SERUM MAGNESIUM LEVELS IN HEALTHY PREGNANT WOMEN IN A TEACHING HOSPITAL IN SOUTH-SOUTH NIGERIA

Enaruna NO, *Ande ABA, *Osemwenkha AP, **Idemudia JO, **Aikoriogie PI

[*]*Department of Obstetrics and Gynaecology, University of Benin Teaching Hospital, Benin City.*
[**]*Department of Chemical Pathology, University of Benin Teaching Hospital, Benin City*

ABSTRACT

Context: Magnesium plays a crucial role in metabolism especially with respect to carbohydrate, protein and energy syntheses. Its decline in pregnancy has been associated with conditions like preeclampsia and preterm delivery. We assess the prevalence of hypomagnesaemia in our locale and examine the associated maternal characteristics.

Objectives: The primary objective was to determine the level of serum magnesium at which hypomagnesaemia could be diagnosed, while secondary objective was to define maternal characteristics associated with hypomagnesaemia.

Study Design, Setting and Subjects: A pilot study was done to document the mean serum magnesium level for the population of female patients attending UBTH. The main study was a cross-sectional study of healthy antenatal women recruited between 24 and 26 weeks of pregnancy. Serum magnesium estimates were done with samples collected at recruitment. The magnesium levels determined were used to divide the subjects into two groups of hypomagnesaemic and normomagnesaemic patients. Their sociodemographic characteristics were used to generate a database for analysis.

Results: Serum magnesium levels were higher in the non-pregnant subjects than the pregnant women in the pilot study. The prevalence of magnesium deficiency in the main study was 16.25%. Hypomagnesaemia was more likely in teenagers (P=0.00), women of higher parities (P=0.02) and lower social class (P=0.00).

Conclusion: Hypomagnesaemia in pregnancy is common in teenagers, women of high parity and low social class. Magnesium supplementation or consumption of magnesium-rich food is recommended for these groups of women, while discouraging too early, frequent or many deliveries.

Keywords: serum magnesium, pregnant women, south-south Nigeria.

INTRODUCTION

Magnesium is a vital co-enzyme for many biochemical processes; yet its deficiency is not readily detectable since less than 1% of the total body magnesium is found in the plasma and red blood cells[1,2]. Moreover, ionized magnesium assays are non-routine and are expensive[3]. Studies from different regions report a decline in magnesium levels during pregnancy[4,5], with values reaching their lowest point at the end of the first trimester[5]. Olatubosun et al[4] in Lagos, Nigeria found an average serum magnesium level of 1.03mg/dl (0.87mEq/L) in

Correspondence: Dr Nosakhare O Enaruna, Department of Obstetrics and Gynaecology, University of Benin Teaching Hospital, Benin City. E-mail: osaseruns@yahoo.com

the 8th month of pregnancy, dropping from a non-pregnant average of 1.47mg/dl (1.24mEq/L).

The rates of magnesium deficiency in pregnancy have been reported in some developing countries to be 25.6%[6], 43.6%[7] and 48%[8]. Gestational magnesium deficiency is believed to induce maternal, foetal, neonatal and paediatric consequences which may last throughout life. There is convincing evidence from animal studies that hypomagnesaemia has marked effects on the processes of parturition, postpartum uterine involution and on foetal growth and development[9]. Many researchers have thus associated magnesium lack with preterm labour and an increased incidence of leg cramps and constipation during pregnancy[10-13]. Magnesium deficiency has also been associated with the development of preeclampsia and foetal growth restriction[1], as well as the sudden infant death syndrome[10].

Several years ago in the United States, Johnson and Phillips[14] documented that lower magnesium intakes correlated with lower birth weights. Other studies have shown that lower income women who were noted to have lower magnesium intake had better magnesium balances following supplementation[11,13,15-17]. Magnesium nutritional status can therefore be influenced by increasing magnesium intake. Magnesium intake plays a crucial role in magnesium status, hence the link between magnesium deficiency and poor socioeconomic status.

Recently, Ramakrishnan et al[18] in a review article of micronutrients and pregnancy outcome concluded that the evidence for magnesium improving outcome was strong, especially in high risk groups. However, most of the studies included in their review were from developed countries. Considering the level of poverty and other social deprivation in our environment, it is important to examine the situation in our pregnant women. This study aims at determining the frequency of magnesium deficiency in pregnancy and the associated maternal characteristics at the University of Benin Teaching Hospital (UBTH), Benin City. The findings we hope will set the stage for a new vista of prospective and interventional research to improve maternal and perinatal outcome.

