Comparative Study of the Serum Magnesium levels and the Foeto-Maternal Outcomes In Pre-Eclamptic and Normotensive Pregnant Women In South Eastern Region of Nigeria

Wokoh D. N[1], Adizua U. C[2], Nduka E. C[1], Okali U. K[1]

[1]Department of Obstetrics and Gynaecology, Federal Medical Centre, Umuahia, Abia State. Nigeria
[2]Department of Chemical pathology, Federal Medical Centre, Umuahia, Abia State. Nigeria.

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Abstract

Pre-eclampsia is a multi-organ disorder of pregnancy characterized by elevated blood pressure and proteinuria. It complicates 2 - 8% of pregnancies, and results in significant foetal and maternal morbidity and mortality worldwide. Inspite of various theories of the aetiology, the exact cause has not been identified. Its association with low serum magnesium levels has been postulated. This study aimed to compare the serum magnesium levels in healthy pregnant women and pre-eclamptic women as well as to determine their foetomaternal outcomes. This hospital based comparative study recruited 42 pregnant women (21 in the healthy group and 21 in the pre-eclamptic group) at the Federal Medical Centre, Umuahia, who satisfied the inclusion criteria. Blood samples were collected and analyzed for quantitative serum magnesium, and urine samples for urinalysis. Ultrasonography ruled out multiple gestation and molar pregnancy. No significant difference was found between serum magnesium levels in pre-eclamptic and the normotensive pregnant women (P=0.570). Prematurity, birth asphyxia, Neonatal Intensive Care Unit admissions, perinatal deaths and Caesarean delivery were higher among pre-eclamptic subjects. There was no significant difference in the serum magnesium levels of pre-eclamptic and healthy normotensive pregnant women.

Keywords: *pre-eclampsia, serum magnesium, pregnant women, proteinuria, birth asphyxia, normotensive.*

1. Introduction

Pre-eclampsia is a form of hypertensive disorder of pregnancy [1]. It is a multisystem, idiopathic disorder of pregnancy and puerperium, characterized by hypertension and proteinuria [1,2]. It complicates about 2 - 8% of all pregnancies [3,4]. Pre-eclampsia is defined as hypertension (elevated blood pressure) occurring after 20 weeks of gestation in a woman with previously normal blood pressure; systolic blood pressure of 140mmHg or higher, diastolic blood pressure of 90mmHg or higher measured on two occasions at least 6 hours apart, with proteinuria, defined as urinary excretion of 0.3g or more protein in a 24-hour urine specimen and this correlates with a finding of +1or greater (if specific gravity is less than 1.030) on a dipstick, or 2+ (1g protein/L) on two random clean-catch or catheter urine specimen[5,6].

Pre-eclampsia can be mild or severe [7]. Mild when the blood pressure is 140/90mmHg or higher but less than 160/110mmHg with proteinuria of 300mg/24 hours or greater but less than 5g/24 hours, and severe when the blood pressure is 160/110mmHg or higher with proteinuria of 5g or higher in a 24 hour urine specimen or 3+ or more on two random urine samples collected at least 4 hours apart [6,7,8]. When convulsions occur in the presence of pre-eclampsia in a patient with no known seizure disorder, the term eclampsia is ascribed [1].
Major maternal complications of pre-eclampsia include placental abruption, HELLP syndrome (hemolysis, elevated liver enzymes, low platelets) and eclampsia [9].

Pre-eclampsia is associated with sig-

*Corresponding author email: davidbuisi@gmail.com

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nificant maternal and perinatal morbidity and mortality in both developed and developing world [10,11,12,13]. However, its impact is felt more in developing countries where it remains one of the most common causes of maternal mortality [6,14]. Pre-eclampsia/eclampsia contributes about 31.5% of maternal deaths in some part of Nigeria [15]. Thus prevention of this disorder will significantly lower maternal and perinatal morbidity and mortality.

