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Effets of Trace Elements Supplementation on Preeclampsia-Related Morbidities in Pregnant Women in Kisangani, Democratic Republic of Congo: A Double-Blind Randomized Clinical Trial

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Abstract **Original Research Article**

Introduction: The need for trace elements increases more than the dietary energy needs increase during pregnancy. Maternal undernutrition is a common public health problem and a key driver of poor perinatal outcomes in sub-Saharan Africa. The objective of this study is to determine the impact of micronutrient supplementation on preeclampsia-related morbidities during pregnancy in Kisangani. ***Material and methods****:* This was a double-blind, randomized controlled trial, which compared 2 regimens of supplementation in pregnant women with micronutrient deficient concentrations (calcium, selenium and zinc). The supplements were made of calcium, selenium and zinc on the one hand, and placebo supplements. Research carried out in Kisangani from 10 January 2024 to 10 October 2024. R software version 4.3.0 was used to perform all statistical analyses. ***Results****:* the rate of preterm delivery was higher in the control group (22.4%) than in the intervention group (8.5%) with a p-value of 0.03; the same was true for IUGR: 26.5% versus 10.6% (p-value=0.02) and gestational arterial hypertension: 30.6% versus 14.9% (p-value: 0.04). Neonatal asphyxia was more observed in the control group than in the intervention group: 28.6% versus 10.6%. ***Conclusion****:* Supplementation with trace elements in pregnant women with a deficiency contributes to a significant reduction in several morbidities related to the occurrence of preeclampsia, especially when it is done during pregnancy, it improves the prognosis and outcomes of pregnancy.

Keywords: trace element, supplementation, calcium, selenium, zinc, morbidity, pregnant, Kisangani.

INTRODUCTION

The course of pregnancy requires additional energy and a better supply of nutrients from the maternal body, to promote ideal fetal growth [1]. Micronutrients, including essential vitamins and minerals, play an important role in the health of pregnant women and the growing fetus [2]. Trace minerals can be used as cofactors and coenzymes for nutrient metabolism and are useful for preventing different diseases in pregnant women [3]. The need for trace elements increases more than the dietary energy requirement increases during pregnancy [4].

Maternal undernutrition is a common public health problem and a key driver of poor perinatal outcomes in sub-Saharan Africa [5]. Pregnant women are primarily vulnerable to the effects of micronutrient deficiency due to the high needs of the growing fetus, placenta, and maternal tissues [6]. Failure to meet these increased needs has potentially harmful consequences for both the mother and the fetus [7].

During pregnancy, micronutrient reserves or insufficient intake can lead to deficiencies, which can lead to anemia, hypertension, various complications during labour, maternal death and stillbirth, premature delivery, intrauterine growth restriction, birth defects, decreased immune capacity, and fetal hypotrophy [8].

Currently, preeclampsia contributes to approximately 78,000 maternal deaths and 540,000 fetal deaths per year [9]. Pregnant women in low- and middle-income countries are particularly at risk of preeclampsia and its serious complications [10]. Despite the severity and prevalence of preeclampsia, the exact etiology of this disorder remains unknown, although impaired placental perfusion has been proposed as a key factor [11].

Preeclampsia can be considered a state of oxidative stress and, in fact, several lines of evidence support the oxidative hypothesis of preeclampsia. The optimal functioning of antioxidant enzymes (glutathione peroxidase, thioredoxin reductase, catalase, superoxide dismutase, etc.) remains dependent for most of the trace elements, the demand for which is accentuated during pregnancy. Based on the oxidative hypothesis of preeclampsia, micronutrient supplementation could help prevent preeclampsia and its multiple consequences on maternal fetal health [12,13].

As the causes of preeclampsia are unknown, immediate delivery is the most effective established treatment; however, it can lead to perinatal problems. Thus, it becomes very important to reduce the rate of preeclampsia and all related morbidities in pregnant women. [11,13].

