

Seric Calcium and Magnesium in Normal and Pre Eclamptic Pregnant Women: A Case-Control Study in Kinshasa, D R Congo

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Abstract

Goal: The present study aimed to determine the profile of seric calcium and magnesium in pre-eclamptic and eclamptic pregnant women of Kinshasa province in the Democratic Republic of Congo where preeclampsia is characterized not only by a high incidence, but also by a seasonal variation probably related to nutritional intake. **Study Design:** This is a case-control study that took place during the period from September 2014 to March 2015 in four quaternary and tertiary maternity hospitals in Kinshasa. A total of 113 healthy pregnant women (controls) and 112 pre-eclamptic and eclamptic pregnant women (cases) were included in this study. Seric calcium and magnesium were measured in all these gravidas by the principle of spectrophotometry with a HUMALYSER Primus semi-automaton. **Results:** The mean age of those gravidas was 26.8 ± 6.3 years (26.7 vs 26.9 , $p = 0.11$). The majority of these gravidas were primiparous. The mean gestational age in both groups was 31.35 ± 0.9 weeks (32.1 vs 30.6 , $p = 0.21$). The average seric calcium value was 4.47 ± 0.23 mEq /L in healthy pregnant women compared to 3.80 ± 0.71 mEq/l in pre-eclamptics ($P < 0.001$). The mean of seric magnesium was 1.56 ± 0.15 mg/dL in healthy pregnant women compared to 1.20 ± 0.41 mg/dL in pre eclamptics ($P < 0.001$). Seric calcium and magnesium values were low in the pre-eclamptic group and lower in the eclamptic group ($P < 0.001$). **Conclusion:** This study establishes a relationship between the low concentration of seric calcium and magnesium with pre-eclampsia and eclampsia, which could

be one of the determinants of the high prevalence and seasonality of the disease in Kinshasa.

Keywords

Seric, Calcium, Magnesium, Preeclampsia, Kinshasa

1. Introduction

Preeclampsia affects 3% - 10% of pregnancies and is responsible for a large maternal and fetal morbidity and mortality worldwide [1]. Although the oxidative stress generated by hypoxia is a major component in the set of mechanisms that contribute to the occurrence of this condition and associated complications, studies in the most affected regions in Africa and Asia have established a relationship between low intakes of certain micronutrients and the occurrence of the disease, which would probably be one of the determinants of the high prevalence and seasonality of the disease in these regions of the world [2]-[7].

Some of these studies indicate that nutritional deficiency of calcium and magnesium is associated with a high risk of preeclampsia and its complications [8]. On the one hand hypocalcemia and hypomagnesemia lead to spasms and increase in vascular resistance that lead to arterial hypertension. On the other hand, by stimulating the N-methyl-D-aspartate receptors, hypoxia promotes the penetration of calcium into the cellule reversing the intracellular Mg/Ca ratio, resulting in significant cellular alterations with consequent release of oxygen free radicals, generalized endothelial dysfunction and the release of certain neuromediators causing preeclampsia and eclampsia [9] [10].

Thus, fluctuations in blood levels of calcium and magnesium seem to play a significant role in the pathophysiology of preeclampsia and its complications alongside hypoxia.

The present study aims to determine the profile of seric calcium and magnesium in pre-eclamptic and eclamptic gravidas in the city of Kinshasa province, one of the most populated urban areas in sub-Saharan Africa where not only the incidence of preeclampsia is high, but it also has seasonal variation [11], probably related to nutritional intakes of micronutrients, particularly calcium and magnesium.

2. Material and Methods

This is a case-control study that took place during the period from September 2014 to March 2015 in four maternity hospitals at the quaternary and tertiary level in the city of Kinshasa Province (DR Congo), namely the university clinic of Kinshasa, the Kinshasa General Hospital, the St. Joseph Hospital and the Mother and Children Center of Bumbu.

The size of our sample was calculated from the following formula: $n = z^2$

$(pq)/e^2$, where n = sample size, z = level of confidence according to the reduced normal centered law (for a 95% confidence level, $z = 1.96$; p = estimated proportion of the population with the characteristic; $q = 100 - p$, e = acceptable margin of error.

A total of 113 healthy pregnant women (controls) and 112 pre-eclamptic and eclamptic pregnant women (cases) were included in this study. These gravidas were recruited from units specialized in the management of hypertensive disorders of pregnancy (for cases) or during prenatal consultations (for controls). The study protocol was approved by the Ethic Committee of the Public Health School/University of Kinshasa. Participation in the study was voluntary after informed consent from the pregnant woman herself or her family in case of eclamptic coma.

Preeclampsia and eclampsia were defined according to the criteria set by the High Blood Pressure Education Program (NHBPEP) by a blood pressure greater than 140/90 mmHg after 20th week of gestation, associated with a significant proteinuria greater than 300 mg/24 hours [12].