Certain measures have been employed in attempt to prevent the disease. These include the use of low dose aspirin, fish oil (marine n-3 fatty acids) and calcium supplementation, with little or no recorded success in those women who are at above-average risk for development of hypertensive disorders of pregnancy [16,17,18]and in those with low dietary calcium intake[18]. Identification of the biochemical or biophysical markers of the disease and a reliable screening tests for the disease at earlier gestational age will help identify those women at risk of developing pre-eclampsia later. These women at risk may then benefit from interventional measures, should any therapeutic intervention prove successful. However, there is currently no such screening test for accurate prediction of pre-eclampsia [19,20]. Some biochemical markers of pre-eclampsia in maternal serum have been identified and certain biochemical tests have been proposed for more accurate identification of those patients at increased risk of developing the disease [20,21]. These include magnesium, albumin, lipids, creatinine, uric acid, vascular endothelial growth factor (VEGF), placental growth factor (PGF) among others [3,21].

Studies have reported reduced serum levels of magnesium in pregnancy [4,22,23]. A study in Lagos, Nigeria found the average serum magnesium level of 1.03mg/dl (0.87mEq/L) in the 8th month of pregnancy, and a non-pregnant average of 1.47mg/dl (1.24mEq/L) [23] Enaruna et al. working in South-south Nigeria found the mean serum magnesium levels of 2.46+/-0.43mEq/L and 1.70 mEq/L for the non - pregnant and pregnant population respectively, with values decreasing as pregnancy advanced [23]. Another study in Ekiti, South-western Nigeria found a mean serum magnesium level of 0.73 (+/-0.14) mmol/L in the healthy pregnant women and 0.53 (+/ -0.17)mmol/L among pre-eclamptic group [4]. A study in Abakaliki, South-east Nigeria recorded mean levels of 4.2 ± 0.78 µg/dl for healthy pregnant normotensive women, and 3.2 ±1.10 µg/dl in those with pre-eclampsia [24]. Magnesium deficiency or low serum levels has been suggested as possible cause of pre-eclampsia [4,23]. Interventional therapeutic measures such as nutritional counselling, administration of magnesium or magnesium-rich diets to those women with deficient or low serum magnesium levels could be of immense benefit [4,25] should magnesium deficiency be found a risk factor for development of pre-eclampsia. This could be in form of dietary magnesium supplementation, especially in early pregnancy [23,26].

Most of the studies comparing serum magnesium levels in normal and pre-eclamptic women were done in the developed countries while there is paucity of such in developing countries like ours where most of the morbidities and mortalities from the disorder occur [27,28]. Such studies had not been conducted at the Federal Medical Centre, Umuahia. This made it necessary to undertake such a research that compared the serum magnesium levels of normal pregnant women with those who developed pre-eclampsia during the course of their pregnancy.
The aim of this study was to determine and compare the serum magnesium levels in healthy normotensive pregnant women and those with pre-eclampsia attending the Federal Medical Centre, Umuahia as well as their foetomaternal outcomes.

2. Materials and Methods

2.1 Study Design

The study was a hospital-based comparative study that compared the serum magnesium levels in healthy normotensive pregnant women and pre-eclamptic women receiving obstetric care at the Federal Medical Centre (FMC), Umuahia as well as their foetomaternal outcomes.

2.2 Study population

The subjects for the study were drawn from the population of healthy pregnant women and pre-eclamptic women managed at the Federal Medical centre, Umuahia who satisfied the inclusion criteria.

2.2.1 Inclusion criteria

1. Booked pregnant women with pre-eclampsia.
2. Unbooked pregnant women with pre-eclampsia.
3. Those whose gestational ages were greater than 20 weeks, and up to 41 weeks attending antenatal care clinic, booking clinic, labour room and emer gency room diagnosed of pre-eclampsia.
4. Controls were booked and unbooked normoten sive non-proteinuric pregnant women at gestational ages greater than 20, up to 41weeks.
5. Those who gave consent to be included in the study.

2.2.2 Exclusion criteria

1. Pregnant women with medical illnesses such as essential hypertension, renal disease, diabetes melli tus, sickle cell disease and cardiac disease
2. Patients who had medical complication with su perimposed pre-eclampsia
3. Patients with pre-eclampsia on treatment with magnesium sulphate
4. Patients with molar pregnancy
5. Subjects with multiple gestation
6. Patients on medication containing magnesium for treatment or supplementation
7. Those who refused to give consent

2.3 Ethical consideration.

Ethical clearance for this study was sought and obtained from the Health Research and Ethics Committee of the Federal Medical Centre, Umuahia.

