Owusu Darkwa et al., *Cogent Medicine* (2017), 4: 1376898
https://doi.org/10.1080/2331205X.2017.1376898

cogent medicine

OBSTETRICS & GYNECOLOGY | RESEARCH ARTICLE

Serum sodium and potassium levels in preeclampsia: A case-control study in a large tertiary hospital in Ghana

Ebenezer Owusu Darkwa[1]*, Robert Djagbletey[1], Charles Antwi-Boasiako[2], George Aryee[1], Daniel Sottie[3] and Alexander Akowuah[3]

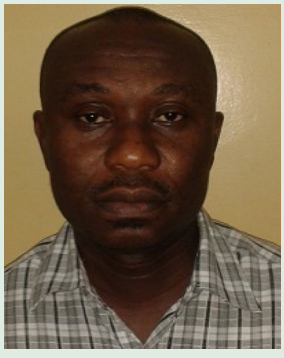
Abstract: *Background*: Preeclampsia remains a poorly understood complication of pregnancy affecting 5–14% pregnancies worldwide. Recent studies indicate that serum electrolytes may play a role in preeclampsia since it is a vascular endothelial disorder. *Aim*: To compare serum sodium and potassium levels between preeclamptics and normotensive pregnant women in a tertiary hospital in Ghana. *Methods and materials*: This was a case-control study consisting of 30 preeclamptics and 30 normotensive pregnant women recruited consecutively at their first third trimester pre-natal visit at Korle-Bu Teaching Hospital. Serum sodium and potassium were analysed using Sherwood Flame Photometer (Model 420 Sherwood Scientific Ltd, UK). Analysis was done using Statistical Package for Social Sciences (SPSS®) software version 20.0 and presented as means (standard deviation). A *p*-value of ≤0.05 was judged significant. *Results*: There was a significantly reduced ($p < 0.001$) serum sodium levels in preeclamptics (mean = 136.13; SD = 4.17 mmol/L) compared to normotensive pregnant women (mean = 142.17; SD = 5.66 mmol/L). There was a significantly reduced ($p < 0.001$) serum potassium levels in preeclamptics (mean = 3.45; SD = 0.54 mmol/L) compared to normotensive pregnant women (mean = 3.98; SD = 0.36 mmol/L). *Conclusion*: The reduced levels of serum sodium and potassium in preeclampsia as compared to normotensive pregnant women, suggests that changes in these electrolytes may be associated with preeclampsia.

Received: 19 June 2017
Accepted: 31 August 2017
First Published: 09 September 2017

*Corresponding author: Ebenezer Owusu Darkwa, Department of Anaesthesia, School of Medicine and Dentistry, College of Health Sciences, University of Ghana, Accra, Ghana
E-mail: eoddarquah@yahoo.co.uk

Reviewing editor:
Udo Schumacher, University Medical Center Hamburg-Eppendorf, Germany

Additional information is available at the end of the article



Ebenezer Owusu Darkwa

ABOUT THE AUTHOR

Ebenezer Owusu Darkwa was an MPhil student at the department of Physiology, University of Ghana at the time of carrying out this study. This study is part of the research on the role of some selected serum electrolytes and nitric oxide in the pathophysiology of preeclampsia in Ghanaian women. He is a consultant Anaesthesiologist and a lecturer at the Department of Anaesthesia, University of Ghana, Korle-Bu Teaching Hospital. The research team has a large interest in body fluid and electrolytes physiology in general. His research interest is in electrolyte physiology of pregnant women and how it affects their general health perioperatively.

PUBLIC INTEREST STATEMENT

Preeclampsia is a complication of pregnancy with most deaths occurring in low to middle income countries. The cause of preeclampsia largely remains unknown. Changes in maternal serum mineral ions during pregnancy have been suggested as a possible cause. Research on maternal deficiencies of mineral ions during pregnancy in Ghana is lacking. This study was therefore carried out to examine the role maternal blood levels of sodium and potassium play in the development of preeclampsia. We observed in our study, a marked reduction in maternal sodium and potassium in pregnancies complicated by preeclampsia.

Subjects: Health Conditions; Medicine; Midwifery

Keywords: preeclampsia; pathophysiology; sodium; potassium

1. Introduction

Preeclampsia is one of the commonest aetiologies of foetal and maternal mortality and morbidity (Sukonpan & Phupong, 2005). It is a multi-system disorder affecting approximately 5–7% of all pregnancies worldwide and it is the commonest, yet least understood disease of pregnancy (Ziaei, Ranjkesh, & Faghihzadeh, 2008). The incidence of preeclampsia in developing nations is estimated to be 4–18% (Villar, Betran, & Gulmezoglu, 2001). Sixteen percent of all maternal mortality in developed countries and 9% of maternal mortalities in Asia and Africa is said to be due to hypertensive disorders in pregnancy (Khan, Wojdyla, Say, Gülmezoglu, & Van Look, 2006). Eighteen percent of 724 total maternal deaths at Korle-Bu Teaching Hospital in Ghana between 1984 and 1994 were due to hypertensive disorders in pregnancy including preeclampsia (Lassey & Wilson, 1998). Whilst earlier studies suggested that preeclamptics after delivery had no increased risk of adverse long term outcomes than non-preeclamptics from the general population (Chesley, Annitto, & Cosgrove, 1976), current studies, however, suggest the reverse (Wilson et al., 2003).

Theories of the pathophysiology of preeclampsia involve both maternal and foetal factors. Though the aetiology of preeclampsia remains unclear, many theories suggest abnormal placental implantation and abnormal trophoblastic invasion as a possible cause (Smith & Kenny, 2006). It has been postulated that fluctuations in maternal serum ions may be the precipitating cause of elevated blood pressures in preeclampsia (Sidahmed & Abubaker, 2017; Tabassum, Al-Jameil, Ali, Khan, & Al-Rahed, 2015).