Subjects, Materials and Methods

This was a cross-sectional study conducted at the Obstetrics and Gynaecology Unit of UBTH, Benin City in July 2011 with the approval of the Institutional Ethics Committee. The study population was healthy pregnant women with uncomplicated pregnancies attending antenatal care clinic during the study period. Those with peptic ulcer disease placed regularly on magnesium-containing antacids, multiple pregnancy, pre-gestational diabetes, chronic hypertension, chronic renal disease, sickle cell anaemia, intrauterine growth restriction, retroviral infection or acquired immune-deficiency syndrome (AIDS) were excluded.

The sample size was calculated[17] based on a previous study which reported 43.6% hypomagnesaemia in rural pregnant Indian population[7]. We aimed at detecting a 50% decrease in pregnant Nigerian women in the current study who were largely urban dwellers. Accepting a statistical power of 80%, confidence interval of 90%, with the level of significance set at 0.05, and up to 10% of the participants expected to drop out, a sample size of 160 patients was obtained. All patients who met the inclusion criteria were recruited after obtaining an informed written consent.

Recruitment of the patients was carried out between 24 and 26 weeks gestation. This period was chosen because many existing data were in agreement that serum magnesium levels in pregnancy decreased before the third trimester[4,5], while others suggest a fall in the third trimester[4]. Hence the effects due to changes in serum magnesium levels in pregnancy may be most marked in the later part of pregnancy.

An initial pilot study involving both pregnant and non-pregnant women attending outpatient clinic in UBTH we conducted found the mean serum magnesium level to be 2.01±0.49mEq/L. Thus in this study hypomagnesaemia was defined as serum magnesium level lower than mean minus 2 SD, that is, 1.03mEq/L. The subjects were divided into two groups of hypomagnesaemia or normomagnesaemia depending on the determination of their serum magnesium levels.

Five milliliters of venous blood was taken from each patient at recruitment. The blood was collected in a 20ml plain plastic container and immediately transferred to the clinical chemistry laboratory where serum was separated by centrifugation at 2000rpm following clot retraction. The separated serum was then analyzed for magnesium or frozen at -80^{0}C if analysis was not immediately possible. Analysis was done by a direct method (Calmagite method) in the clinical chemistry laboratory using the kit manufactured by TECO DIAGNOSTICS, CALIFORNIA, USA, which defines adult reference range as 1.3 - 2.5 mEq/L[19].

Primary outcome measure was the prevalence of hypomagnesaemia in pregnancy. The hypomagnesaemic and normomagnesaemic groups were also compared for maternal socio-demographic characteristics. For all participants, sociodemographic data including age, parity, occupation and level of education of the patient and her spouse, estimated gestational age, as well as relevant clinical parameters were entered into a data extraction sheet and used to generate a database. The social classes of the women were determined using the Olusanya *et al*[20] classification, making use of the educational status of the woman and her husband's occupation.

All data were entered into a proforma and analysis was done with a personal computer using the SPSS for Windows version 15.0. Categorical variables were expressed as absolute numbers and percentages and significant differences were determined using the Chi square test or Fisher exact test where appropriate, while continuous variables were presented as means with standard deviations and significant differences were determined with the Student *t* test. The level of significance was set as $p<0.05$.

RESULTS

There were 120 subjects in the pilot group, made up of 60 pregnant women with 20 from each of 1st, 2nd, and 3rd trimesters, and 60 non-pregnant women. The mean age, parity and body mass index of the pregnant and non-pregnant subjects were not significantly different. The mean serum magnesium for the pilot group was 2.01±0.49mEq/L; SE 0.039, 95% CI 1.93--2.09 (Table 1; Figure 1). The mean serum magnesium for the non-pregnant population in the pilot study was higher than that of the pregnant women and the levels decreased as pregnancy advanced (Table 1).

The mean serum magnesium level in the main study was 1.54±0.46mEq/L, and the prevalence of hypomagnesaemia in the group was 16.25%.

The age of the subjects ranged from 19 years to 36 years with a mean age of 30.14±3.76 years. The teenage mothers were 5 times more likely to have hypomagnesaemia than women 20 years or older (100% versus 20.75%, P=0.00; Table 2). Most (67.5%) of the patients had a parity of between 1 and 4 while the nulliparas made up the remaining 32.5%. The risk of having hypomagnesaemia in this study was 30% higher in women of parity 4 than the nulliparas (36.4% versus 6.9%, P=0.03; Table 2). Social Class 1 contributed 48.8% of the patients, Social Class 2 and 3 combined made up 46.2% while only 5% of the women were in Social Class 4. Even so, Social Class 4 was almost 5 times more likely to be associated with hypomagnesaemia than Social Class 1(100% versus 23%, P=0.0001; Table 2). Obesity in the group was observed in 21.3% of the subjects and its presence was 100% protective against hypomagnesaemia (P=0.00). Normal weight and overweight had similar risks of association with hypomagnesaemia (21.7% versus 20% respectively; Table 2).