2.4 Analysis of Data

All results were recorded in a proforma. Data generated from the study were analyzed using statistical package for social science (SPSS) version 17. Descriptive statistics such as frequency and percentages were used to summarize categorical variables, while means and standard deviations were obtained for continuous variables. Association between categorical variables were done using chi square, while means of continuous variables were compared using student's t-test and ANOVA. The significant value was set at $p<0.05$. Results were presented in tables.

3. Results and Discussion

3.1 Results

The mean serum magnesium level in healthy normotensive pregnant women was 1.41 ± 0.21mEq/L while that of their pre-eclamptic counterparts was 1.36 ± 0.36 mEq/L. However, the difference was not significant (t = 0.576, P = 0.570) as shown in Table 1.

Table 1: Mean comparison of serum magnesium (mEq/L) levels between the healthy normotensive and pre-eclamptic groups

	Pre-eclamptic Mean ± SD	***Normo-tensive Mean ± SD***	***T***	***P value***
Magnesium	1.36 ± 0.36	1.41 ± 0.21	0.573	0.570

Table 1 shows that the mean serum magnesium of healthy normotensives was 1.41±0.21mEq/L while that of the pre-eclamptic subjects was 1.36±0.36mEq/L. However this was not significantly different (t = 0.573, P = 0.570)

The age of the respondents ranged from 19 to 40 years with a mean age of 29.38 ±5.53 years for the healthy pregnant women and 29.71±6.05 years for the pre-eclamptic subjects (Tables 2 and 3).

Table 2 shows that the age of respondents ranged between 19 and 40 years. It also shows that similar number of subjects were either nulliparous or parous. Majority of them presented at term (83.3%).

The mean gestational age at delivery for the pre-eclamptic subjects (36.19±4.32 weeks) and that for the normotensive women (38.86±0.91 weeks). The difference was statistically significant (t= 2.768, P= 0.009; Table 3).

Table 2: Socio-demographic characteristics of respondents

	Frequency	*Percent*
Age group (years)		
19 – 25	13	31.0
26 – 32	14	33.3
33 – 40	15	35.7
Socio-economic class		
Lower	10	23.8
Middle	12	28.6
Upper	20	47.6
Parity		
0	18	42.9
1 – 3	17	40.5
≥4	7	16.7
Gestational Age (weeks)		
<28	1	2.4
28 – 33	2	4.8
34 – 36	4	9.5
37 – 41	35	83.3

Table 3: Mean age and gestational age of respondents

	Groups		*T*	*P value*
	Pre-eclamptic Mean ± SD	*Normotensive Mean ± SD*		
Age (years)	29.71 ± 6.05	29.38 ± 5.53	0.186	0.853
Gestational Age (weeks)	36.19 ± 4.32	38.86 ± 0.91	2.768	0.009

Table 3 shows that the mean age of the pre-eclamptic women was 29.71± 6.05 years whereas that of the normotensive pregnant women was 29.38±5.53 years. There was no significant difference between these mean ages, (t=0.186,P= 0.853). It also shows the mean gestational at delivery, of pre-eclampsia (36.19±4.32 weeks) is significantly lower (t=2.768, P=0.009) than that of normotensive women (38.86±0.91weeks).

More (28.6%) of the pregnant women who developed pre-eclampsia were in the lower socio-economic class when compared with their normotensive counterpart (19.0%). This difference was statistically significant (x^2=6.600, P=0.037; Table 4).

Inasmuch as majority (47.6%) of those who develop pre-eclampsia were nulliparous, 42.9% of them were parous (para 1-3). Among the normotensive women, equal number 8 (38.17%) were both nulliparous and parous. Parity did not appear to have contributed to development of pre-eclampsia (x^2=1.567, P=0.457; Table 4).

Table 4: Parity and socio-economic class

	Pre-eclamptic n (%)	*Normotensive n (%)*	x^2	*P value*
Parity				
0	10 (47.6)	8 (38.1)	1.567	0.457
1 – 3	9 (42.9)	8 (38.1)		
≥4	2 (9.5)	5 (23.8)		
Socio-economic class				
Lower	6 (28.6)	4 (19.0)	6.600	0.037
Middle	9 (42.9)	3 (14.3)		
Upper	6 (28.6)	14 (66.7)		

Table 4 shows that a greater proportion of the pre-eclamptic subjects were nulliparous (47.6%), and that 38.1 % of normotensive women were also nulliparous. This difference is not statistically significant, (x^2= 1.567, P=0.457). A statistically significant difference exists between the socio-economic status of the pre-eclamptic (28.6% in lower class) and the normotensive women, (x^2=6.600, P=0.037).

