

Study of Serum IMA and Electrolytes in Patients of Pre-eclampsia in Central India

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ABSTRACT

Background: Pre-eclampsia (PE) a pregnancy specific disorder is the most common cause of fetal and maternal death, yet no specific prevention and treatment is available. Reliable biochemical markers for prediction and diagnosis of PE can have a better impact on maternal health and therefore several markers have been suggested till now. Recently Ischemia Modified Albumin (IMA) has emerged as a marker in different diseases where ischemia is the origin or consequence behind disease pathology. The normal sodium level is in the range of [137-145 mmol/L] and that of the potassium is [3.5-5.0 mmol/L].

Materials & methods: 30 patients with PE were selected for the study and compared with 30 pregnant healthy controls.

IMA, IMA/albumin ratio & Serum Electrolytes were estimated in these patients.

The results were then statistically analyzed. It was a record based cross-sectional comparative study, carried out in the department of Biochemistry at Shri Shankracharya Institute of Medical Sciences and Hospital, Bhilai (Chhattisgarh) a tertiary care institute.

Results: IMA levels were found significantly raised in PE patients as compared to normal pregnant controls (p value<0.001)

The mean serum sodium level in preeclamptics was 123.9±3.03 mmol/l and mean serum sodium levels in controls was 140.6±1.73 mmol/l. On applying significance test it was found that the difference in serum levels of sodium in both the groups was highly significant (p value < 0.001). The mean serum potassium levels in preeclamptics were 2.49±0.23 mmol/l and mean potassium levels in controls was 3.96±0.32 mmol/l. On applying significance test it was

found that the difference in serum levels of potassium in both the groups was highly significant (p value < 0.001).

Conclusion: IMA generated by hypoxia/ischemia driven oxidative stress is raised in PE, hence it can be used as a biomarker in PE.

Serum sodium level was observed to be reduced in pre-eclamptics as compared to normotensive pregnant and non-pregnant women. The identification and counselling of preeclampsia relies fundamentally on the frequency of antenatal care and if their blood pressure was measured during the visit. Many women with pre-eclampsia, particularly, at the community level are missed due to the lack of antenatal care.

Keywords: Pre-eclampsia, IMA, Electrolytes

INTRODUCTION

Preeclampsia is a multisystem disorder of unknown aetiology characterized by development of hypertension to the extent of 140/90 mmHg or more with proteinuria after the 20th week of pregnancy in a previously normotensive and non-proteinuric women.

Impaired endovascular invasion of cytotrophoblast into the spiral arteries is implicated as a causal factor in pathogenesis of the disease. Many other theories regarding its pathogenesis such as increased insulin resistance, oxidative stress, immunological intolerance between maternal and foetal tissue etc. are also postulated.

Hypertensive disorders of pregnancy are the leading cause of maternal mortality.

It occurs in approximately 6-8% of all pregnancies, 10% of first pregnancies and 20-25% of women with a history of chronic hypertension. It accounts for approximately a quarter of all antenatal admissions. Incidence of pre eclampsia in India is reported to be 8-10% of all pregnancies. [1,3]

Pre-eclampsia is associated with defective endovascular trophoblast invasion and inadequate remodelling of uterine spiral arteries leading to hypoxic intrauterine environment and generation of oxidative free radicals. Accumulation of biomarkers of oxidative stress accompanied by depletion of antioxidant reserves is considered as a hallmark of pre-eclampsia.

As placental hypoxic conditions are found in pre-eclampsia and oxidative stress is implicated in its pathogenesis, maternal serum Ischemia Modified Albumin (IMA) can be a potent biomarker of pre-eclampsia.

Under physiological conditions the amino terminal of Human Serum Albumin (HSA) binds to transition metals. Ischemia reperfusion injury generates reactive oxygen species which modify the N-terminal region of HSA, reducing its capacity to bind to the transition metals. This chemically changed albumin is called as ischemia modified albumin.

In preeclampsia, there is alteration in cell membrane sodium transport leading to extravascular accumulation of sodium with reduced plasma sodium level. [7] Preeclampsia remains an important maternal health problem in India. However, other studies found no significant change in serum sodium levels of preeclamptics compared to normal pregnant women. [2]

Objectives

To determine and compare the values of IMA and serum Electrolytes in pre-eclamptic primigravida and healthy pregnant females.