However, there are not yet enough clinical studies evaluating the effectiveness of micronutrient supplementation in preventing preeclampsia and its consequences [14]. Therefore, micronutrient supplementation initiated early, between 8- and 14-weeks' gestation, may have better results in the prevention of preeclampsia than that given late, as in most previous studies conducted after 20 weeks' gestation [12,14].

Given the many complications of preeclampsia [15,16], the significant reduction in micronutrient concentrations in preeclamptic women, and the antioxidant and anti-inflammatory effects of antioxidant enzymes, and the links between micronutrients and antioxidant enzymes, we designed the present trial to investigate the impact of deficiency micronutrient supplementation in the prevention of preeclampsia and its consequences in the couple Feto-maternal.

To do this, we asked ourselves the question: does the intake of trace elements that are deficient in pregnant women in the prevention of preeclampsia minimize the consequences of the latter in pregnant women in Kisangani?

The objectives of this study are to contribute to improving the management of pregnant women with micronutrient deficient concentrations to reduce the risk of developing preeclampsia and other hypertensive disorders during pregnancy in Kisangani; to determine the impact of this supplementation on preeclampsia-related morbidities.

CHAPTER I. MATERIALS AND METHODS

I.1.Type and terrain of the study

This was a double-blind, randomized controlled trial, which compared 2 supplementation regimens in pregnant women with micronutrient deficiency statuses (calcium, selenium and zinc). The supplements were made of calcium, selenium and zinc on the one hand, and placebo supplements. The investigators and the pregnant women did not know which treatment (supplementations) each of the participants was receiving. The surrogates were recruited in 8 health facilities, including the Makiso-Kisangani General Referral Hospital, the Kabondo General Referral Hospital, the Mangobo General Referral Hospital, the Lubunga General Referral Hospital, Matete Referral Health Center, Saint Joseph Referral Health Center, the Social Foyer Referral Health Center and the Kisangani University Clinics. all located in the city of Kisangani, in the Democratic Republic of Congo.

I.2. Period and Sample of the Study

This research took place from the period from 10 January 2024 to 10 October 2024. During this period, all pregnant women who came to the prenatal consultation were asked to sort according to the selection criteria to participate in the study.

Referring to the research by Guna Balasingam S et al [17], the minimum sample size was calculated with the G-Power software version 3.1.9.7. To calculate this sample size, we used the α cut-off of 0.05 and a power of 90% and an effect size of 0.3. There were 88 individuals. By adding 10% of individuals (about 8) lost to follow-up, the size of this sample was reduced to 96 individuals, including 48 individuals for each arm. The study consisted of two arms: one arm of 48 pregnant women to be supplemented with trace elements (calcium, selenium and zinc) and the other arm of 48 pregnant women to be supplemented with placebo.

I.3. Selection criteria

- **Inclusion criteria**

Be a pregnant woman in the first trimester of pregnancy; Have consented to participate in the research by signing the informed consent form; Have a concentration of trace elements (calcium: < 2.20 mmol/l, selenium: < 0.75 µmol/l and zinc: < 11.5 µmol/l) lower than normal; Pregnant not being on any other form of micronutrient supplementation.

- **Non-inclusion criteria**

Pregnant beyond the first trimester of pregnancy; Not having consented to participate in the study; pregnant with chronic high blood pressure; Pregnant in other form of micronutrient supplementation.

- **Exclusion criteria**

Pregnant women who have experienced untolerable side effects during supplementation; Pregnant woman who has personally decided to leave the research with or without a valid reason; who received other forms of supplementation during the research.

- **Criteria for Discontinuation of Supplementation (Treatment)**

Occurrence of a major side effect; Non-compliance with the supplementation protocol; Withdrawal of informed consent.