None of the normotensive women had preterm delivery while 33.3% of the pre-eclamptic women had preterm births (x^2= 8.400, P=0.0004;

Table 5: Maternal outcomes

	Pre-eclamptic n (%)	*Normotensive n (%)*	X^2	*P value*
Gestational Age				
Term	14 (66.7)	21 (100.0)	8.400	0.004
Preterm	7 (33.3)	0.(0.0		
Delivery				
SVD	9 (42.9)	21(100.0)	16.800	<0.001
C/S	12(57.1)	0.(0.0)		

tables 5 and 6). A 100% of the normotensive women had spontaneous vaginal delivery while a significant percentage (57.1%) of the pre-eclamptic women had Caesarean deliveries(x^2=16.800, P=<0.001; Table 5).

Table 5 shows that 100% of normotensive women had term deliveries whereas significant number 7 (33.3%) of the pre-eclamptic group had preterm deliveries (x^2=8.400, P=0.004). It also shows that all 21 (100%) of normotensive women had Spontaneous Vaginal Deliveries (SVD) whereas 57.1% of the pre-eclamptic women were delivered via Caesarean section (C/S) (x^2=16.800, P <0.001).

Moderate birth asphyxia was significantly more among babies of the pre-eclamptic women as against those of the normotensive mothers (x^2=10.615, P=0.005 and x^2=11.455, P=0.003 respectively; Table 6).

Table 6: Foetal outcomes

	Pre-eclamptic n (%)	***Normo-tensive n (%)***	***x^2***	***P value***
Premature				
Nil	14 (66.7)	21 (100.0)	8.400	0.004
Yes	7(33.3)	0 (0.0)		
Birth asphyxia(1st)				
Normal	3 (14.3)	18 (85.7)	10.615	0.005
Moderate	8 (38.1)	3 (14.3)		
Severe	10 (47.6)	0 (0.0)		
Birth asphyxia (5th)				
Normal	3 (14.3)	21(100.0)	11.455	0.003
Moderate	12 (57.1)	0 (00)		
Severe	6 (28.6)	0 (0.0)		
Admission (SCBU)				
Yes	8 (38.1)	0 (0.0)	9.882	0.002
No	13 (61.9)	21 (100.0)		
Perinatal death				
Yes	7 (33.3)	0 (0.0)	8.400	0.004
No	14 (66.7)	21 (100.0)		
Birth Weight(Kg)	2.94±1.72	3.28±1.81	2.02	0.105

Table [6] shows that 38.1 % and 57.1% of babies born to pre-eclamptic women were moderately asphyxiated in the 1st and 5th minute respectively and that 47.6% and 28.6% of the were severely asphyxiated within the 1st and 5th minute respectively whereas none of the babies delivered to the normotensive women were severely asphyxiated. These differences in the Apgar scores were significant (x^2=10.615, P=0.005 and x^2=11.455, P=0.003 respectively). A significant percentage (38.1%) of babies of the pre-eclamptic women required Special Care Baby Unit (SCBU) admission while none of those born to the normotensive women was admitted (x^2=9.882, P=0.002). More perinatal deaths were recorded among babies of pre-eclamptic mothers as against the normotensive mothers (33.3% versus 0.0%). This is statistically significant (p=0.004). There was no significant different between the mean birth weights of babies born to pre-eclamptic women compared to those of normotensive mothers (p=0.105)

More babies (38.1%) born to the pre-eclamptic women were admitted into the Special Care Baby Unit (SCBU) than those (0.0%) of the normotensive mothers (x^2=9.882, P=0.002; Table 6). A significant number 7(33.3%) of perinatal deaths occurred among babies of pre-eclamptic subjects whereas none (0.0%) was recorded among babies of normotensive women (x^2=8.400, P=0.004; Table 6).

