ORIGINAL ARTICLE

Comparative Evaluation of Serum Magnesium Level in Pre-eclamptic and Non Pre-eclamptic Women in a tertiary Hospital in Southern Nigeria

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Received: July 25th, 2018
Accepted: September 26th, 2018

DISLOSURE
There was no conflict of interest declared and the study was self sponsored

ABSTRACT

Background: Magnesium is a micronutrient found in the human body whose major function is to maintain nerve and muscle function. Magnesium sulphate has been used over time as a prophylactic drug in pre-eclamptic women. There is paucity of studies on the role of serum magnesium level in preeclampsia in South-South Nigeria.

Objective: The main objective of this study was to determine the serum levels of magnesium in cohorts of pre-eclamptic and non pre-eclamptic patients in a tertiary hospital in South-South Nigeria.

Methodology: This was a comparative study in which 104 women who satisfied the eligibility criteria were enrolled for the study (52 pre-eclamptic and 52 non- pre-eclamptic women). Data analysis was done using statistical software (IBM SPSS® for windows version 21.0.) Data was analyzed for mean and standard deviation. Comparison of serum levels of magnesium between the two groups was performed by student t-test and *P* value < 0.05 was considered as statistically significant.

Results: The study showed that the serum magnesium level was not statistically different between the pre-eclamptic and non-pre-eclamptic women (1.79±0.24mg/dl vs. 1.88±0.37mg/dl respectively, $p = 0.10$). There was no correlation between serum magnesium level and the systolic and diastolic blood pressures in either group.

Conclusion: This study showed that women with preeclampsia did not demonstrate reduced serum magnesium level. This support the hypothesis that hypomagnesaemia is not a possible aetiology of preeclampsia.

Key words: *Pregnancy, Micronutrients, Hypertension, Primigravida.*

INTRODUCTION

The relationship between preeclampsia and nutritional deficiencies has been well researched and documented.[1,2] However, there are conflicting results depending on the location, nutritional status of the patients and sample size. The results of clinical trials showed the aggravation of hypertensive complications and the change in concentration of various trace elements.[1,2,3] One of such elements is magnesium which is a micronutrient found naturally in the human body.[4] Magnesium is needed for more than 300 biochemical reactions in the body. It helps to maintain nerve and muscle function, it has a relaxant effect on blood vessel of pregnant women, it helps to regulate blood glucose levels and aids in the production of energy and proteins.[4,5]

Changes in the serum levels of this element can lead to changes in blood pressure leading to preeclampsia. It has however been speculated that low serum magnesium level i.e. <1.46mg/dl (0.6mmol/L) may lead to preeclampsia and its complications. The efficacy of magnesium sulphate during preeclampsia as prophylaxis for eclampsia may be attributed to corrections of this deficiency.[4,5]

The risk factor for preeclampsia includes family history, primigravidity, diabetes, renal diseases, black race, and hypertension prior to pregnancy.[6] Others include oocyte donation or insemination, stress, hydatidiform mole, new partner and the use of barrier contraception.[6,7,8]

The prevention of preeclampsia is difficult, because the aetiology of the diseases is not fully known.[1,2] However, it is known that endothelial dysfunctions and oxidative stress play key role. There is interest in supplementation with low dose aspirin, calcium and anti-oxidants like vitamins C and E. Some trials of the use of calcium and antioxidant vitamins in high doses have reported improvements in biochemical markers of endothelial activation in addition to a reduction in preeclampsia.[6,7,8,9]

Preeclampsia is a progressive disorder and when not promptly and properly managed may lead to complications which may affect all the systems of the body. The complications include eclampsia, cerebral heamorrhage, cerebral oedema and cortical blindness. Others include pulmonary oedema, disseminated intravascular coagulopathy, haemolysis, elevated liver, low platelets count (HELLP) syndrome and abruption placenta.[10,11] Fetal complications are also common and include prematurity, preterm birth and intrauterine fetal death.[6,7,8]

This study was aimed at determining if there is any significant difference in serum magnesium levels between pre-eclamptic and non pre-eclamptic women, and also to contribute to the understanding of the role of magnesium in preeclampsia.