In developing countries, dietary deficiency of various mineral ions have been established to have a role in blood pressure regulation in pregnant women with a consequent development of preeclampsia (Aziz & Mahboob, 2014; Ephraim, Osakunor, Denkyira, Eshun, & Anto, 2014; Kanagal et al., 2014).

Studies have reported that serum calcium and magnesium levels have a vasomotor activity on blood vessels in pregnancy, whilst others have reported a varying conclusion on the effects of serum sodium and potassium levels on vasomotor activity during pregnancy (Ephraim et al., 2014; Yussif, Salih, Sami, & Mossa, 2009).

Serum sodium levels has been observed to be reduced in both preeclampsia and pregnancy induced hypertension as compared to normotensive pregnant and non-pregnant women (Indumati, Kodliwadmath, & Sheela, 2011; Pitkin, Kaminetzky, Newton, & Pritchard, 1972; Ravid, Massarwa, Biron-Shental, & Fejgin, 2005; Searcy, 1969; Tarik & Ward, 2011). There is a reduced intrarenal production of cyclic GMP (cGMP), endothelin and prostaglandin E2 (PGE2) with resultant sodium retention, hypertension and thrombosis in preeclampsia (Clark, Cotton, Hankins, & Phelan, 1997). In preeclampsia there is alteration in cell membrane sodium transport leading to extravascular accumulation of sodium with a reduced plasma sodium level (Clark et al., 1997; Searcy, 1969). However, other studies found no significant change in serum sodium levels of preeclamptics compared to normal pregnant women (Adewolu, 2013; Bera et al., 2011; Rizk, 1997; Yussif et al., 2009). Caughey and colleagues also noted increased sodium levels in preeclampsia compared to normotensive pregnant women (Caughey, Stotland, Washington, & Escobar, 2005).

Various studies have reported a statistically non-significant change in the serum potassium levels in preeclampsia and hypertensive pregnant patients compared to normotensive pregnant women

(Adewolu, 2013; Bera et al., 2011; Clark et al., 1997; Siddiqui & Rana, 1993; Singh, Dighe, Singh, & Othman, 1993). However, Yussif et al. (2009) observed a significantly reduced serum potassium level in hypertensive pregnant women compared with normal pregnant women and proposed a raised serum sodium and a reduced serum potassium level as a pathologic cause of hypertension in pregnancy. Yussif et al. (2009) concluded that a low potassium diet combined with a normal sodium diet can cause sodium retention and therefore development of hypertension. Handwerker, Altura, & Altura (1995) however noted an elevated serum potassium level in preeclampsia compared to normal pregnant women.

Considering the above mentioned literatures, the serum sodium and potassium profile in preeclampsia compared with normal pregnancy is inconclusive. These electrolytes seem to play a role in vasomotor activity during pregnancy and may possibly have a role in the pathophysiology of preeclampsia. Literature, however, is yet to reach an agreement on the role these electrolytes play in the development of preeclampsia. This study sought to compare the serum sodium and potassium levels between preeclamptic and normotensive pregnant women in a tertiary hospital in Ghana.

2. Materials and methods

2.1. Study design

This was a case-control study conducted at the Obstetrics and Gynaecology clinic of Korle- Bu Teaching Hospital, Ghana between March and June, 2016.

2.2. Study site

The survey site was the Korle-Bu Teaching Hospital, the premiere and the largest tertiary hospital in Ghana affiliated to the University of Ghana School of Medicine and Dentistry. The hospital has a 2,000 bed capacity. The obstetrics and gynaecology department of the hospital has a 350 bed capacity with 3 operating theatre suites. The department has 65 doctors, 200 nurses and midwives, with a daily antenatal attendance of 100 patients, and a total annual delivery between 10,000 and 12,000.

2.3. Subjects/Target population

The study population included normotensive pregnant women and preeclamptics aged 18-35 years attending the obstetrics and gynaecology clinic at Korle-Bu Teaching Hospital and who gave their informed consent, except:

(1) Pregnant and preeclamptics on any medical treatment other than iron and folic acid.

(2) Pregnant and preeclamptics with chronic hypertension, history of kidney disease, diabetes mellitus, cardiac diseases and neuromuscular disorders.

The International Society for the Study of Hypertension in Pregnancy criteria (Tranquilli et al., 2014) was used for the diagnosis of preeclampsia.

2.4. Sampling and sample size determination

At their first third trimester (29–40^{+} weeks) pre-natal visit to the hospital, patients fulfilling the inclusion criteria were consecutively recruited into the study after obtaining an informed consent. Considering a total of 10,000 deliveries at Korle-Bu Teaching hospital, with 1.5% difference between normotensive pregnant women and preeclamptics and 5% margin of error. Using the formula $n = N^{*}X/(X + N - 1)$ where $X = Z^{2}_{\alpha/2} {}^{*}p^{*}(1 - p)/E^{2}$, 30 preeclamptics and 30 normotensive pregnant women were recruited consecutively into the study at the ratio of 1:1.

2.5. Procedure used

After obtaining an informed consent, participants' age, parity, height and weight were recorded on a data collection form.

Blood pressure measurements were taken at the first third trimester pre-natal visit using a sphygmomanometer (Accuson, Italy) and a stethoscope. Measurements were done on the right arm with the patients in the sitting position. Two measurements were done per patient at 15 min interval and averaged.

