room temperature. Serum for electrolyte analysis was separated by centrifugation at 3000 rpm for 15 minutes and stored at -20°C for long-run analysis. Serum samples were subjected to a chemistry analyzer (SA-20 CLINDIAG, Belgium) to check the electrolytes by using commercially available kits (Dia Sys Diagnostic System). Serum sodium, potassium, chloride, and calcium levels (Cat # 1480809910021, 1 5221 99 10 021, 1 1221 99 10021, 1 1181 99 10 021, respectively) were determined using colorimetric assays while bicarbonate levels were determined using an enzymatic test using phosphoenolpyruvate carboxylase (PEPC) and a stable NADH analog (Dia Sys Diagnostic System Cat #1 0950 99 10 026). Statistical analysis was performed using Graph Pad Prism (V.6.0) software. The inter and intragroup comparisons were executed by one-

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way ANOVA at p<0.05 as significant.

RESULTS

The study comprises of total 90 participants that were divided into three groups (30 subjects in each group). All relevant information related to pregnancy are enlisted in Table 1.

Table 1: Personal and pregnancy history of normotensive, hypertensive and pre eclamptic pregnant females of the study

Variables	Normotensive pregnant	Hypertensive pregnant	Preeclamptic pregnant
	N (%)	N (%)	N (%)
Number of kids			
0	0 (0)	0 (0)	4 (13.3)
1	4 (13.3)	3 (10)	6 (20)
2	6 (20)	9 (30)	13 (43.3)
3	12 (40)	9 (30)	5 (16.6)
4	8 (26.6)	9 (30)	2 (6.66)
Gravida			
1	0 (0)	0 (0)	5 (16.6)
2	4 (13.3)	3 (10)	5(16.6)
3	6 (20)	9 (30)	13 (43.3)
4	12 (40)	8 (26.6)	5 (16.6)
5	7 (23.3)	9 (30)	2 (6.66)
6	1 (3.33)	1 (3.33)	0 (0)
Para			
1	4 (13.3)	3 (10)	5 (16.6)
2	6 (20)	9 (30)	13 (43.3)
3	12 (40)	9 (30)	6 (20)
4	7 (23.3)	9 (30)	2 (6.66)
Abortion			
Yes	0 (0)	0 (0)	0 (0)
No	1 (100)	1 (100)	1 (100)
Trimester			
2nd	4 (13.3)	4 (13.3)	4 (13.3)
3rd	26 (86.6)	26 (86.6)	26 (86.6)
Edema			
Yes	6 (20)	30 (100)	24 (80)
No	24 (80)	0 (0)	6 (20)
Convulsion			
Yes	6 (20)	30 (100)	6 (20)
No	24 (80)	0 (0)	24 (80)

The anthropometric and biophysical characteristics of recruited participants are shown in Table 2. A significant difference was observed in the BMI (p<0.0001), mean systolic (p<0.0001), and diastolic (p<0.0001) blood pressure.

Table 2: Comparison of Maternal Anthropometric and Biophysical Variables

Variable	Normotensive pregnant (Mean ± SEM)	Hypertensive pregnant (Mean ± SEM)	Preeclamptic pregnant (Mean ± SEM)	p-value
Age (Years)	32.33±0.70	32.17±0.62	30.23±0.67	0.051
BMI (kg/m2)	22.25±0.22	24.34±0.16	25.72±0.18	<0.0001****
Systolic Blood Pressure (mmHg)	123±1.18	138±1.21	152.1±1.41	<0.0001****
Diastolic Blood Pressure (mmHg)	83.33±0.87	94±0.90	95.67±0.92	<0.0001****
Pulse Rate (bpm)	83.90±0.82	84.40±0.87	85.67±0.85	0.322

****significant at p<0.0001, SEM = Standard Error of the Mean

A significant reduction (p<0.0001) in mean sodium level was observed in preeclamptic (129.1±0.89) as compared to normotensive (133.4±0.38) and hypertensive (128.1±0.89). In comparison with normotensive (11.73±0.12), preeclamptic females (10.36±0.25) had significantly lower serum calcium levels. Serum levels of other electrolytes such as K^+, Cl^-, and HCO^{3-} had non-significant variations in preeclamptic patients as compared to other groups (Table 3).

Table 3: Comparison of Electrolytes in Normotensive, Hypertensive, and Preeclamptic pregnant females

Variables	Normotensive Pregnant (Mean ± SEM)	Hypertensive Pregnant (Mean ± SEM)	Preeclamptic Pregnant (Mean ± SEM)	p-value
Na^+ (mEq/L)	133.4±0.38	128.1±0.89	129.1±0.89	<0.0001****
K^+ (mEq/L)	4.303±0.05	4.203±0.12	3.98±0.12	0.7860
Cl^- (mg/dL)	100.4±0.37	99.37±0.45	100.3±0.46	0.2379
$HCO3^-$ (mEq/L)	24.73±0.34	24±0.39	25.13±0.41	0.3794
Ca^{++} (mg/dL)	11.73±0.12	10.26±0.25	10.36±0.25	<0.0001****