I.4. Enrolment of pregnant women

Out of a total of 196 pregnant women selected, 115 were excluded because they had not met the inclusion criteria, or because they did not consent to participate in this research; 102 others were included. The pregnant women recruited were randomized into two groups: 51 were subjected to micronutrient supplementation (intervention group), and 51 others to placebo supplementation (control group). During follow-up, none of the pregnant women had experienced a severe side effect. In the intervention group, 3 pregnant women versus 2 others in the control group were removed from the analyses because they were lost from sight (see Figure 1).

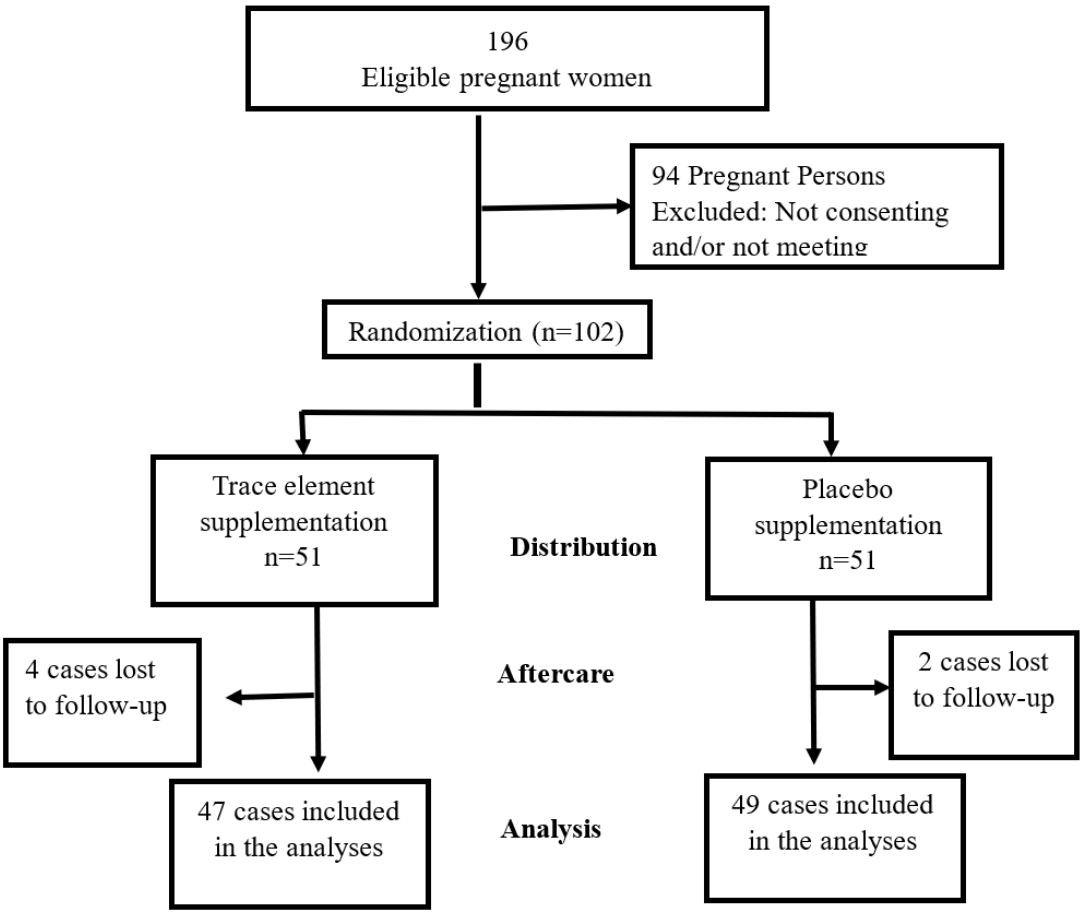

Figure 1: Enrolment of pregnant women

I.5. Randomization, intervention and follow-up

The data collection for this research was prospective. The investigation team was made up of 19 people, including a supervisor (principal investigator), per health facility, 1 doctor, 1 nurse, 1 medical biologist and 1 community relay. The investigation team had received explanations on the completion of the data collection forms and training on interview techniques, randomization, follow-up of pregnant women and maintenance of the register of adverse reactions. Physicians were more trained in the identification and management of major adverse events related to supplemented micronutrients. The medical biologist was briefed on the speed of blood sample collection. The community relay was more trained in the home monitoring of pregnant women in their area of responsibility to ensure compliance or daily use of medication.