Three millilitres of blood was drawn from the cubital vein using a sterile 19G hypodermic needle fixed on a 5 ml syringe after cleansing the site to be punctured with methylated spirit. Aseptic conditions were adhered to. The blood sample was transferred into a plain test tube, immediately sent to the laboratory and then spun at a speed of 4,000 rpm for 10 mins to separate serum from cells. Serum obtained was stored in a freezer at a temperature of −20°C prior to analysis. Serum sodium and potassium were analysed using Sherwood Flame Photometer (Model 420 by Sherwood Scientific Ltd, UK) and values recorded on data collection forms.

2.6. Statistical analysis

Data collected was entered into Microsoft Access database 2010 (Microsoft® USA) and analysis done using Statistical Package for Social Sciences (SPSS®) software version 20.0. The demographic and anthropometric parameters such as age, weight, height and BMI were reported as means (standard deviations) in a tabular form. The serum sodium and potassium levels were presented in a bar chart. Independent t-test was employed to compare the significant difference in the means of serum sodium and potassium between preeclampsia and normotensive pregnant women. A *p*-value ≤ 0.05 was considered statistically significant.

3. Results

A total of 60 third trimester pregnant women were recruited into the study. This consisted of 30 preeclamptics and 30 normotensive pregnant women. The characteristics of the recruited women are shown in Table 1. Compared to the normotensive pregnant women, a significant difference was observed in the mean systolic ($p < 0.001$), diastolic ($p < 0.001$) and mean arterial pressures ($p < 0.001$) of the preeclamptics

There was a significantly reduced ($p < 0.001$) serum sodium levels in preeclamptics [136.13(4.17) mmol/L] compared to normotensive pregnant women [142.17(5.66) mmol/L] (Figure 1).

There was a significantly reduced ($p < 0.001$) serum potassium levels in preeclamptics [3.45 (0.54) mmol/L] compared to normotensive pregnant women [3.98(0.36) mmol/L] (Figure 2).

4. Discussion

Our study showed no statistically significant difference between maternal age and preeclampsia ($p = 0.358$), similar to the findings of other studies (Ganesh, Unnikrishnan, Nagaraj, & Jayaram, 2010;

Table 1. Demographic and clinical characteristics of the patients

Parameter	Preeclamptics	Normotensive pregnant women	*p-value*
	Mean (SD)	Mean (SD)	
n	30	30	
Age (years)	30.97 (5.51)	29.93 (2.60)	0.358
Parity	1.70 (1.42)	1.13 (1.41)	0.567
BMI (kg/m^2)	32.03 (7.52)	30.50 (5.50)	0.374
SBP (mmHg)	170.13 (23.69)	116.47 (13.38)	<0.001*
DBP (mmHg)	106.30 (18.79)	67.57 (8.54)	<0.001*
MAP (mmHg)	126.20 (20.86)	83.87 (8.85)	<0.001*

*Significant at $p < 0.05$; *n*—sample size; SD—standard deviation; BMI—body mass index; SBP—systolic blood pressure; DBP—diastolic blood pressure; MAP—mean arterial pressure.

Figure 1. Mean serum sodium levels of preeclamptic and normotensive pregnant women.

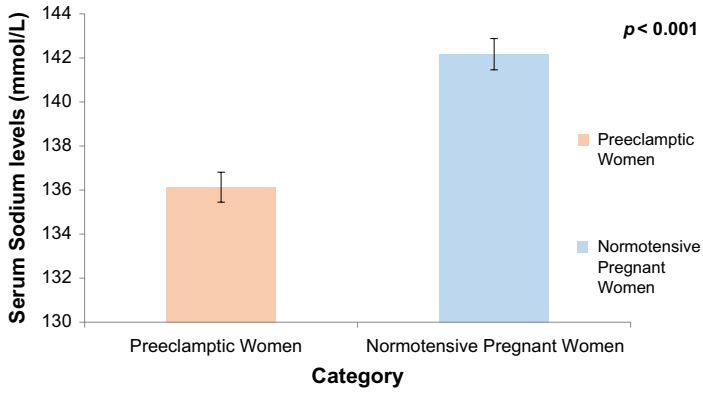
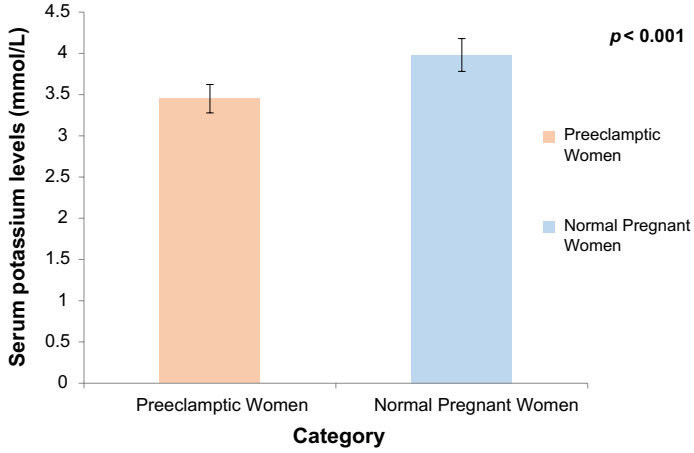


Figure 2. Mean serum potassium levels for preeclamptic and normotensive pregnant women.



Shamsi et al., 2010) but contradicts the findings of Macdonald-Wallis et al. (2011). This difference may be accounted for by the differences in population characteristics.

Our study also showed no statistically significant difference between BMI and preeclampsia ($p = 0.374$) similar to the findings of Onyebule et al. (2014); however, other studies have reported an association of high BMI with preeclampsia (Hauger, Gibbons, Vik, & Belizán, 2008; Munazza et al., 2011; Poorolajal & Jenabi, 2016).