3.2 Discussion

In this study, the age range of the respondents was 19 to 40 years. The mean age for the cases was 29.71±6.05 years which was not significantly different *(P= 0.853)* from the mean age for the normal pregnant women which was 29.38±5.53 years. This is similar to other studies [4,24].

There was no significant difference between serum magnesium levels in the pre-eclamptic women and that of their normotensive counterpart, *p= 0.570*. This finding was similar to the results from other studies, [13,29,30,31] but differs from many others [3,11,14,24] who observed significantly

reduced serum magnesium with pre-eclampsia and therefore proposed hypomagnesaemia as a possible cause or predictor of pre-eclampsia, and suggested magnesium supplementation in pregnancy [4,25].

Another study from South Africa reported a higher serum magnesium in pre-eclampsia than in the healthy normotensive pregnancies [10]. This was probably because some of the pre-eclamptic women were given magnesium sulphate seizure prophylaxis.

Preterm labour and prematurity were common complications of pre-eclampsia (33.3%) in this study. This finding was similar to that observed by Onyiriuka and Okolo in Benin City, Nigeria [8]. Another research in India also recorded a high incidence (46.6%) of prematurity, [28] which again, is in consonant with the finding of delivery at a significantly lower gestational age by Adeosun and coworkers in South-west Nigeria [32].

A significant number of pre-eclamptic women in the study had Caesarean delivery when compared with the normotensive subjects among which none had abdominal delivery. Similar findings were noted by other researchers [32,33]. The Caesarean sections are due to prematurity, foetal distress and the need to promptly deliver the placenta as this is the only known cure for the disease.

Moderate (38.1% and 57.1% in the 1st and 5th minute respectively) and severe (47.6% and 28.6% in the 1st and 5th minute respectively) birth asphyxia were recorded among babies born to the pre-eclamptic mothers in this study. Similar observation was made by Onyiriuka and Okolo in Benin City, Nigeria [8]. A study in Kano, northern Nigeria recorded 39.1% birth asphyxia among babies of pre-eclamptic women [34]. Unlike babies born to the normotensive women, 38.1% of babies of pre-eclamptic mothers were admitted into the Special Care Baby Units due to prematurity and birth asphyxia. Another study had recorded 26.6% of Neonatal Intensive Care Unit admissions [28]. Perinatal deaths recorded in this study was 33.3% among babies of pre-eclamptic mother while none was observed among the babies of their normotensive counterparts. The mean birth weight of babies of pre-eclamptic mothers was lower than that of those born to normotensive women; 2.94±1.72kg against 3.28± 1.81kg, although not statistically significant (*p=0.105*).

Nulliparity and low socio-economic status are widely considered risk factors for development of pre-eclampsia [2,5,6,28]. This study found that majority (47.6%) of those women who developed the disease were nulliparous and that 42.9% of them were of low parity as well. Only 9.5% were of parity ≥ 4. Among the healthy normotensive pregnant women, 38.1% of them were also nulliparous, showing no significant difference in parity among the two groups *(p=0.457).* An earlier study from South-west Nigeria however reported significantly lower parity among pre-eclamptic women compared to normotensive women [4].

Lower socio-economic status was found to be significantly associated with pre-eclampsia in this study. Women who developed pre-eclampsia were found to deliver at a significantly lower gestational age *(P=0.009)* than their normotensive counterparts, (36.19±4.32 weeks versus 38.86±0.91 weeks). This finding was consistent with the observation in similar studies [4,8]. This also supports the fact that pre-eclampsia is associated with preterm delivery [8,28].

4.0 Conclusion

This study showed that there is no significant difference between serum levels of magnesium in both normotensive and pre-eclamptic women. It is yet to be proven universally and with certainty that low serum magnesium levels (which is a common finding in pregnancy) plays a major role in the pathogenesis of pre-eclampsia considering the variegated nature of the results obtained by various researchers on this subject matter. However, what appears to be well documented is the association of pre-eclampsia with preterm delivery, birth asphyxia, increased operative delivery, increased neonatal intensive care unit admissions, increased perinatal and maternal morbidity.

4.1 Limitations of Study

This hospital- based study was conducted in a tertiary centre which is a referral hospital sub-serving the neighboring towns and states, and therefore may not be a true representative of the population of Umuahia, Abia state.

4.2 Recommendation

From the above study findings, a multi-centre study will further support or counter the findings.

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