METHODOLOGY

Study Area

This study was carried out in the University of Port Harcourt Teaching Hospital. It is a 650-bed hospital located at Alakhahia in Obio-Akpor local government area of Rivers state, South-South Nigeria. It is a tertiary health center that provides all levels of health care services to Rivers, Bayelsa, Delta, Imo,

Abia and Akwa Ibom states. The Obstetrics and Gynaecology department is a key department in the hospital with 18 Consultants staff. On average, between 400 and 450 pregnant women are booked for antenatal care services in the hospital every

week. Primigravidae constitute about 41% of total attendance. Follow up attendance rate is between 250 and 300 patients per week. The annual delivery rate in the hospital is about 3500 which gives an average of 290 deliveries monthly. The hospital has a chemical pathology department staffed by consultants, resident doctors, laboratory scientists and interns. Over 40 different tests are conducted in the chemistry laboratory including serum magnesium quantization.

Study Design

Ethical approval for this study was obtained from the Ethics Committee of the hospital.

This was a comparative case control study, designed to evaluate the levels of magnesium in pregnant women with and without preeclampsia. This study was performed between 1st of July 2015 to 22nd of February 2016.

The control and study group were chosen from women attending ante natal care in the Hospital. The control group was chosen from women who fulfilled the inclusion criteria and were followed up from booking till delivery but did not develop preeclampsia in the third trimester. The study group was those that were followed up from booking, developed preeclampsia in the third trimester and fulfilled other selection criteria, were enrolled in the study.

A proforma developed for the study was used to record the socio-demographic characteristics, clinical and laboratory data of the patients. The content of the questionnaire include age, marital status, occupation, educational status, religion, parity, booking status, last menstrual period, gestational age, past history of diabetes or hypertension, family history of diabetes or hypertension, presence or absence of pedal oedema, serum magnesium level, onset of delivery, mode of delivery, birth weight, APGAR score and admission into special care baby units.

Inclusion Criteria

All those who developed preeclampsia based on: Blood pressure equal to or greater than 140/90 mm Hg on two occasions 6 hours apart and proteinuria greater than 300mg in 24 hours urine sample or one plus (+) of protein in 2 mid-stream urine sample collected 6 hours apart in the 3rd trimester. Also included in the study were pregnant women with singleton fetus, third trimester gestational age, primigravida, no history or evidence of urinary tract infection, age range 18 to 35 years and non diabetics

Exclusion Criteria

Excluded were those with multiple pregnancies, diabetics, pregnancy with renal disease, gestational trophoblastic diseases, chronic hypertension, pregnancy with heart disease, patients already on magnesium sulphate and maternal age greater than 35 years

Sample Size Determination

The sample size was calculated using the formula for comparison of two means.

$$N = \frac{(U+V)^2 \ (SD_1^2 + SD_2^2)}{U_1 + U_2}$$

Where

N= minimum required sample size

U= one sided percentage point of the normal distribution corresponding to 100% the power. Thus when power is 90% then U= 1.28

V= percentage point of the normal distribution corresponding to the two sided significance level. Thus at 5% significance level V= 1.96

SD_1= standard deviation in study group= 0.37

SD_2= standard deviation in control group= 0.69

U_1= mean of observation in study group=1.92

U_2= mean of observation in control group=2.29

$$N= \frac{(1.28+1.96)^2 (0.37^2 + 0.69^2)}{(1.92-2.29)^2}$$

N= 47.

Therefore a minimum sample size of 47 patients is required for each group. Adjusting for a drop out of 10% this study will require a total of 104 patients (52 patients in each group).

Data Collection and Processing

The participants in this study were followed up from booking in the second trimester (the minimum gestational age at booking was 16 weeks). And a written informed consent was obtained from each participant before recruitment into the study. A detailed history was taken to ensure each patient fulfilled the selection criteria. Data regarding socio-demographic characteristics, clinical, family history and laboratory results were recorded in the proforma. A thorough clinical examination was done for each patient. The height and weight of each participant was measured (using a weighing scale ZT-120, METLAR) and the body mass index calculated by dividing the weight in kilogram by the square of the height in meter.