The mean systolic, mean diastolic and mean arterial pressures of the preeclamptics were significantly higher than that of the normotensive pregnant women ($p < 0.001$). This was however expected in view of the criteria used for diagnosis of preeclampsia. Mean arterial pressure has been observed to be predictive of preeclampsia even though other studies have reported otherwise (Redman, Beilin, Bonnar, & Wilkinson, 1976).

There are two mechanisms by which sodium has been proposed to affect blood pressure. Excess sodium intake causes expansion of intravascular and extravascular fluid volume resulting in increased venous return and cardiac output and therefore increased blood flow to tissues. Persistence of this triggers an autoregulatory mechanism causing increased peripheral resistance (Sullivan & Martin, 1994). The "peripheral arterial vasodilation hypothesis" also postulates an increased endothelial damage with sodium and water retention and hence an increase in sensitivity to angiotensin (Schrier & Briner, 1991).

Though literature is inconclusive on the picture of serum sodium levels in preeclamptics compared to normotensive pregnant women, with some observing no significant difference (Adewolu, 2013; Bera et al., 2011; Rizk, 1997; Yussif et al., 2009) and others observing a significant increase (Caughey et al., 2005), this study, in agreement with findings of other studies (Indumati et al., 2011; Pitkin et al., 1972; Searcy, 1969; Tarik & Ward, 2011), noted a significantly reduced serum sodium levels in preeclamptics in comparison to normotensive pregnant women ($p < 0.001$).

Preeclampsia clinically manifests as hypertension, proteinuria with or without oedema during pregnancy. Even though preeclamptics have an adequate electrolyte and water content, these are mainly situated in the interstitium with a resultant decreased intravascular circulating volume. This decrease in intravascular circulating volume results in activation of baroreceptors and release of antidiuretic hormone (ADH) causing water retention and natriuresis. This sequence of events leads to a reduction in serum sodium and may account for the observed significantly reduced serum sodium levels in preeclamptics. It has also been observed that a defective placenta seen in preeclamptics is unable to produce a vasopressinase, an enzyme which inactivates ADH and therefore a build-up of ADH in preeclamptics (Chung, Kluge, Schrier, & Anderson, 1987). The ADH levels of the subjects in this study were however not measured.

Alteration of natriuretic factors as being responsible for reduced serum sodium levels seen in preeclampsia has also been suggested in literature. Atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) levels has been noted to be increased in preeclamptics even though this is not a uniform finding (Graves, 2007; Reis et al., 2003; Tihtonen, Kööbi, Vuolteenaho, Huhtala, & Uotila, 2007). These factors cause natriuresis and hence a fall in serum sodium levels. This study however did not measure the levels of natriuretic factors.

The reduced serum sodium levels in preeclamptics observed in this study could also be dilutional. There are reports of dilutional hyponatraemia in preeclamptics with or without associated nephrotic syndrome in literature (Hayslett, Katz, & Knudson, 1998; Magriples, Laifer, & Hayslett, 2001). Preeclampsia is one of the commonest causes of nephrotic syndrome that occurs during pregnancy (Fisher, Ahuja, Luger, Spargo, & Lindheimer, 1977). There is a difficulty distinguishing between preeclampsia and renal disease as a cause of hyponatraemia. The distinction is usually possible in retrospect, as clinical signs of preeclampsia generally resolve within 12 weeks postpartum, whilst proteinuria due to underlying renal disease does not (Chua & Redman, 1992).

From this study, there was a significant reduction in mean serum potassium levels in preeclamptics compared to normotensive pregnant women ($p < 0.001$) as shown in Figure 2. Manjareeka and Nanda (2012) and Yussif et al. (2009) made a similar observation in an Indian and Iraqi population respectively while other studies (Adewolu, 2013; Bera et al., 2011; Siddiqui & Rana, 1993; Singh et al., 1993) observed no statistically significant difference in the serum potassium level between hypertensive pregnant women and normotensive pregnant women in India. However, Handwerker et al. (1995) have also reported a statistically significant elevation of serum potassium levels in preeclamptics compared to normotensive pregnant women.

Ninety percent of total body potassium is located intracellularly whilst sodium is mainly located extracellularly. The difference in predominant locations is influenced by the Na^+/K^+-ATPase (Delgado, 2004). In preeclampsia and pregnancy induced hypertension there is an abnormality in the transport of sodium and potassium across the cell membrane of vascular smooth muscles which regulates blood pressure (Arumanayagam & Rogers, 1999). An earlier study (Pikilidou et al., 2007) has established an inverse relationship between serum potassium levels and severity of hypertension. This shows that raised serum potassium may have a beneficial effect on blood pressure regulation. The mechanism explaining the relationship between reduced serum potassium levels and poor blood pressure control is poorly understood. Reduced levels of serum potassium enhance vascular responsiveness to vasopressors such as norepinephrine (Bianchetti, Weidmann, Beretta-Piccoli, & Ferrier, 1987). Decreased release of nitric oxide by the endothelial cells may be the mediating factor

