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Serum Magnesium among Women with Preterm Labour in a Tertiary Health Institution in South-East Nigeria: A Comparactive Study

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Abstract

Background: Preterm delivery is a major health concern. It is the leading cause of perinatal morbidity and mortality. Besides varied aetiology, it may be due to alteration in basic biochemical function of the body at cellular level making emphasis on trace elements especially Magnesium. **Objective:** The objective of this study is to determine the relationship between maternal serum magnesium levels and preterm labour. **Methodology**: This is a cross sectional comparative study of 70 women presenting at the labour ward of Federal Medical Centre Owerri with spontaneous preterm labour (cases) and 70 women with uncomplicated pregnancies at term(controls). Relevant clinical data were obtained from participants using a proforma, after which blood samples were collected and serum magnesium levels were determined using a direct method (calmagite method). The data obtained was analyzed using the statistical package for social science (SPSS) for Windows version 22. The results were expressed in mean ± standard deviation and evaluated with unpaired student "t" test, chi square test, ANOVA and post-HOC test. Significance was defined as P values < 0.05. **Results:** Patients with preterm labour had a highly significantly depressed serum magnesium level (mean 1.7 mg/dl ± 0.33 vs. 2.05 ± 0.26 mg/dl) ($p < 0.001$) as compared to women at term. It was found that there was a highly significant ($p < 0.001$) difference between mean serum magnesium levels in patients of low socio-economic class (1.69 mg/dl ± 0.29) and those of other social classes (high social class = 1.99 mg/dl ± 0.31, middle class = 2.02 mg/dl ± 0.29). There was also a statistically significant relationship ($p = 0.027$) between low magnesium levels and maternal age above 35 years. This study also showed that patients belonging to the middle and low socio-eco-

nomic classes were 3.4 and 4.5 times more likely to have preterm labour. Also those above 35 years were 1.2 times more likely to have preterm labour. **Conclusion:** Low serum magnesium level is associated with preterm onset of labour hence magnesium supplementation in pregnancy is recommended especially for those of low social class and advanced maternal age.

Keywords

Preterm Labour, Serum Magnesium

1. Introduction

Preterm delivery is the leading cause of perinatal morbidity and mortality [1] [2]. Fifteen million children each year are born preterm [3]. World Health Organization (WHO) defines preterm labour as onset of labour before 37 completed weeks (259 days) of gestation [3] [4]. The burden of preterm delivery is disproportionately concentrated in Asia and Africa, where about 85% of all preterm births occur (54% and 31% respectively) [5] [6]. In Nigeria, preterm babies account for 40-60% of perinatal deaths [7]-[9]. In addition, preterm delivery has long term consequences such as impaired neuro-developmental function, cerebral palsy, learning impairment and visual disorders [10].

Preterm labour is a syndrome with a variety of causes which can be classified into two broad subtypes: Spontaneous preterm birth (spontaneous onset of labour or following premature rupture of membranes (PROM) and provider initiated preterm birth (defined as induction of labour or elective caesarean birth before 37 completed weeks of gestation for maternal or fetal indications or other non-medical reasons) [11]. In 50% of cases the cause of spontaneous preterm labour is unknown although several potential risk factors have been identified [12]. The main one is premature rupture of membranes, and others are multiple pregnancy, genital tract infection, polyhydramnios, cervical incompetence, antepartum haemorrhage, fetal and uterine anomalies, anemia, and smoking. It is also related to socioeconomic status and geographic location [13]-[15].

Besides varied aetiology of preterm labour, it may be due to alteration in basic biochemical functions of the body at cellular level with emphasis on trace elements, of which magnesium being one of them is a subject of interest in recent times [16]. Moreover, the final common pathway of all the pathophysiologic mechanisms of spontaneous preterm labour is calcium mediated uterine contraction which is inhibited by magnesium. Magnesium is the fourth most common cation in the body and the second most common intracellular cation [17]. It has a fundamental role as a co-factor in more than 300 enzymatic reactions in the body [12] [17]. It is also involved in several processes, including hormone receptor binding, gating of calcium channel, muscle contraction, neuronal activity, cardiac excitability and neurotransmitter release [17] [18]. Many of these actions, are at-

tributed to its calcium antagonism [17] [18].

Studies have reported a fall in magnesium during pregnancy [12] [19] [20]. A significant decline has been reported by various studies in cases of preterm labour [12] [16] [21] [22]. Magnesium supplementation have been recommended for prevention of preterm labour as well as preeclampsia, low birth weight and other maternal, fetal, neonatal and paediatric consequences which may last throughout life [21]-[25].

The aim of this study is to determine the relationship between maternal serum magnesium levels and preterm delivery in our environment. The result of this study can help to reduce the high morbidity and mortality related to preterm delivery.

2. Methodology

This was a cross sectional comparative study carried out in Federal Medical Centre Owerri, South-east Nigeria between March, 2016 and February, 2017. The study included 70 pregnant women presenting with idiopathic preterm labour as cases, and 70 pregnant women at term who are not in labour. Approval for the study protocol was granted by the Health Research Ethics Committee of the Federal Medical Centre, Owerri. All patients who met the inclusion criteria were recruited after informed written consent was obtained. Structured questionnaire was used to obtain socio-demographic data and relevant clinical data.