On admission, in addition to the personal data collected, the measurements of trace element concentrations were carried out in all consenting pregnant women. In this way, the identification of pregnant women with deficiency trace elements was

effective for their integration into the further research. In addition to socio-demographic data, the anamnesis had insisted on the date of the last menstrual period, the history related to previous pregnancies in search of a notion of arterial hypertension and its complications. The standard paraclinical assessment consists of the Hemoglobin assay, the hematocrit, the RDT for malaria and the direct examination of the stool; An ultrasound was also performed to confirm the diagnosis of a pregnancy in the first trimester. During this meeting, all possible explanations related to this research (objectives, procedure, drugs used with their roles and adverse effects) were provided to the pregnant women. Those who met the inclusion criteria were randomized using the stratified block randomization technique, with stratification according to Body Mass Index (< 25 vs. ≥ 25 kg/m2); and age (< 30 years vs. ≥ 30 years). These randomization blocks were established based on assignment sequences generated by an independent statistician in research. The supplementation drugs were distributed in envelopes of the same color closed. Each envelope contained either the trace element tablets in 3 different boxes, or the Placebo tablets for a 30-day intake. The withdrawal of the next envelope or dose was done on every 28th day, i.e. 2 days before the end of the initially withdrawn batch. The research team was only aware of the assignment group of pregnant women at the end of the research during the sequential code analysis on the different envelopes.

Pregnant women assigned to the intervention group or who received micronutrient supplementation received calcium tablets (caltrate 600mg/day), selenium tablets 65 µg (organic selenium 65 mg) and +zinc tablets 15 mg (zinc 15 mg); while those in the control group received three placebo tablets: two white tablets for calcium and zinc, and a red tablet for selenium, all made with microcrystalline cellulose. All pregnant women were informed of the maternal-fetal benefits of taking the drugs to encourage them to comply with this supplementation. The community relays went every 7 days to the selected pregnant women to reassure themselves that they were taking the medication by counting the number of tablets remaining. The appointment was set after 4 weeks, for clinical evaluation, monitoring of adverse drug reactions and paraclinical control.

At each prenatal consultation appointment, the pregnant women presented themselves with the medication envelopes received at the previous appointment to allow the doctor and nurse to ensure compliance or compliance. And after these different evaluations, the pregnant woman received the second envelope with the same code as the previous envelope.

All drugs used in this trial were subject to quality control at the Laboratory for the Analysis and Control of Medicines and Foodstuffs of the University of Kinshasa at the Faculty of Pharmacy (LACOMEDA, Kinshasa, DRC).

The data on the characteristics of the medicinal products used in this research are given in Table 01

Table 01: Characteristics of the drugs used in this research

Medicine	Registered Name	Galenic form	Manufacturer	Lot number	Expiration Date
Calcium carbonate	Caltrate	600mg tablet, film-coated, 30 tablets per box	Pfizer consumer manufacturing Italy	488R	January, 2025
Selenium	Selenium organic yeast 65µg	65µg capsule, 30 capsules per box	Granions Laboratoire,France	SE338J	December,2026
Zinc	Zinc 15mg	15mg capsule, 30 capsules per box	Granions Laboratoire, France	CO20	October,2026
Placebo	Placebo	100mg tablet	Granions Laboratoire,France	PX356S	Nombre,2025

I.6. Management of adverse reactions

During this research, any self-medication or other supplementation by pregnant women, which is common practice in Congo, was discouraged. The pregnant women had been given explanations about the adverse effects of the trace elements in the study and were asked to report them. A grid of side effects has been developed to allow an objective and standardized assessment of the respondents. In this evaluation system, the severity of adverse effects was established as follows: 0 (symptom not reported by the respondent), 1 (mild symptom, not affecting lifestyle), 2 (moderate symptom, affecting lifestyle but controlled with simple means), 3 (severe symptom, justifying immediate cessation of treatment and requiring hospital management of the patient). This evaluation was carried out each time a side effect was reported by the respondents. This information was collected when pregnant women came to the appointment for antenatal consultations and collected the next batch of supplementation.