Excluded from this study were women with multiple pregnancies, those taking diuretic medication, those who received magnesium sulphate and those with renal insufficiency, diabetes, anemia, cardiovascular disease, malabsorption

Serum calcium and magnesium were measured in all these gravidas by the principle of spectrophotometry with a HUMALYSER Primus semi-automaton.

The reference values for these assays are 4.5 to 5.5 mEq/L for serum calcium, and 1.6 to 2.6 mg/dl for magnesium.

Descriptive statistics calculations (frequency, mean, median) were performed and the Mann-Whitney test was used to compare the values obtained in the two groups, with a significance level of 0.01.

3. Results

A total of 225 pregnant women were included in this study, including 113 healthy pregnant women (controls) and 112 pregnant patients (96 pre-eclamptic and 16 eclamptic women)

The average age of gravidas was 26.8 ± 6.3 years (26.7 vs 26.9 , $p = 0.11$). The majority of these gravidas were primiparous (58/113 healthy pregnant Vs 57/112 preeclampsics, $p = 0.23$). The mean gestational age in both groups was 31.35 ± 0.9 weeks (32.1 Vs 30.6 , $p = 0.21$).

The values for serum calcium and magnesium are given in **Table 1**. The average serum calcium value was 4.47 ± 0.23 mEq/L in healthy pregnant women compared to 3.80 ± 0.71 mEq/L in patients (pre-eclamptic and eclamptic) ($P < 0.001$). Mean magnesium level was 1.56 ± 0.15 mg/dL in the control group compared to 1.20 ± 0.41 mg/dL in the case group ($P < 0.001$).

The comparison of mean serum calcium and magnesium values in pre-eclamptic and eclamptic pregnancies is given in **Table 2**. The average serum calcium value was 3.70 ± 0.56 mEq/l in pre-eclamptic pregnant women compared to 3.20 ± 0.41 mEq/l for eclamptic ($P < 0.001$); that of serum magnesium

Table 1. Comparison of the means of calcemia and magnesemia between the groups of healthy and pre eclamptic pregnant.

	GESTANT HEALTHY	GESTANT PRE ECLAMPTIC	P Value
CALCEMIA (mEq/l)	4.47 ± 0.23	3.80 ± 0.71	<0.001
MAGNESEMIA (mg/dl)	1.56 ± 0.15	1.20 ± 0.41	<0.001

Table 2. Comparison of mean values of serum calcium and magnesium between pre-eclamptic and pre-eclamptic pregnant.

	PRE ECLAMPTIC PREGNANT	ECLAMPTIC PREGNANT	P Value
CALCEMIA (mEq/l)	3.70 ± 0.56	3.20 ± 0.41	<0.001
MAGNESEMIA (mg/dl)	1.25 ± 0.36	1.15 ± 0.46	<0.001

was 1.25 ± 0.36 mg/dl in pre-eclamptic pregnant women compared to 1.15 ± 0.46 eclamptic women ($P < 0.001$).

The comparison of values of seric calcium and magnesium between the group of healthy pregnant, pre-eclamptic and eclamptic women is given in **Table 3**. There is a very significant difference of the values obtained in these 3 sub-groups: the values obtained decreased going from healthy pregnant groups to pre-eclampsics and eclampsics ($P < 0.001$).

4. Discussion

The pathophysiology of pre-eclampsia is still less well known today. Of all the hypotheses put forward to explain the occurrence of this condition, it seems that the oxidative stress generated by the metabolism and homeostasis disorder of certain minerals and vitamins play a significant role by the fact that it is responsible for endothelial dysfunction at the origin of clinical manifestations of the disease especially, the occurrence of arterial hypertension and its severity. Studies show that nutritional deficiencies are common during pregnancy and pregnant women in developing countries have been reported to consume diets that are low in minerals and vitamins [13]. Dietary deficiencies of calcium and magnesium during pregnancy have been implicated in preeclampsia, eclampsia, pre-term birth and intrauterine growth retardation [14]. Several epidemiological studies in developing nations indicate an association between reduced calcium intake and preeclampsia. These observations led to the hypothesis that the incidence of preeclampsia can be reduced in populations of low calcium intake by calcium supplementation [15]. Magnesium has been known as an essential co-factor for many enzyme systems. It also plays an important role in neurochemical transmission and peripheral vasodilatation [16]. Magnesium supplementation during pregnancy may be able to reduce fetal growth retardation and preeclampsia and increase birth weight [17]. The modification of calcium and magnesium metabolism during pregnancy could be a potential cause of pre-eclampsia.