DISCUSSION

Our pilot study revealed that serum magnesium level was significantly lower in the pregnant population than the non-pregnant women. Serum magnesium in pregnancy reduced as pregnancy advanced. The fall in serum magnesium value was most marked between the first and second trimesters. The main study revealed that 16.25% of our pregnant women had deficiency of magnesium at recruitment. Young age, previous delivery and low social class were associated with magnesium deficiency.

The preliminary pilot study served as a basis for the validity of our results despite the cross-sectional design which lacked temporality. The sample size of 160 pregnant women was adequate, though it was smaller than some previous study population[4,6,7]. This was a tertiary hospital-based study in an urban setting; even then, its results may be representative of the general patient population because of the referral status of the hospital**.** Absorption spectrophotometry is a better method than our direct (Calmigite) measurement of serum magnesium in this study. However, this method has acceptable precision and coefficient of variation[21].

The reduction in serum magnesium with advancing gestation reported in this study is similar to findings of previous workers[4,5,11,16]. Some suggested reasons for the low levels of magnesium in pregnancy include inadequate intake, increased metabolic demand of pregnancy especially as gestation advanced, physiological haemodilution in pregnancy, increasing parity and low socio-economic status[1,7]. The prevalence of 16.25% in our study is different from figures reported by other investigators working in different populations. Pathak et al[7] reported 43.6% amongst rural Indian women in a community-based cross-sectional study and found a higher prevalence in higher parity women, while another hospital-based pilot study involving urban Indian dwellers reported magnesium deficiency in 4.6% of all pregnant women included in the study[21]. Kassu et al[6] reported a prevalence of 25.6% while Kumar and coworker[8] in Mauritius reported magnesium deficiency of 48% but found no difference in prevalence between their urban and rural participants.

In our study, previous delivery was associated with a significantly higher frequency of magnesium deficiency. This is closely related to the finding by Pathak et al that there was a decrease in serum magnesium with increase in parity. In their study, pregnant women with parity 2 or more had a significantly lower serum magnesium level (1.77±0.35mg/dl) than nulliparous pregnant women (2.01±0.57mg/dl); and further logistic regression analysis showed that women with a parity 2 or more were at a 2.59 times higher risk of magnesium deficiency (P=0.002) than the nulliparous pregnant women. Kumar and coworker[8] also reported a high prevalence of magnesium deficiency with high parity. To explain this relationship some investigators have proposed that frequent cycles of reproduction exert a significant stress that leads to a greater risk of malnutrition in pregnant women[22].

Another reason for this difference in prevalence may be the period in pregnancy included in the study. The present study evaluated pregnant women at the end of their 2nd trimester, which is similar to the work by Pathak et al[7] who recruited women from their 28th week of pregnancy. This may explain the high prevalence of magnesium deficiency reported in both studies; though the prevalence in our study was lower probably due to the involvement of largely urban dwellers. Again the documented magnesium deficiency in 4.6% of pregnant women by Kapil et al[21] is low but this observation can be explained by their inclusion of pregnant women from as early as 12 weeks gestation.

In this study, being a teenager was significantly associated with magnesium deficiency, and to a lesser degree, the age group 30-39 years was associated with magnesium deficiency. The similarity with the findings of Pathak et al[7] may be explained considering that 75% of their study population was in the age group 18-22 years. However, the high prevalence in the group of 30-39 years may be reflective of the role of higher parity which is expected at this age group, rather than the influence of age alone.

Social Class 4 was significantly correlated with the occurrence of magnesium deficiency in our study. This finding is related to a previous report that lower income women had lower magnesium intake[23], resulting in a higher negative magnesium balance; hence the association of low socio-economic status with magnesium deficiency. Low socio-economic status has also been associated with preterm labour/delivery, intrauterine growth restriction and low birth weight, which have all been linked to magnesium deficiency[1,10-13]. A similar study also reported that high levels of serum magnesium were found in women of high social class[24]. However, Kumar and coworker[8] did not find any correlation between the prevalence of magnesium deficiency and social class. It is likely that low social class imposes low consumption of magnesium-rich diet like green leafy vegetables, legumes, nuts, peas and soya flour. A recent study has disappointingly revealed that most fortified foods and beverages for pregnant and lactating women do not contain magnesium[25].

The use of multivitamin supplements by a small group of the participants in this study was not associated with a better serum magnesium status. In contrast, previous studies have shown improvement in magnesium balance when patients are put on adequate magnesium supplements leading to a better clinical outcome[11,13,15-17]. It is noteworthy that in our study the patients who were taking additional multivitamin drugs did not aim to take magnesium supplements, and should magnesium be present in their multivitamin the content is likely to be negligible. This may explain the lack of association.