Any side effects presented by the pregnant women, but not included in the study drug prospectus, had to be reported for analysis by the Congolese National Pharmacovigilance Center to determine whether the reported event was attributable to the drugs (supplements) administered. Any pregnant woman who had mild and moderate adverse effects had to be followed on an outpatient basis, and those with severe symptoms should be hospitalized in one of the facilities

where the research was carried out and close to her address. At the halfway point, the data on adverse effects had to be communicated to the ethics committees of the University of Kisangani and the health committee for approval of the continuation of the trial.

I.7. Laboratory examination

Serum micronutrient assays were performed using Agilent 7700X inductively coupled plasma mass spectrophotometry (Agilent 7700X ICP-MS). Dosages were made at the beginning of supplementation at 13 weeks of amenorrhea, at 23 weeks and at 33 weeks, and also when the diagnosis of preeclampsia was made.

I.8. Expected results

The primary outcomes targeted in this research were the reduction of the incidence of preeclampsia and the improvement of serum levels of trace elements (calcium, selenium and zinc). The improvement of biological markers was determined by the determination of the serum concentration of these different trace elements. The targeted secondary outcomes were a reduction in preterm birth and intrauterine growth restriction related to preeclampsia; and the reduction of complications related to preeclampsia.

I.9. Data Processing and Analysis

The data from this research were presented as frequencies, percentages, and averages with standard deviation (SD). The primary objective was to compare the incidence of preeclampsia between the two groups of pregnant women with a low micronutrient concentration in the first trimester of pregnancy (one group received a deficiency or low-level micronutrient supplementation, and the other a placebo). To determine the membership of a pregnant group, a sequence was generated by the Excell software to assign pregnant women in one group or the other.

The Pearson $\chi 2$ test at the significance level of $p< 0.05$ was calculated to compare proportions. The Ficher exact test at the significance level of $p< 0.05$ was calculated when the conditions for the application of the chi-square test were not met. The hazard ratio (RR) with its 95% confidence interval (CI) was determined to measure the strength of the association between the qualitative variables. To compare the averages, the t-Student test was calculated. The homogeneity of the variances was tested between the 2 assignment groups... When the P-value was less than 0.001, the difference was considered significant. To eliminate confounding factors, multivariate logistic regression was calculated. R software version 4.3.0 was used to perform all statistical analyses.

I.10. Ethical considerations

This study was approved by the Ethics Committee of the University of Kisangani, UNIKIS/CER/024/2023 on7th of June 2023 and the Ethics committee of the School of Public Health at the University of Kinshasa: ESP/CE/43/2024.

I.11. Nomenclature declaration of targets and ligands

The key targets and ligands mentioned in this research are permanently archived in The Concise Guide to Pharmacology 2021/22[17] and ESPEN Micronutrient guideline [18].

1.12. Expression of Interest

We have no conflicts of interest to declare for this work.