2.1. Inclusion Criteria

Women presenting to Federal Medical Center Owerri with singleton pregnancies and gave consent to participate in the study. Primigravid and multiparous women who met the inclusion criteria were enrolled. Their gestational ages were calculated from the first day of their last menstrual period or an early ultrasound scan for those unsure of their dates.

Cases: women with spontaneous preterm labour (between 28 and less than 37 completed weeks' gestation) and had preterm deliveries.

Controls: women with uncomplicated pregnancies at term (37 completed weeks to less than 42 weeks).

2.2. Exclusion Criteria

For cases: pregnant women known to have high risk factor(s) for preterm labour will be excluded from the study as follows;

a) Patients with premature rupture of membrane.

b) Women with multiple pregnancy.

c) Women with preeclampsia, polyhydramnios, oligohydramnios, congenital anomalies.

d) Women with history of diabetes, Human Immunodeficiency Virus, significant intercurrent infection or other illness.

e) Women that have received any form of magnesium therapy prior to contact.

f) Women with a previous history of preterm labour.

g) Women unsure of their dates and don't have an early ultrasound scan.

h) Women who refused consent to participate in the study.

For controls:

a) Women who refused consent to participate in the study.

b) Women unsure of their dates and don't have an early ultrasound scan.

c) Women that have received any form of magnesium therapy prior to contact.

d) Women with history of diabetes, Human Immunodeficiency Virus, significant intercurrent infection or other illness.

e) Women with preeclampsia, polyhydramnios, oligohydramnios, congenital anomalies.

f) Women with multiple pregnancy.

2.3. Sample Collection

A total volume of eight milliliters of venous blood was collected from the antecubital vein without stasis and dispensed into a plastic vacuum plain bottle. Blood in the plain bottle was allowed to clot and then centrifuged at 3000 rpm for ten minutes and the serum was aspirated and dispensed into plain tubes and stored at −20˚C until the time of analysis.

Five milliliters of venous blood were collected from the antecubital vein without a tourniquet and dispensed into a plastic vacuum plain bottle. Blood in the plain bottle was allowed to clot and then centrifuged at 3000 rpm for ten minutes and the serum aspirated and dispensed into plain tubes and stored at −20˚C until the time of analysis.

2.4. Methodology

The serum magnesium level was then determined by direct measurement (calmagite method) using the kit manufactured by Teco Diagnostics, California USA, which defines adult reference range as 1.4 - 2.5 millequivalent per litre.

2.5. Statistical Analysis

Statistical analysis was performed using SPSS version 22. The data were expressed as mean ± standard deviation and evaluated with unpaired students "t" test, chi square test, ANOVA and post-HOC test. A logistic regression analysis was used to predict the roles of maternal age and social class as risk factors for preterm labour. "p" value of < 0.05 will considered as significant and 0.001 highly significant.

3. Results

Table 1 shows the socio-demographic characteristics of participants. The mean and standard deviation (Mean ± SD) of age in the case and control groups were 31.1 ± 4.12 and 31.09 ± 4.70 respectively. Social class and booking status differed significantly between the case and control groups $P = 0.03$ and <0.01, respectively.

Distribution of the participants by serum magnesium levels (Table 2) showed

that hypomagnesaemia (*i.e.,* Mg^{++} < 1.8 mg/dl) occurred more significantly among the case group 75.9% compared to the control group 24.1% (p value < 0.001). A comparison of the mean serum magnesium for the cases and controls is shown in Table 3. The mean serum magnesium level for the cases, 1.79 ± 0.33 was significantly lower than mean for controls, 2.05 ± 0.26 (P-value ≤ 0.001).

Table 1. Distribution by socio-demographic characteristics of subjects.

Characteristics	Total	Case (Preterm labour) N (%)	Control (Term labour) N (%)	P-Value
Age				
20 - 24	4	0 (0.0)	4 (100.0)	0.924
25 - 29	54	34 (63.0)	20 (37.0)	
30 - 34	43	15 (34.9)	28 (65.1)	
35 - 39	37	21 (56.8)	16 (43.2)	
≥40	100	0 (0.0)	2 (100.0)	
Mean ± SD (years)		**31.16 ± 4.12**	**31.09 ± 4.70**	
Parity				
Primigravidae	40	20 (50.0)	20 (50.0)	0.872
Primipara	28	12 (42.9)	16 (57.1)	
Multipara	63	33 (52.4)	30 (47.6)	
Grand multipara	8	4 (50.0)	4 (50.0)	
Social class				
Upper class	40	11 (27.5)	29 (72.5)	0.03*
Middle	62	35 (56.5)	27 (43.5)	
Lower	38	24 (63.2)	14 (36.8)	
Booking status				
Booked	127	57 (44.9)	70 (55.1)	<0.01*
Unbooked	13	13 (100.0)	0 (0.0)	

Table 2. Distribution by serum magnesium levels of the patients for cases and controls.