MATERIALS AND METHODS

This cross sectional study was conducted taking women with gestational hypertension and pre-eclampsia

as cases and healthy pregnant females were taken as controls from April 2018 to April 2019.

The cases and controls were selected from tertiary care hospitals in local geographical area.

Written informed consent was taken from each study subject.

I. Selection of study subjects

- Based on inclusion and exclusion criteria total 60 study subjects (30 cases and 30 controls) were selected for the study. A proforma was used to record relevant information and patient's data.
- CASES = 30 women with hypertensive disorders of pregnancy were selected on the basis of definition given by National High Blood Pressure Education Programme (NHBPEP 2000).
- CONTROLS = 30 healthy pregnant females.
- **INCLUSION CRITERIA**
 - 30 diagnosed cases of pre-eclampsia in the age group of 20-45 years.
 - Pregnant females of ≥ 20 weeks of gestation with blood pressure of $\geq 140/90$ mm of Hg noted first time during pregnancy on ≥ 2 occasions at least 6 hours apart with proteinuria of $\geq 1+$ by dipstick method in a random urine sample was considered to have pre-eclampsia.
 - Control = healthy age & sex matched 30 controls were taken.
- **EXCLUSION CRITERIA**
 - History of chronic hypertension that was present before pregnancy.
 - History of diabetes mellitus and/or who are on insulin therapy.
 - Subjects taking anti-hypertensive drugs.
 - Liver disease patients.

Collection of Blood samples

- About 6ml of venous blood was drawn under aseptic precautions from selected subjects after overnight fasting of 12 hours.
- 3 ml of blood was collected in plain vial for serum IMA (maternal).

- The blood samples were centrifuged at 3000 rpm for 10 minutes to obtain the serum.

Parameters Measured

- The parameters which were to be measured in the cases and controls are maternal serum IMA, Na⁺ & K⁺.

Measurement of serum ischemia modified albumin, Na⁺ & K⁺

- It is done according to Bar Or et al 2000. Known amount of cobalt was added to the serum sample and unbound cobalt was measured by the intensity of coloured complex formed after reacting with dithiothreitol by spectrophotometer at 470 nm.

- Na⁺ & K⁺ was measured by SENSACORE ELECTROLYTE ANALYZER. [4,5]

RESULTS

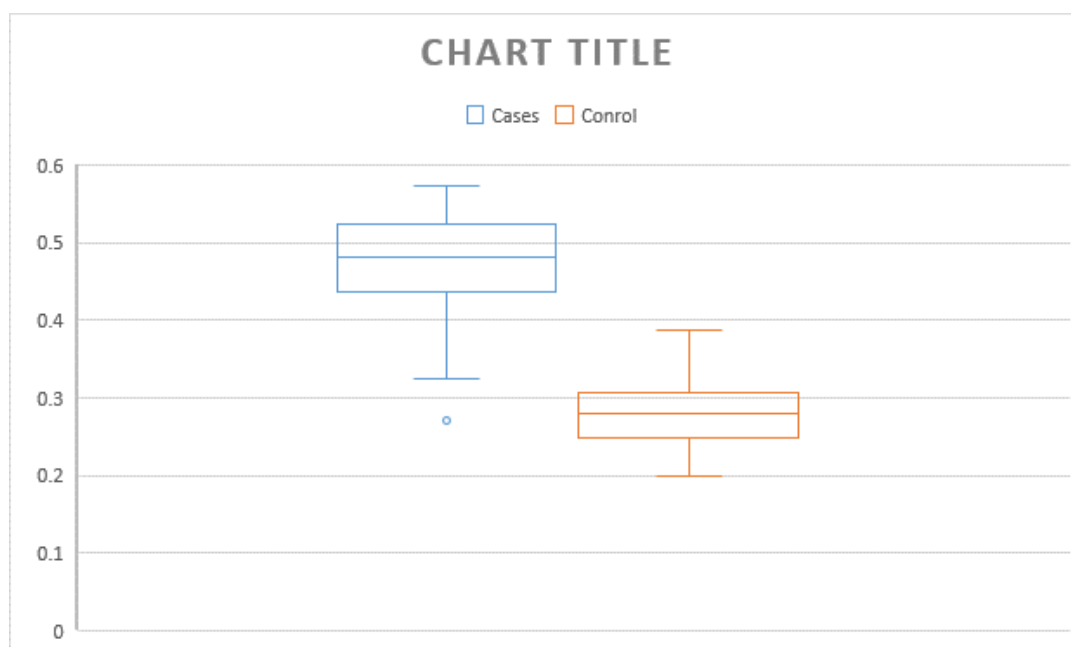
Table No. 1: Descriptive information of subjects