The factors in the pregnant woman which may suggest magnesium lack were shown in this study to include young age, high parity and low socio-economic status. To reduce the high prevalence of magnesium deficiency in pregnancy, magnesium balance needs to be improved. This can be attained through nutritional counselling. We recommend that the average diet in this environment be evaluated in a nutritional survey to determine the content of magnesium. The diet with the highest amounts of magnesium can be advised for women who are at risk of magnesium deficiency. From the findings of this study, magnesium lack is likely to be pronounced in the last trimester of gestation; alternatively, routine supplementation with oral magnesium may be directed at young, lower income women or those with high parities commenced in the second trimester of pregnancy.

We also recommend that a population-based cross-sectional study be conducted to strengthen the findings of this study. This is necessary so that the limitations arising from a hospital-based study will be eliminated. Furthermore, a prospective follow up study is desired to assess magnesium status with respect to maternal and perinatal outcome. In the same vein, interventional studies can be embarked on to prove the efficacy or otherwise of dietary counselling or magnesium supplementation in pregnancy.

In conclusion, discouraging teenage pregnancy and delivery, improving the socio-economic status of every woman through education and social emancipation, as well as economic empowerment will directly translate to giving them the means to better their magnesium balance in or out of pregnancy and thus reduce the risk of magnesium deficiency in pregnancy. Similarly, emphasizing birth-spacing to allow the body to replenish its stores of essential nutrients including magnesium will help to reduce the prevalence of low magnesium in pregnancy.

ACKNOWLEDGEMENTS

The following people deserve special thanks: Mr. RE Okosun for his assistance with laboratory assay of magnesium, and Mr. TO Asieba for his role in the secretarial work and data analysis.

Tables:

Table : Baseline serum magnesium levels amongst pregnant and non-pregnant women in UBTH.

Trimester of pregnancy	Serum magnesium concentration (mEq/L)			
	mean	SD	SE	95% CI
Non-Pregnant	2.46	0.43	0.013	1.90 – 1.95
First Trimester	1.93	0.57	0.065	1.59 – 1.87
Second Trimester	1.73	0.29	0.042	1.36 – 1.53
Third Trimester	1.45	0.19	0.055	2.35 – 2.57
P-value	0.00			

SD – Standard Deviation

SE – Standard Error of the Mean

CI – Confidence Interval

Table 2: Maternal socio-demographic characteristics in relation to hypomagnesaemia

Characteristic	Frequency (%)		P-value
	Gp A(n=26)	Gp B(n=134)	
Age(years)			
<20	4(15.38)	0(0)	0.00
20-29	0(0)	50(37.31)	
30-39	22(84.62)	84(62.69)	
Parity			
0	8(46.15)	40(29.85)	0.03
1	4(15.38)	22(16.42)	
2	5(19.23)	37(27.61)	
3	6(23.10)	28(20.90)	
4	3(11.54)	7(5.22)	
Body Mass			
Index(BMI)	10(38.47)	36(26.87)	0.00
Kg/M^2	16(61.53)	64(47.76)	
Normal	0(0)	34(25.37)	
Overweight			
Obese	18(69.23)	60(44.78)	0.00
Social Class	0(0)	42(31.34)	
1	0(0)	32(23.88)	
2	8(30.77)	0(0)	
3			
4			

Figure:

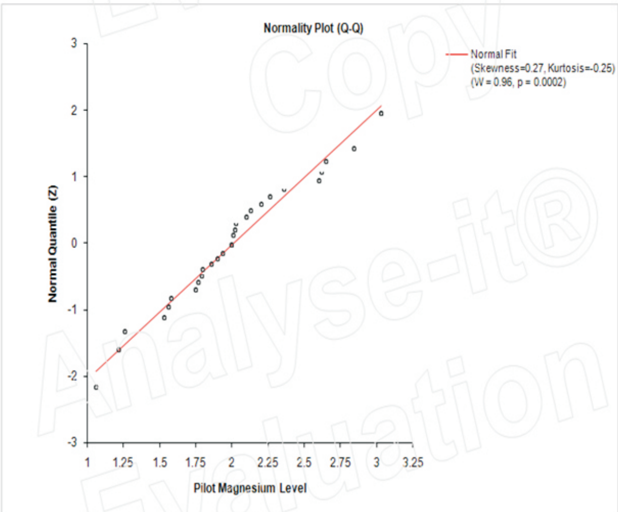

Figure 1: Dot plot of serum magnesium levels of pilot study

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