****significant at p < 0.0001, SEM = Standard Error of the Mean

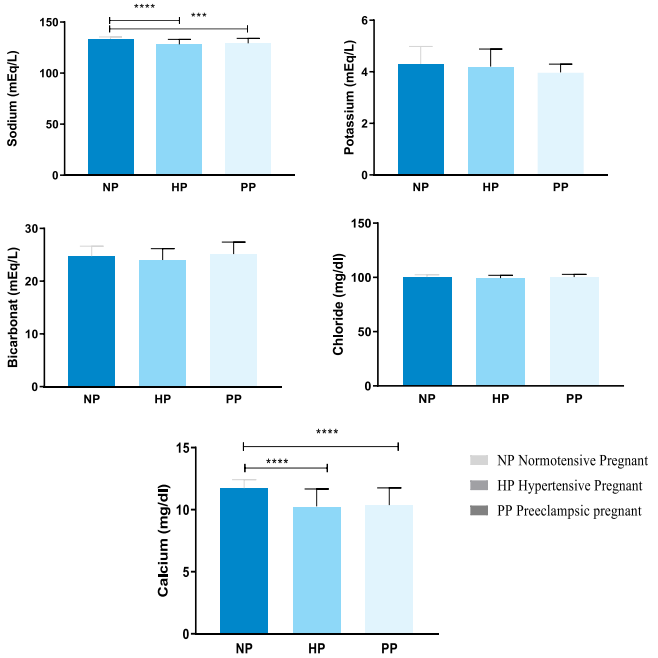

Figure 1: Average sodium (mEq/L), Potassium (mEq/L), Bicarbonate (mEq/L), Chloride (mg/dl) and Ca^{++} concentration (mg/dl) in comparable groups. Values are Mean±SEM. Significant at <0.0001****, CI 95%

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DISCUSSION

Preeclampsia is a multifactorial and multiorgan dysfunction with no factor considered strictly necessary to cause it [14]. It has been labeled as a dreaded disease affected women and their pregnancies since ancient times. Factors such as gestational diabetes, hypertension in family history, and mental stress during pregnancy can be used as screening tools to predict preeclampsia. Assessment of electrolytes in preeclampsia provides a very helpful index for the study of pathological and physiological changes during pregnancy [15]. We observed a significant ($p<0.0001$) increase in the BMI of preeclamptic patients as compared to normotensive and hypertensive pregnant females. Body mass index is correlated with complications connected with pregnancy such as preeclampsia. Several trials have shown that obese women are at elevated danger of developing pregnancy hypertension owing to enhanced BMI. Our findings are consistent with Munazza *et al.*, (2011) and Poorolajal and Jenabi (2015) who reported a similar association of increasing BMI with preeclampsia and concluded that having a high BMI is connected with an increased risk of preeclampsia thus, being overweight or obese might be a risk factor for preeclampsia [16, 17]. Significantly ($p<0.0001$) higher mean systolic and mean diastolic pressure in preeclampsia as compared to normotensive and hypertensive pregnant females was also observed. Hypertension induced by pregnancy could be an early indication of sodium and potassium transport abnormality across the vascular smooth muscle cell membrane, which is responsible for regulating blood pressure [10]. In this study, a statistically significantdecrease in Na^+ levels were observed in the preeclamptic group however the decrease in K^+ level was statistically non-significant. The findings of the current research in accordance with Adewolu *et al.*, (2013) who claimed that serum potassium are level reduced within the normal limit therefore serum electrolytes picture may vary in different population and environment [18]. The findings are also supported by Owusu *et al.*, 2017 who conducted a case control study in Ghana and found reduced serum sodium and K levels in preeclamptic pregnant females [19]. Hypokalemia and hypocalcemia were also reported by other researchers but contradiction exist in sodium concentration as the author reported hypernatremia rather than hyponatremia [20-22]. A significant decline in serum calcium levels in preeclamptic females was noted. This decrease in calcium level may be due to suboptimal absorption of calcium by the intestines because of a reduction in 1, 25-dihydroxy vitamin D. It has been suggested that increased calcium secretion during the urinary system or a decreased parathyroid hormone secretion can play a role in this regard [23]. Reduced serum calcium levels in pregnant women may be partially attributed to hemodilution. By stimulating parathyroid hormone and release of renin, low serum calcium can trigger high blood pressure, which in turn improves intracellular calcium in the soft vascular muscle. This creates vasoconstriction, increased resistance to the vascular, and increased blood pressure in preeclamptic women [24]. Calcium and other mineral in serum calcium may be associated with onset and progression of preeclampsia in pregnant females [25, 26].

CONCLUSIONS

The present study concludes that serum electrolytes level could have an important function in the development of preeclampsia or eclampsia and possibly link the pathogenesis of different disorders. This study also shows the significant alteration in the essential minerals and electrolytes that may contribute to the growth of preeclampsia. Hypocalcemia, hypomagnesemia, hypokalemia, and hypernatremia are linked with preeclampsia and can perform a significant causative role in preeclampsia. Adjuvant supplementation of Ca^{++}, Na^+, K^+, and Cl^- with nutritional sodium restriction may minimize further preeclampsia development.

Authors Contribution

Conceptualization: TM
Methodology: SS
Formal analysis: TM, SS
Writing-review and editing: TM, NM

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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