Those in the control group were all normotensive from booking and did not develop preeclampsia. While those in the study group were followed up from booking and on development of preeclampsia in the third trimester for the first time and fulfillment of the selection criteria, were recruited for the study. Patients in both groups were followed up till delivery.

Blood pressure was measured with the use of manual sphygmomanometer while the patient was in supine position on a couch with a left sided tilt. An appropriate sized cuff that covers at least 2/3rd of the upper arm was used. The systolic blood pressure was taken at the first point the sound was heard while, the diastolic blood pressure was taken as Korotkoff 5(the absence of sound). A patient was said to be hypertensive when her blood pressure was equal to or greater than 140/90 mmHg measured at least 6 hours apart.

Urine collection was done in the ante natal clinic between 8 to 9 am. Urine samples were collected under the supervision of trained nurses. Patients were given clean, dry, wide-mouthed, leak-proof containers with their names and numbers. Each patient cleaned her vulva with copious clean water and parts her labia. The first stream of urine was discarded and the next stream collected into the container.

Samples were analyzed for protein estimation using dip stick. Protein estimation was made based on the colour change of the dip stick compared to the corresponding colour chart on the reagent container. The diagnosis of proteinuria was made when two samples of mid-stream urine collected at least four hours apart showed one or more plus (+) of albumin. Urine microscopy culture and sensitivity test was routinely done in suspicious cases to exclude infection. Therefore, a patient was said to be pre-eclamptic when her blood pressure was equal to or greater than

140/90mmHg measured at least six hours apart accompanied by proteinuria of at least one plus.

Blood samples (5ml) was taken from the ante cubital vein and sent to the laboratory for magnesium estimation. Blood samples were taken from women in the control group at the time of presentation in the labour ward after an informed consent was obtained, while for patients with preeclampsia blood samples was collected at the time the diagnosis was first made and before the administration of magnesium sulphate. Then they were followed up till delivery.

At the laboratory, the samples were centrifuged to get the serum which was stored in the refrigerator until the time of analysis.

Serum magnesium level Analysis was done by the direct calmagite method. Magnesium was analyzed using the kit manufactured by Teco Diagnostics, California, USA.

At birth data were collected regarding onset of labour, mode of delivery, birth weights, APGAR score and information on whether the baby was admitted into the special care baby unit or not were entered into the proforma as well as the development of any complication.

Statistical Analysis

The statistical analysis was done using statistical software (IBM-SPSS for window, version 21.0). Data was analyzed for mean and standard deviation. Comparison of serum levels of magnesium between the two groups was performed by student t-test and p value < 0.05 at 95% was considered statistically significant. Pearson correlation was used to measure the degree of association between variables.

RESULTS

A total of one hundred and four booked women were enrolled in the study. The socio-demographic characteristic of the patients were shown in tables 1. In the case group 32.7% had spontaneous vaginal delivery while in the control group 73.1% had spontaneous vaginal delivery. In the pre-eclamptic group 30.8% of babies were admitted into the special care baby unit and 7.7% were admitted into the special care baby unit in the non pre-eclamptic group.

In table 2, the mean serum magnesium level was 1.79±0.24mg/dl for pre-eclamptic patients. In the non pre-eclamptic group the mean serum magnesium level was 1.88±0.37mg/dl. There was no significant difference in mean serum magnesium level between the two groups (p value = 0.10).

The mean body mass index range of the cases group was 28.09±3.50 Kg/m^2. The mean body mass index of the control group was 26.42±2.42Kg/m^2. There was a statistical difference in body mass index between the two groups (p value = 0.01).

The mean systolic blood pressure of the pre-eclamptic group was 158.88±11.80 mmHg. The mean systolic pressure of the control group was 113.65±7.15 mmHg. There was a statistical difference in systolic blood pressure between the two groups. The p value was 0.01.The mean diastolic blood pressure for the pre-eclamptic group was 101±8.20mmHg. The mean diastolic blood pressure of the control group was 71.35±6.57mmHg. There was a statistical difference in diastolic blood pressure between the two groups. The p value = 0.01.