Variable	Normotensives mean±SD	Preeclampsics mean±SD
Age in years	27.86±4.46	27.5 ±4.88
Gestational age in weeks	32.6±2.8	30±2.3
Blood Pressure		
Systolic	121.8 ±5.15	147.6±5.85
Diastolic	84.06 ±4.44	97.8±6.39

Table No. 2

Parameter	Case	Control	P-value
Age	27.7 ± 4.99	26.93 ± 4.55	0.5367
IMA	0.468 ± 0.05	0.279 ± 0.047	<0.001*

*significant difference



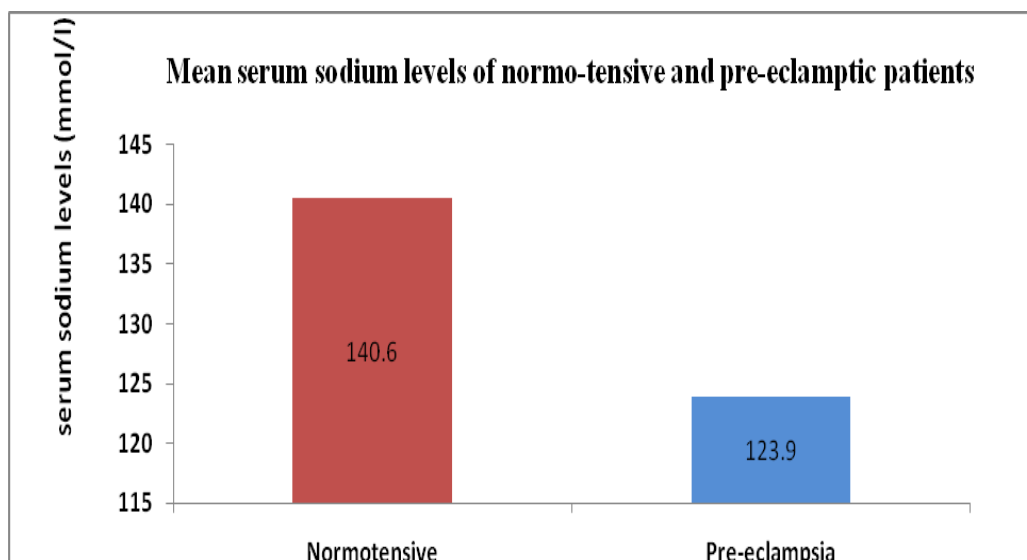
The mean value of IMA was 0.468 ± 0.075 in the cases and in controls it was 0.279 ± 0.047.

The IMA variables were noted in cases as well as controls. All the variables were continuous in nature. T-test for two independent samples was applied to data as the samples were independent. Cases and controls were matched for age and there was no significant difference found in age of cases and control. IMA levels were found to be higher in cases compared to control. This type of graph is used to show the shape of the distribution, its central value, and its variability.