Table 3. Comparison of mean values of serum calcium and magnesium between the three different groups of pregnant women (healthy, pre-eclamptic and eclamptic).

	GESTANT HEALTHY	PRE ECLAMPTIC GESTANT	ECLAMPTIC GESTANT	P Value
CALCEMIA (mEq/l)	4.47 ± 0.23	3.70 ± 0.56	3.20 ± 0.41	<0.001
MAGNESEMIA (mg/dl)	1.56 ± 0.15	1.25 ± 0.36	1.15 ± 0.46	<0.001

It has been demonstrated by numerous studies that abnormalities of calcium and magnesium homeostasis could lead to increased vascular hypersensitivity, highly incriminated in the occurrence of pre-eclampsia and its complications.

In their studies Sukonpan K *et al.* [18], Standley CA *et al.* [19], Frenkel Y *et al.* [20], Handwerker SM *et al.* [21], Hassan TJ *et al.* [22], Kosch M *et al.* [23], Malas NO *et al.* [24], Richards SR *et al.* [25] note a low seric calcium and magnesium rate in pre-eclamptic pregnant compared to healthy pregnant. The results obtained from these different studies show a significant decrease of the seric magnesium and calcium in pre-eclamptic pregnant women compared to normal pregnant women, with a still very significant decrease in eclamptic pregnant. The results obtained from our study showed low levels of calcium and magnesium in pregnant women with pre-eclampsia and even more pronounced in those with eclamptic seizures. These results are similar to those obtained in many studies. However the validation of our results requires the realization of other studies on large samples. Indeed, this study took into account only four hospitals in the city of Kinshasa province with a very small effective, which is a weak point for this study.

It appears from these studies that, fluctuations in blood levels of calcium and magnesium play an important role in the pathophysiology of pre-eclampsia and its complications alongside hypoxia and are probably the determinants of the high prevalence and the seasonality of the disease in the poor regions of the globe.

Studies show that N-methyl-D-aspartate receptor stimulation in hypoxia is associated with high calcium intracellular penetration reversing the intracellular Mg/Ca ratio, leading significant cellular alterations with the release of oxygen-free radicals, what ends to generalized endothelial dysfunction and release of some neuromediators that cause pre-eclampsia and eclampsia [8] [9] [10]. On the other hand, it has been demonstrated by in vivo and in vitro studies that hypomagnesemia and hypocalcemia are responsible for vascular spasms with elevated vascular resistance, which results in high blood pressure, a symptom major in pre-eclampsia.

Observational studies have revealed an inverse association between calcium intake and hypertensive disorders during pregnancy. Clinical trials have also confirmed that calcium supplementation reduces blood pressure and hypertension-related disorders. In fact, during pre-eclampsia, there are endothelial lesions that cause an increase in thromboxane A2 which is responsible for vascular spasm leading to arterial hypertension and placental ischemia. Calcium prevents this

vasospasm, which leads to vasodilatation. A Cochrane review analysed 12 high quality trials after excluding 24 trials on supplementation of calcium to prevent pre-eclampsia in normotensive pregnant women. The dose of calcium evaluated was 1.5 to 2 gm daily. There was less high blood pressure associated with calcium supplementation rather than placebo [26].

Magnesium competitively inhibits the binding of Ca^{2+} to troponin C in the myocyte and the formation of the calmodulin- Ca^{2+} complex in the smooth muscle cell preventing the occurrence of vascular spasms. At the whole heart, the negative inotropic effect of magnesium is compensated by peripheral vasodilatation and tachycardia leading to retention or even increase in cardiac output [27] [28]. Clinical studies indicate that magnesium has an anti-thrombotic property that would be beneficial in the prevention of pre-eclampsia and these complications [29]. In a Cochrane review selected randomised and quasi randomised trials of dietary magnesium supplementation during pregnancy, it showed that magnesium treatment was associated with a reduced risk of low birth weight and of small for gestational age babies compared with placebo. But, there was no apparent effect of magnesium treatment on maternal systolic or diastolic blood pressure during pregnancy [17]. However, numerous studies reveal the role of magnesium in calcium conduction whose low serum levels are implicated in the occurrence of pre-eclampsia. Extracellular magnesium inhibits also the release of noradrenaline, dopamine, acetylcholine, alters receptor sensitivity to acetylcholine and blocks the central N-methyl-D-aspartate (NMDA) receptors who are involved in the occurrence of pre eclampsia and eclampsia [10].

5. Conclusion

To conclude, our study shows a significant reduction of serum calcium and magnesium levels in pre-eclamptic compared to normotensive pregnant women, and establishes a relationship between the low concentration of those minerals with preeclampsia and eclampsia. Further studies should specify if low calcium and magnesium dietary intakes are determinants of the high prevalence and seasonality of the disease in our city.

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