Serum magnesium (mg/dl)	Total	Cases (n = 70) N (%)	Controls (n = 70) N (%)	P-value
<1.8 mg/dl	58	44 (75.9)	14 (24.1)	<0.001*
≥1.8 mg/dl	82	26 (31.7)	56 (68.3)	

Table 3. Comparison of mean serum magnesium levels between cases and controls.

Group	No of patients	Serum magnesium levels(mg/dl)				
		Range	Mean	SD	't'	P-value
Group I (cases)	70	1.46 - 2.44	1.79	± 0.33	4.816	<0.001*
Group II (controls)	70	1.21 - 2.81	2.05	± 0.26		

Serum magnesium levels were compared for various socio-economic classes using the one-way ANOVA with post-HOC test (Table 4 and Table 5). The difference in serum magnesium levels between high socio-economic class (1.99 mg/dl ± 0.31) and low socio-economic class (1.69 mg/dl ± 0.29) was significant ($p \leq 0.001$). Also, serum magnesium levels were significantly higher in the middle socio-economic class (2.02 mg/dl ± 0.29) than in the low socio-economic class (1.69 mg/dl ± 0.2) ($p \leq 0.001$).

Table 4. Relationship between serum magnesium and social class.

Social class	Total serum magnesium level				
	N = 140	Mean ± SD	Min	Max	P-value
Higher	40	1.99 ± 0.3	1.51	2.44	
Middle	62	2.02 ± 0.29	1.41	2.81	<0.001*
Lower	38	1.69 ± 0.29	1.21	2.28	

Table 5. Comparative analysis of serum magnesium levels in pregnant women between different socio-economic classes.

Socio-economic class	No of cases	Serum magnesium level			P-value
		Range	Mean	SD	
High Vs	40	1.51 - 2.44	1.99	± 0.31	0.819
Middle	62	1.41 - 2.81	2.02	± 0.29	
Middle Vs	62	1.41 - 2.81	2.02	± 0.29	<0.001
Lower	38	1.21 - 2.28	1.69	± 0.29	
Higher Vs	40	1.51 - 2.44	1.99	± 0.31	<0.001
Lower	38	1.21 - 2.28	1.69	± 0.29	

Table 6 shows the distribution by age of patients for mean serum Magnesium levels. The mean serum Magnesium level was significantly higher in age groups 20 - 24 (2.19 mg/dl ± 0.06) (P = 0.027).

Table 6. Distribution by age of subjects for mean serum magnesium levels.

Maternal age	N = 140	Mean ± SD (mg/dl)	P-value
20 - 24	4	2.19 ± 0.06	
25 - 29	54	1.89 ± 0.38	
30 - 34	43	2.003 ± 0.29	0.027*
35 - 39	37	1.83 ± 0.26	
≥40	2	1.84 ± 0.14	

4. Discussion

Preterm labour is associated with perinatal mortality and morbidity. The exact

aetiology of preterm labour is still unknown though alterations in trace elements especially magnesium has been linked with preterm labour [12] [25].

In this study, the mean magnesium level was 1.79 ± 0.33 mg/dl for the patients with preterm labour and 2.05 ± 0.26 for the women at term. The mean difference was found to be statistically highly significant ($p < 0.001$). This result is found to be similar to and supported by findings of other investigators. In a study by Sahid A.R, and Co-workers, serum magnesium level in those women with preterm labour was found to be 1.87 ± 0.34 and 2.1 ± 0.4 in those presenting with labour at term [12]. Okunade and Co-workers in Lagos Nigeria found that the patients with preterm labour had significantly depressed serum magnesium level and the mean was 1.73 ± 0.4 [25]. They also found the relative risk of preterm labour to be 1.83 times among the patients with serum magnesium levels less than 1.6 mg/dl [25]. A recent study by Kamal *et al.*, the mean serum magnesium level in preterm labour cases to be 1.4 mg/dl ± 0.22 and concluded that estimation of serum magnesium might prove to be a valuable tool in predicting the preterm onset of labour [26]. In the present study, hypomagnesaemia was significantly higher among the patients with preterm labour as compared to pregnant women at term. Similar findings were reported by other investigators [12] [16] [25] [26].

The present study found that magnesium was significantly lower among advance maternal age and lower social class. Cunningham *et al.* reported similar findings [27]. Kamal *et al.* also showed that low serum magnesium level was found in patients belonging to the low socio-economic status, thus relating it to a dietary deficiency [26]. In contrast, in a study in Lagos, Nigeria, there was no relationship between preterm labour, maternal age and socio-economic status [25]. This disparity may be attributable to dietary differences in the environment studied.

5. Conclusion

Most available interventions for preterm labour in our environment aim at stopping an ongoing labour process and these are not effective in reducing morbidity and mortality associated with this condition. The findings of this study support that there's an association between hypomagnesaemia and idiopathic preterm labour hence the need for prophylactic therapy (consumption of magnesium rich diet and/or oral magnesium supplementation) for pregnant women at high risk of preterm labour.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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