CHAPTER II. RESULTS

II.1. Socio-demographic characteristics of the respondents

Table 1 presents the respondents according to their sociodemographic characteristics

Table 1: Socio-demographic characteristics of pregnant women

Characteristic	Placebo	Supplementation	Total
	N = 49[1]	N = 47[1]	N = 96[1]
Age (year)			
< 30 years	31 (63.3%)	38 (80.9%)	69 (71.9%)
≥ 30 years	18 (36.7%)	9 (19.1%)	27 (28.1%)
Address			
Kabondo	9 (18.4%)	15 (31.9%)	24 (25.0%)
Kisangani	5 (10.2%)	5 (10.6%)	10 (10.4%)
Lubunga	9 (18.4%)	3 (6.4%)	12 (12.5%)
Makiso	9 (18.4%)	5 (10.6%)	14 (14.6%)
Mangobo	11 (22.4%)	11 (23.4%)	22 (22.9%)
Tshopo	6 (12.2%)	8 (17.0%)	14 (14.6%)
Level of education			
Primary	4 (8.2%)	8 (17.0%)	12 (12.5%)
Secondary	34 (69.4%)	35 (74.5%)	69 (71.9%)
Higher or University	11 (22.4%)	4 (8.5%)	15 (15.6%)
Marital status			
Single	1 (2.0%)	7 (14.9%)	8 (8.3%)
Maried	48 (98.0%)	40 (85.1%)	88 (91.7%)

Profession			
State agent	2 (4.1%)	2 (4.3%)	4 (4.2%)
Merchant	10 (20.4%)	4 (8.5%)	14 (14.6%)
Dressmaker	1 (2.0%)	3 (6.4%)	4 (4.2%)
Cultivator	1 (2.0%)	4 (8.5%)	5 (5.2%)
Teacher	5 (10.2%)	1 (2.1%)	6 (6.3%)
Student	0 (0.0%)	1 (2.1%)	1 (1.0%)
Nurse	4 (8.2%)	1 (2.1%)	5 (5.2%)
Housewife	16 (32.7%)	19 (40.4%)	35 (36.5%)
Unemployed	10 (20.4%)	12 (25.5%)	22 (22.9%)
Parity			
Large multiparous	4 (8.2%)	0 (0.0%)	4 (4.2%)
Multiparous	18 (36.7%)	12 (25.5%)	30 (31.3%)
Nulliparous	1 (2.0%)	8 (17.0%)	9 (9.4%)
Primiparous	14 (28.6%)	16 (34.0%)	30 (31.3%)
Second-parous	12 (24.5%)	11 (23.4%)	23 (24.0%)
Weight (in kg)	66.8 (7.8)	64.0 (8.4)	65.4 (8.2)
Size (in cm)	159.4 (6.5)	159.7 (5.8)	159.6 (6.1)
IMC (Kg/m^2)			
< 25	19 (38.8%)	27 (57.4%)	46 (47.9%)
≥ 25	30 (61.2%)	20 (42.6%)	50 (52.1%)

It can be seen from this Table 1 that the two randomization groups (Placebo versus Micronutrients) were compared in terms of age of the pregnant women, their address, level of education, marital status, occupation, parity, weight, height and BMI. The average age among pregnant women was 28.1± 5.6 years versus 24.5 ± 5.7 years; and the mean BMI was 26.3± 3.2 kg/m2 versus 25.1± 3.4 kg/m2; respectively in the control group (who received placebo) and in the intervention group (supplemented with micronutrients).

II.2. Mean trace elements during pregnancy

Table 2 shows the different averages of micronutrient concentrations during pregnancy in the different research groups.