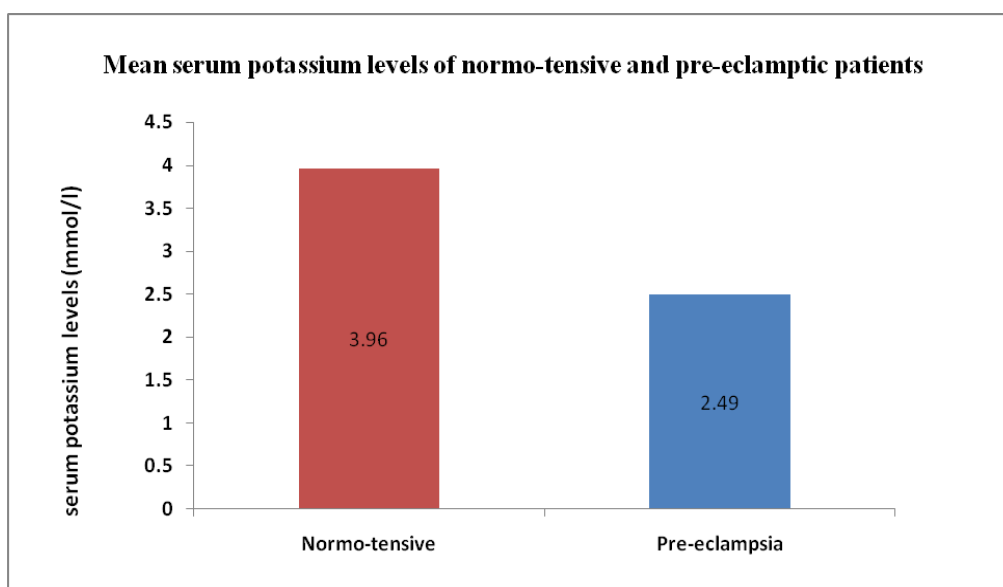
The mean serum sodium level in preeclampsics was 123.9±3.03 mmol/l and mean serum sodium levels in normotensives was 140.6±1.73 mmol/l. On applying significance test it was found that the difference in serum levels of sodium in both the groups was highly significant (p value < 0.0001) (Graph no.1).

The mean serum potassium level in preeclampsics was 2.49±0.23 mmol/l and mean potassium levels in normotensives was 3.96±0.32 mmol/l. On applying significance test it

was found that the difference in serum levels of potassium in both the groups was highly significant (p value < 0.0001) (Graph no.2).



Graph no.1: Mean serum sodium levels in pre eclamptics and controls



Graph no.2: Mean serum potassium levels in pre eclamptics and controls

DISCUSSION

Pre-eclampsia is associated with defective placentation which results in failure of conversion of small diameter high resistance vessels to large diameter low resistance vessels, leading to ischemic reperfusion injury and thus oxidative stress and generation of free radicals. Eclampsia is the end stage of the disease characterized by generalized seizures. Pre-eclampsia and eclampsia complicate 2%-8% of pregnancies and overall 10%-15% of direct

maternal deaths are associated with these conditions. [6,7]

Biochemical markers not only allow early detection of patients at risk, but can also help in grouping patients into different categories according to their severity for timely intervention. Many different biochemical markers have been investigated based upon pathophysiology of the disease but their reliability in predicting pre-eclampsia has been inconsistent.

Serum IMA has been observed to be significantly increased in diseases where

oxidative stress is the consequence of the disease process. In the present study a significant rise in serum IMA was seen in pre-eclamptic women compared to normal pregnant women. There occurs haemodilution in pregnancy leading to decrease in plasma albumin concentration so IMA was normalized to albumin by calculating IMA/Albumin ratio. These observations were in accordance with the studies done by GafSou et al and Yusuf Ustun et al. Placental hypoxia causing ischemic reperfusion injury results in the generation of free radicals which in turn causes alteration of NH₂ terminus of human serum albumin resulting in reduced binding of albumin to cobalt compared to normal pregnant control. [8,9]

However in a limited study done by Van Rijn et al serum IMA was found elevated in normal pregnant controls compared to the non-pregnant controls (p=0.015) but the IMA levels in pre-eclampsia were similar to those of normal pregnant controls (p=0.65). The discrepancy in these studies could possibly be explained by smaller number of patients and differences in severity of pre-eclampsia.

The mean serum sodium levels in preeclamptic women was 123.9±3.03 mmol/l and mean serum sodium levels in normotensive women was 140.6±1.73 mmol/l and the mean serum potassium levels in preeclamptic women was 2.49±0.23 mmol/l and mean potassium levels in normotensive women was 3.96±0.32 mmol/l. In a similar type of study conducted by Dhokikar Gajanan D et al in 2015 in Mumbai not much difference is observed in serum sodium [138 ± 4.03 mEq/L] and serum Potassium [4.0±0.5 mEq/L]. [10,11]

In a study conducted by Indumati et al in 2011 in Karnataka, it was observed that serum sodium and potassium levels were 130.84±3.03 and 3.57±0.27 respectively. Serum sodium levels were decreased significantly in the preeclamptic cases as compared to those in the normal pregnancy controls (p<0.001), but there was no

significant change in the serum potassium levels (p<0.457). [11]