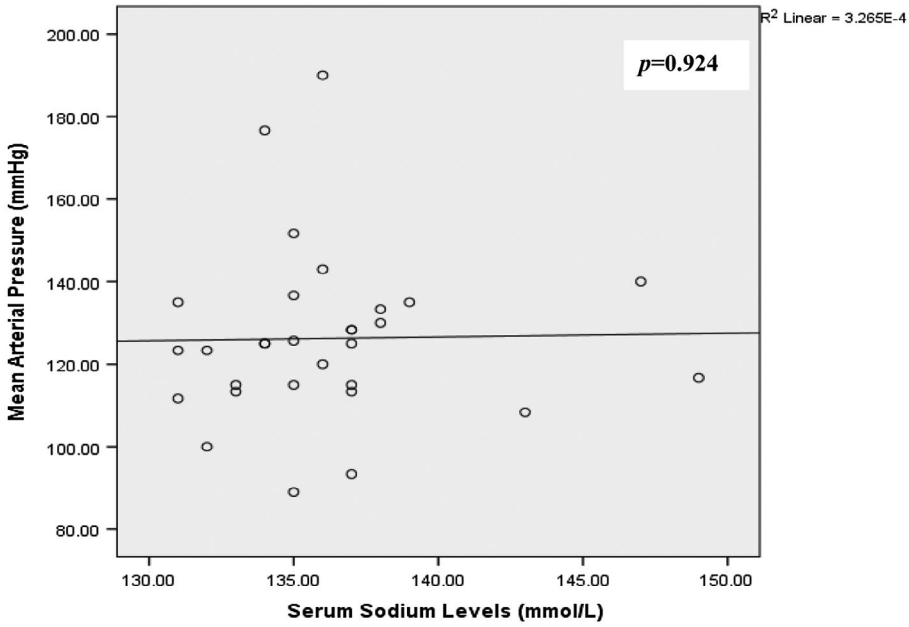


Figure 3. Correlation between serum sodium levels and mean arterial pressure in preeclamptics.

(Taddei et al., 1994). This leads to vasoconstriction and increased platelet aggregation which increases blood pressure and therefore poor protection against hypertension caused by induced endothelial injury which has been implicated in the pathogenesis of preeclampsia (Vane, Änggård, & Botting, 1990).

It has also been observed that reduced serum potassium levels also reduce sodium excretion through probable changes in reabsorption of sodium in the proximal tubule or loop of Henle of the kidney resulting in elevated blood pressure (Gallen et al., 1998). In fact it has been observed that a diet low in potassium coupled with individual's usual sodium intake can lead to sodium retention and therefore hypertension (Yussif et al., 2009).

There was weak non-significant correlations between mean arterial pressures and serum sodium and potassium levels (Figures 3 and 4). An R^2 value of 0.3 and 4% was obtained respectively for sodium and potassium. This implies that serum sodium levels and serum potassium levels may

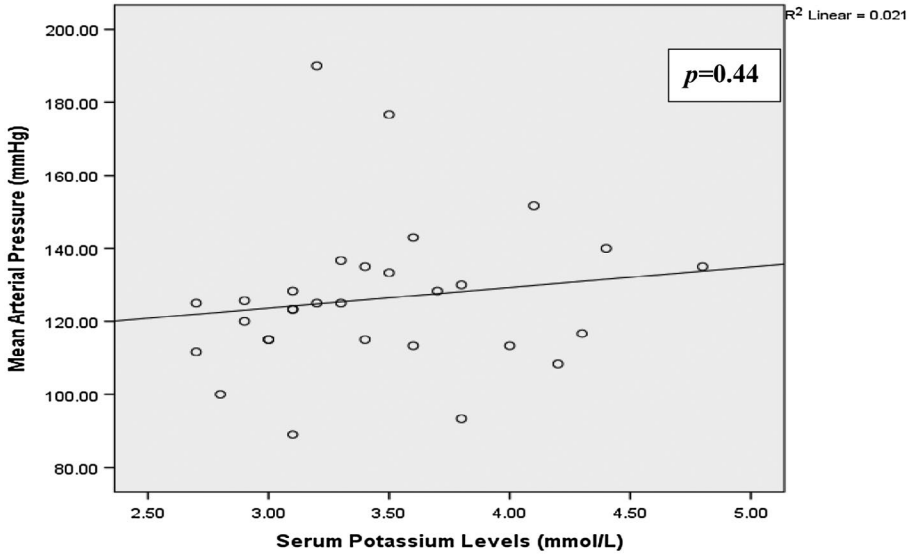


Figure 4. Correlation between serum potassium levels and mean arterial pressure in preeclamptics.

account for only 0.3 and 4% in the variability of mean arterial pressure in preeclamptics respectively. Other factors may therefore be involved, hence, it would be difficult predicting mean arterial pressures in preeclamptics using only their serum sodium and potassium levels.

5. Conclusion

We observed a significantly reduced serum sodium and potassium levels in preeclamptics compared to normotensive pregnant Ghanaian women. A non-significant weak positive correlation was found between the two serum ions (sodium levels and potassium levels) and mean arterial pressure in preeclamptics.

The observed reduced levels of serum sodium and potassium in preeclampsia as compared to normotensive pregnant women, suggests that changes in these electrolytes may be associated with preeclampsia.

Authors' contribution

Ebenezer Owusu Darkwa is a consultant Anaesthetist of the Department of Anaesthesia, Korle-Bu Teaching Hospital. The author designed the study and wrote the manuscript which is part of his MPhil. Physiology thesis.

Robert Djagbletey is a consultant Anaesthetist of the Department of Anaesthesia, Korle-Bu Teaching Hospital. He participated in designing the study.

Charles Antwi-Boasiako, Head of Physiology Department, School of Allied Health and Biomedical Sciences, University of Ghana helped in preparing the manuscript.

Alexander Akowuah and Daniel Sottie of the Department of Anaesthesia, Korle-Bu Teaching assisted in data collection

George Aryee of the Department of Anaesthesia, University of Ghana assisted in data analysis.