There was no correlation between the systolic blood pressure and serum magnesium level. Pearson correlation = -0.105, p value was 0.300. There was no

correlation between diastolic blood pressure and serum magnesium level. Pearson correlation = - 0.170, *p* value = 0.09.

Table 1. Social and demographic characteristic of the cases and control

	Cases	Percentage (%)	Control	Percentage (%)
Age				
15-19	10	19.2	4	7.7
20-24	12	23.1	14	26.9
25-29	11	21.2	18	34.6
30-35	19	36.5	16	30.8
Educational status				
Primary	14	27.0	6	11.5
Secondary	23	44.0	26	46.2
Tertiary	15	29.0	22	42.3
No formal education	0	0.0	0	0.0
Marital status				
Single	6	11.0	4	8.0
Married	45	87.0	47	88.0
Divorced	1	2.0	2	4.0
Religion				
Christianity	4 9	92.4	47	90.4
Muslims	3	5.8	5	9.6
Others	0	0.0	0	0.0
Onset of labour				
Induced	15	28.8	8	15.4
Spontaneous	17	32.7	38	73.1
No labour	20	38.5	6	11.5
Mode of delivery				
Vaginal	23	44.2	46	80.5
Caesarean section	29	55.8	6	11.5
Forceps/vacuum	0	0.0	0	0.0
Admission into special care baby unit	16	30.6	4	7.7

Table 2. The characteristics of the study population

Parameter	Cases mean± SD	Control mean± SD	*P* value	Significance
Ages (yrs)	27.58±7.34	26.71±4.21	0.45	Not significant
Gestational age	36.54±2.69	38.67±1.10	0.01	Significant
Body mass index	28.09±3.50	26.42±2.42	0.01	Significant
Blood pressures				
Systolic blood pressure	158.88±11.80	101 ±8.20	0.01	Significant
Diastolic blood pressure	113.65 ±7.15	71.35±6.57	0.01	Significant
Serum magnesium level (mg/dl)	1.79±0.24	1.88±0.37	0.10	Not significant
Birth weight (kg)	2.71±0.70	3.10±0.43	0.01	Significant

DISCUSSION

Decrease in serum magnesium level has been considered as the cause of preeclampsia. The success of magnesium therapy as a treatment for eclamptic seizure and the known effect of magnesium on vascular smooth response in-vitro suggested that magnesium might be deficient in women with preeclampsia.[12]

An important finding in this study is that there was no difference in the mean serum magnesium level for the pre-eclamptic (1.79±0.24mg/dl) and the non pre-eclamptic (1.88±0.37mg/dl). Several other studies have similar outcome.[13,14] However Kanagal *et al.* found a marginal difference in serum magnesium level between pre-eclamptic and non eclamptic women in India where most of the patients used for the study were from the lower class strata with poor dietary consumption of magnesium rich food.[12] The difference in value of magnesium obtained in various studies may be due to variation in the study population and dietary intake.

Our study did not show any statistical significance in age between the two groups. This finding was similar to report from Ugwuja *et al*. in Abakaliki South-East Nigeria.[15] However, Kanagal *et al. found a* significant difference in age between pre-eclamptic and non-pre-eclamptic patients[12]. This may be attributed to the inclusion of both multiparas and grand multiparas in the study.

The study revealed an association between the development of preeclampsia and body mass index. Akinloye *et al.* also found a higher body mass index in the preeclamptic.[10] However, the result of this study was not in keeping with the work done by Onyegbule *et al*. in Nnewi South-East Nigeria.[11]

Limitations of the Study

This study has several limitations. Firstly, the dietary intake of pre-eclamptic women was not taken prior to the commencement of the study to ascertain their magnesium level. Second limitation was the non-use of quantitative method in detecting proteinuria. The direct (Calmagite) method which is easier and cheaper was used in this study instead of the ion-selective electrode which is better but expensive in the analysis of serum magnesium levels.

CONCLUSION

The study revealed that in pre-eclamptic women serum magnesium level is not significantly reduced. This study did not support the hypothesis that hypomagnesaemia is a possible cause of preeclampsia. There was no change in serum magnesium level with increase or decrease in systolic or diastolic blood pressure.

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