In a study conducted by Hajera Tabassum and Noura Al-Jameil in 2015 in Riyadh, Saudi Arabia, found the level of serum sodium significantly increased in preeclampsia [138.27±2.99 mEq/L] which is quite opposite of our findings, while that of potassium significantly decreased [3.56±0.38mEq/L]. [12]

In a study conducted by Ebenezer Owusu Darkwa, Robert Djagbletey et al in 2017 in Ghana found the level of serum sodium and potassium significantly reduced (p <0.001) in preeclampsia [136.13(4.17) mmol/L] & [3.45 (0.54)mmol/L] respectively. [13]

CONCLUSION

IMA normalized to albumin appears to be significantly increased in PE. This suggests that measurement of this oxidative biomarker may be useful in monitoring pregnancies with respect to the development of pre-eclampsia.

Serum sodium level was observed to be reduced in preeclampsia as compared to normotensive pregnant. The identification and counseling of preeclampsia relies fundamentally on the frequency of antenatal care and if their blood pressure was measured during the visit. Many women with pre-eclampsia, particularly, at the community level are missed due to the lack of antenatal care.

Intervention education and communication (IEC) activities and awareness campaigns should be conducted at community levels so that more number of pregnant women should visit ANC clinics and identified for PIH (pregnancy induced hypertension) and preeclampsia at the earliest.

REFERENCES

1. Datta DC. Hypertensive disorders in pregnancy. In:Konor H.(edit). DC Datta's Textbook of obstetrics. 7th ed. Kolkata: New central book agency (P) Ltd.2011; 219-227.
2. Maternal physiology. In: Cunningham F, Lenovo K, Bloom S, Hauth J, Rouse D,

- Spong C (edts). William obstetrics, 23rd ed. USA : The Mc Graw. Hill companies. 2010; 107-131.
3. Preventive medicine in obstetrics, paediatrics and geriatrics. In: Park K (edt). Park's textbook of preventive and social medicine. 21st ed. Jabalpur: M/S Banarasidas, Bhanot publishers. 2011; 514-517.
 4. Saleh R, Dkhil M. Structural changes of placenta in Pre-eclamptic patients: light and electron microscopic study. Turk J Med Sci 2008; 38(3): 232-239.
 5. Solomon C, Seely E. Hypertension in Pregnancy – A manifestation of the insulin resistance syndrome? Hypertension. 2000; 37: 232-239.
 6. Davey DA, MacGillivray I. The classification & definition of the hypertensive disorders of pregnancy. Am J Obstet Gynecol. 1988;158(4):892-98.
 7. Clark, S. L., Cotton, D. B., Hankins, G., & Phelan, J. P. (Eds.). (1997). Critical care obstetrics (3rd ed.). Oklahoma, OK: Black Well Science Limited.95.
 8. 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.
 9. 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.
 10. Dhokikar GD, Birla VH, Ingale PW, Bende SP, Kadam PS. Study of serum electrolytes in preeclampsia. International Journal of Anatomy Physiology and Biochemistry. 2015; 2(1):16-20.
 11. Indumati, V., Kodliwadmth, M. V., & Sheela, M. K. Role of serum electrolytes in pregnancy induced hypertension. JCDR. 2011. 5, 66–69.
 12. Hajera Tabassum, Noura Al-Jameil1, Mir Naiman Ali, Farah Aziz Khan, May Al-Rashed. Status of serum electrolytes in preeclamptic pregnant women of Riyadh, Saudi Arabia. *Biomedical Research* 2015; 26 (2): 219-224
 13. Ebenezer Owusu Darkwa, Robert Djagbletey, Charles Antwi-Boasiako, George Aryee1, Daniel Sottie, Alexander Akowuah. Serum sodium and potassium levels in preeclampsia: A case-control study in a large tertiary hospital in Ghana Owusu Darkwa et al., *Cogent Medicine* (2017), 4: 1376898
- How to cite this article: Roy N, Bachu L. Study of serum IMA and electrolytes in patients of pre-eclampsia in central India. Galore International Journal of Health Sciences & Research. 2019; 4(4): 55-60.