All authors read and approved the final manuscript

Ethical approval

Ethical Approval for the study was obtained from the Ethical and Protocol Review Committee of University of Ghana, School of Medicine and Dentistry (Protocol Identification Number: CHS-Et/M.4-P4.5/2015-2016). Clearance was also received from the Management of the Korle-Bu Teaching Hospital and Heads of Clinical units where the study was conducted.

Acknowledgement

We are grateful to all health workers and patients at the obstetrics and gynaecology unit of the Korle-Bu Teaching Hospital. Special thanks goes to Prof Samuel Obed, Head of Department, Obstetrics and Gynaecology, Korle-Bu Teaching Hospital.

Funding

This work was funded by the authors. We therefore declare that no financial support was sought from any organisation.

Author details

Ebenezer Owusu Darkwa[1]
E-mail: eoddarquah@yahoo.co.uk
ORCID ID: http://orcid.org/0000-0002-8766-6133
Robert Djagbletey[1]
E-mail: r_djag@yahoo.com
ORCID ID: http://orcid.org/0000-0001-5454-9515
Charles Antwi-Boasiako[2]
E-mail: antwiboasiako@chs.edu.gh
ORCID ID: http://orcid.org/0000-0002-2750-3500
George Aryee[1]
E-mail: garyee43@gmail.com
ORCID ID: http://orcid.org/0000-0002-9892-3131
Daniel Sottie[3]
E-mail: dsottie@gmail.com
ORCID ID: http://orcid.org/0000-0002-1166-8802
Alexander Akowuah[3]
E-mail: kwamens05@gmail.com

[1] Department of Anaesthesia, School of Medicine and Dentistry, College of Health Sciences, University of Ghana, Accra, Ghana.

[2] Department of Physiology, School of Biomedical and Allied Health Sciences, College of Health Sciences, University of Ghana, Accra, Ghana.

[3] Department of Anaesthesia, Korle-Bu Teaching Hospital, Accra, Ghana.

Citation information

Cite this article as: Serum sodium and potassium levels in preeclampsia: A case-control study in a large tertiary hospital in Ghana, Ebenezer Owusu Darkwa, Robert Djagbletey, Charles Antwi-Boasiako, George Aryee, Daniel Sottie & Alexander Akowuah, *Cogent Medicine* (2017), 4: 1376898.

Competing Interests

The authors declare no competing interest.

References

Adewolu, O. (2013, January 1). Serum sodium, potassium, calcium and magnesium in women with pregnancy induced hypertension and preeclampsia in Oredo local Government, Benin Metropolis: A pilot study. *African Journal of Medical and Health Sciences, 12*, 1–5. https://doi.org/10.4103/2384-5589.129914

Arumanayagam, M., & Rogers, M. (1999). Platelet sodium pump and sodium potassium cotransport activity in nonpregnant, normotensive, and hypertensive pregnant women. *Hypertension in Pregnancy, 18*, 35–44. https://doi.org/10.3109/10641959909009609

Aziz, R., & Mahboob, T. (2014). Serum calcium, magnesium and parathyroid hormone in normal pregnant and pre-eclamptic women in Karachi. *Pakistan Journal Hyperten, 3*, 143–145.

Bera, S., Siuli, R., Gupta, S., Roy, T., Taraphdar, P., Bal, R., & Ghosh, A. (2011). Study of serum electrolytes in pregnancy induced hypertension. *Journal of the Indian Medical Association, 109*, 546–548.

Bianchetti, M. G., Weidmann, P., Beretta-Piccoli, C., & Ferrier, C. (1987). Potassium and norepinephrine-or angiotensin–mediated pressor control in pre-hypertension. *Kidney International, 31*, 956–963. https://doi.org/10.1038/ki.1987.92

Caughey, A. B., Stotland, N. E., Washington, A. E., & Escobar, G. J. (2005). Maternal ethnicity, paternal ethnicity, and parental ethnic discordance: Predictors of preeclampsia. *Obstetrics & Gynecology, 106*, 156–161. https://doi.org/10.1097/01.AOG.0000164478.91731.06

Chesley, L. C., Annitto, J. E., & Cosgrove, R. A. (1976). The remote prognosis of eclamptic women. *American Journal of Obstetrics and Gynecology, 124*, 446–459. https://doi.org/10.1016/0002-9378(76)90168-X

Chua, S., & Redman, C. (1992). Prognosis for pre-eclampsia complicated by 5 g or more of proteinuria in 24 hours. *European Journal of Obstetrics & Gynecology and Reproductive Biology, 43*, 9–12. https://doi.org/10.1016/0028-2243(92)90236-R

Chung, H.-M., Kluge, R., Schrier, R. W., & Anderson, R. J. (1987). Clinical assessment of extracellular fluid volume in hyponatremia. *The American Journal of Medicine, 83*, 905–908. https://doi.org/10.1016/0002-9343(87)90649-8

Clark, S. L., Cotton, D. B., Hankins, G., & Phelan, J. P. (Eds.). (1997). *Critical care obstetrics* (3rd ed.). Oklahoma, OK: Black Well Science Limited.

Delgado, M. C. (2004). Potassium in hypertension. *Current Hypertension Reports, 6*, 31–35. https://doi.org/10.1007/s11906-004-0008-6

Ephraim, R. K. D., Osakunor, D. N. M., Denkyira, S. W., Eshun, H., & Anto, E. O. (2014). Serum calcium and magnesium levels in women presenting with pre-eclampsia and pregnancy-induced hypertension: A case–control study in the Cape Coast metropolis, Ghana. *BMC Pregnancy and Childbirth, 14*, 416. https://doi.org/10.1186/s12884-014-0390-2

Fisher, K. A., Ahuja, S., Luger, A., Spargo, B. H., & Lindheimer, M. D. (1977). Nephrotic proteinuria with pre-eclampsia. *American Journal of Obstetrics and Gynecology, 129*, 643–646. https://doi.org/10.1016/0002-9378(77)90646-9

Gallen, I. W., Rosa, R. M., Esparaz, D. Y., Young, J. B., Robertson, G. L., Batlle, D., … Landsberg, L. (1998). On the mechanism of the effects of potassium restriction on blood pressure and renal sodium retention. *American Journal of Kidney Diseases, 31*, 19–27. https://doi.org/10.1053/ajkd.1998.v31.pm9428447

Ganesh, K. S., Unnikrishnan, B., Nagaraj, K., & Jayaram, S. (2010). Determinants of pre-eclampsia: A case-control study in a district hospital in South India. *Indian Journal of Community Medicine, 35*, 502–505.

Graves, S. W. (2007). Sodium regulation, sodium pump function and sodium pump inhibitors in uncomplicated pregnancy and preeclampsia. *Frontiers in Bioscience, 12*, 2438–2446. https://doi.org/10.2741/2245

Handwerker, S. M., Altura, B. T., & Altura, B. M. (1995). Ionized serum magnesium and potassium levels in pregnant women with preeclampsia and eclampsia. *The Journal of Reproductive Medicine, 40*, 201–208.

Hauger, M. S., Gibbons, L., Vik, T., & Belizán, J. M. (2008). Prepregnancy weight status and the risk of adverse pregnancy outcome. *Acta Obstetricia et Gynecologica Scandinavica, 87*, 953–959. https://doi.org/10.1080/00016340802303349

Hayslett, J. P., Katz, D. L., & Knudson, J. M. (1998). Dilutional hyponatremia in pre-eclampsia. *American Journal of Obstetrics and Gynecology, 179*, 1312–1316. https://doi.org/10.1016/S0002-9378(98)70153-X

Indumati, V., Kodliwadmath, M. V., & Sheela, M. K. (2011). Role of serum electrolytes in pregnancy induced hypertension. *JCDR, 5*, 66–69.

Kanagal, D. V., Rajesh, A., Rao, K., Devi, U. H., Shetty, H., Kumari, S., & Shetty, P. K. (2014). Levels of serum calcium and magnesium in pre-eclamptic and normal pregnancy: A study from coastal India. *Journal of Clinical and Diagnostic Research, 8*, OC01–OC04.

Khan, K. S., Wojdyla, D., Say, L., Gülmezoglu, A. M., & Van Look, P. F. (2006). WHO analysis of causes of maternal death: A systematic review. *The Lancet, 367*, 1066–1074. https://doi.org/10.1016/S0140-6736(06)68397-9

Lassey, A., & Wilson, J. (1998). Trends in maternal mortality in Korle Bu Hospital, 1984–1994. *Ghana Med Journal, 32*, 910–916.

Macdonald-Wallis, C., Lawlor, D. A., Heron, J., Fraser, A., Nelson, S. M., & Tilling, K. (2011). Relationships of risk factors for pre-eclampsia with patterns of occurrence of isolated gestational proteinuria during normal term pregnancy. *PLoS One, 6*, e22115. https://doi.org/10.1371/journal.pone.0022115

Magriples, U., Laifer, S., & Hayslett, J. P. (2001). Dilutional hyponatremia in preeclampsia with and without nephrotic syndrome. *American Journal of Obstetrics and Gynecology, 184*, 231–232. https://doi.org/10.1067/mob.2001.106798

Manjareeka, M., & Nanda, S. (2012). Serum electrolyte levels in preeclamptic women: A comparative study. *International Journal of Pharma and BioSciences, 3*, 572–578.

Munazza, B., Raza, N., Naureen, A., Khan, S. A., Fatima, F., Ayub, M., & Sulaman, M. (2011). Liver function tests in preeclampsia. *Journal of Ayub Medical College Abbottabad, 23*, 3–5.

Onyegbule, O. A., Meludu, S. C., Dioka, C. E., Udigwe, G. O., Udo, J. N., Ezidigboh, A. N., … Osakue, N. (2014). Comparison of serum levels of calcium and magnesium among preeclamptic and normotensive pregnant women at Nnamdi Azikiwe University Teaching Hospital, Nnewi, Nigeria. *International Journal of Research in Medical Sciences, 2*, 404–408. https://doi.org/10.5455/2320-6012.

Pikilidou, M. I., Lasaridis, A. N., Sarafidis, P. A., Tziolas, I. M., Zebekakis, P. E., Dombros, N. V., & Giannoulis, E. (2007). Blood pressure and serum potassium levels in hypertensive patients receiving or not receiving antihypertensive treatment. *Clinical and Experimental Hypertension, 29*, 563–573. https://doi.org/10.1080/10641960701744103

Pitkin, R. M., Kaminetzky, H. A., Newton, M., & Pritchard, J. A. (1972). Maternal nutrition: A selective review of clinical topics. *Obstetrics & Gynecology, 40*, 7730–7785.

Poorolajal, J., & Jenabi, E. (2016). The association between body mass index and preeclampsia: A meta-analysis. *The Journal of Maternal-Fetal & Neonatal Medicine, 29*, 3670–3676. https://doi.org/10.3109/14767058.2016.1140738

Ravid, D., Massarwa, L.-E., Biron-Shental, T., & Fejgin, M. D. (2005). Hyponatremia and preeclampsia. *The Journal of Maternal-Fetal & Neonatal Medicine, 18*, 77–79. https://doi.org/10.1080/14767050500127682

Redman, C., Beilin, L., Bonnar, J., & Wilkinson, R. (1976). Plasma-urate measurements in predicting fetal death in hypertensive pregnancy. *The Lancet, 307*, 1370–1373. https://doi.org/10.1016/S0140-6736(76)93024-5

Reis, Z. S. N., Cabral, A. C. V., Barra, J. S., Leite, H. V., Demian, A. A., & Reis, A. (2003). Pressão arterial e concentração plasmática do peptídeo atrial natriurético e do peptídeo natriurético tipo B, em gestações complicadas pela pré-eclâmpsia. *RBGO, 25*, 413–418.

Rizk, D. (1997). A study of alpha-human atrial natriuretic peptide in normal pregnancy and in pre-eclampsia. *Journal of Obstetrics and Gynaecology, 17*, 234–238. https://doi.org/10.1080/01443619750113122

Schrier, R. W., & Briner, V. A. (1991). Peripheral arterial vasodilation hypothesis of sodium and water retention in pregnancy: Implications for pathogenesis of preeclampsia-eclampsia. *Obstetrics & Gynecology, 77*, 632–639.

Searcy, R. L. (1969). *Diagnostic biochemistry* (pp. 469–476). New York, NY: McGraw-Hill Book company.

Shamsi, U., Hatcher, J., Shamsi, A., Zuberi, N., Qadri, Z., & Saleem, S. (2010). A multicentre matched case control study of risk factors for preeclampsia in healthy women in Pakistan. *BMC Womens Health, 10*(1), 1.

Sidahmed, M. A. E., & Abubaker, N. E. (2017). Serum total calcium, magnesium, sodium and potassium in sudanese with preeclampsia. *International Journal of Advanced Research, 5*, 2061–2066. https://doi.org/10.21474/IJAR01

Siddiqui, J. A., & Rana, I. (1993). Mineral and parathyroid hormone inter-relationships in normal pregnancy and pregnancy-induced hypertension. *JPMA, 43*, 92–95.

Singh, H. J., Dighe, V., Singh, R., & Othman, N. (1993). Serum levels and urinary excretion of magnesium, calcium and electrolytes in mild pregnancy-induced hypertension. *Hypertension in Pregnancy, 12*, 113–120. https://doi.org/10.3109/10641959309031058

Smith, R. A., & Kenny, L. C. (2006). Current thoughts on the pathogenesis of pre-eclampsia. *The Obstetrician & Gynaecologist, 8*, 7–13. https://doi.org/10.1576/toag.8.1.007.27202

Sukonpan, K., & Phupong, V. (2005). Serum calcium and serum magnesium in normal and preeclamptic pregnancy. *Archives of Gynecology and Obstetrics, 273*, 12–16. https://doi.org/10.1007/s00404-004-0672-4

Sullivan, C. A., & Martin, J. N. J. (1994). Sodium and pregnancy. In R. M. Pitkin, & J. R. Scott (Eds.), *Clinical obstetrics and gynaecology* (pp. 558–573). Philadelphia: Lippincott Co.

Tabassum, H., Al-Jameil, N., Ali, M. N., Khan, F. A., & Al-Rahed, M. (2015). Status of serum electrolytes in preeclamptic pregnant women of Riyadh, Saudi Arabia. *Biomedical Research, 26*, 219–224.

Taddei, S., Mattei, P., Virdis, A., Sudano, I., Ghiadoni, L., & Salvetti, A. (1994). Effect of potassium on vasodilation to acetylcholine in essential hypertension. *Hypertension, 23*, 485–490. https://doi.org/10.1161/01.HYP.23.4.485

Tarik, A., & Ward, E. (2011). Severe hyponatraemia in pregnancy associated with pre-eclampsia. *Endocrine Abstracts, 25*, 39.

Tihtonen, K. M., Kööbi, T., Vuolteenaho, O., Huhtala, H. S., & Uotila, J. T. (2007). Natriuretic peptides and hemodynamics in preeclampsia. *American Journal of Obstetrics and Gynecology, 196*, 328.e1–328.e7. https://doi.org/10.1016/j.ajog.2006.11.033

Tranquilli, A., Dekker, G., Magee, L., Roberts, J., Sibai, B., Steyn, W., … Brown, M. A. (2014). The classification, diagnosis and management of the hypertensive disorders of pregnancy: A revised statement from the ISSHP. *Pregnancy Hypertension: An International Journal of Women's Cardiovascular Health, 4*, 97–104.

Vane, J. R., Änggård, E. E., & Botting, R. M. (1990). Regulatory functions of the vascular endothelium. *New England Journal of Medicine, 323*, 27–36.

Villar, J., Betran, A., & Gulmezoglu, M. (2001). Epidemiological basis for the planning of maternal health services. *WHO/RHR, 111*, 298–298.

Wilson, B. J., Watson, M. S., Prescott, G. J., Sunderland, S., Campbell, D. M., Hannaford, P., & Smith, W. C. (2003). Hypertensive diseases of pregnancy and risk of hypertension and stroke in later life: Results from cohort study. *BMJ., 326*, 845. https://doi.org/10.1136/bmj.326.7394.845

Yussif, M. N., Salih, R., Sami, A., & Mossa, M. (2009). Estimation of serum zinc, sodium and potassium in normotensive and hypertensive primigravide pregnant women. *Tikrit Med Journal, 15*, 13–18.

Ziaei, S., Ranjkesh, F., & Faghihzadeh, S. (2008). Evaluation of 24-hour urine copper in preeclamptic vs. normotensive pregnant and non-pregnant women. *IJFS, 2*, 9–12.

***Cogent Medicine* (ISSN: 2331-205X) is published by Cogent OA, part of Taylor & Francis Group.**