Table 2: Mean micronutrients during pregnancy in both groups

Characteristic	Placebo	Supplémentation	P-value2
	N = 49[1]	N = 47[1]	
Calcium			
In the first trimester	1.7 (0.2)	1.7 (0.2)	0.3
In the second trimester	1.6 (0.3)	2.1 (0.2)	**<0.001**
In the third trimester	1.5 (0.4)	2.2 (0.3)	**<0.001**
At the time of diagnosis	1.5 (0.3)	2.0 (0.4)	**<0.001**
Postpartum	1.4 (0.3)	2.2 (0.3)	**<0.001**
Selenium			
In the first trimester	0.5 (0.1)	0.5 (0.1)	0.7
In the second trimester	0.4 (0.1)	0.7 (0.1)	**<0.001**
In the third trimester	0.4 (0.2)	0.8 (0.2)	**<0.001**
At the time of diagnosis	0.4 (0.1)	0.6 (0.2)	**<0.001**
Postpartum	0.4 (0.1)	0.7 (0.2)	**<0.001**
Zinc			
In the first trimester	7.8 (0.9)	8.0 (0.9)	0.4
In the second trimester	7.7 (1.6)	10.5 (1,1)	**<0.001**
In the third trimester	7.8 (2.5)	12.1 (2.0)	**<0.001**
At the time of diagnosis	7.4 (1.6)	10.5 (2.2)	**<0.001**
Postpartum	7.4 (22)	12.1 (2.0)	**<0.001**
[1] Average (SD)			
[2] Student tests			

The analysis of this Table 5 shows that the mean micronutrient concentrations varied in the direction of increase in the supplementation group versus in the direction of decrease in the control group. The difference was statistically significant for all averages from the second trimester onwards.

II.3. Secondary Outcomes

Table 3 will present the comparative secondary results in the two groups.

Table 3: Presentation of cases according to maternal-fetal complications and pregnancy outcome

Parameter	Placebo group		Supplementation group	P-value	
	N=49	%	N=47	%	
Preterm delivery	11	22.4	4	8.5	0.03
Intrauterine growth restriction	13	26.5	5	10.6	0.02
Gestational hypertension	15	30.6	7	14.9	0.04
HELLP sydrom	3	6.1	1	2.1	0.029
Maternal anaemia	19	38.8	8	17.0	0.01
Died in utero	4	8.2	1	2.1	0.31
Neonatal asphyxia	14	28.6	5	10.6	0.02
Fetal macrosomia	2	4.1	3	6.4	0.61

Reading this table informs us that the rate of preterm delivery was higher in the control group (22.4%) than in the intervention group (8.5%) with a p-value of 0.03; the same was true for IUGR: 26.5% versus 10.6% (p-value=0.02) and gestational hypertension: 30.6% versus 14.9% (p-value: 0.04). Neonatal asphyxia was more observed in the control group than in the intervention group: 28.6% versus 10.6%.

Table 4: Mean weight, APGAR and gestational age

Parameter	Placebo group	Supplementation group	P-value
	n=49	n=47	
Average birth weight (in gramme)	2780 ± 510	3190 ± 420	<0.001
Gestational age at delivery (in week)	36.8 ± 2.1	38.5 ± 1.2	0.002
APGAR SCORE at 5 minutes	7.8 ± 2.1	8.9 ± 0.7	0.01

The mean gestational age at delivery was higher in the supplemented pregnant women than those who received placebo: 38.5 ± 1.2 weeks versus 36.8 ± 2.1 weeks (see table 4).

DISCUSSION

The present research compared the effects of supplementation of deficiency micronutrients (calcium, selenium and zinc) in pregnant women in two groups, one of which received placebo and the other micronutrients, on morbidities probably related to preeclampsia. The two randomization groups had comparable socio-demographic, clinical and biological characteristics (see Table 1, 2,3 and 4). The results observed had pointed out that most morbidities related to the occurrence of preeclampsia were not common in the intervention group than in the control group.

This observation could suggest that micronutrient supplementation (especially deficient) in a population of pregnant women with low or low micronutrient concentrations reduces the risk of developing preeclampsia, and consequently the reduction of certain consequences related to the latter.

The literature insists on the synergistic effects in the actions of trace elements in pregnant women with increased needs for the maintenance of maternal metabolism and fetal growth for a successful pregnancy [19-21], this fact could justify the results observed in this research conducted in Kisangani by our team.

By seeing the individual actions of these trace elements (calcium, selenium and zinc), we notice a similarity and certain particularities for each. This fact justifies the expected or more marked results when supplementation is combined or made with multiple micronutrients than when this supplementation is done with only one trace element [22,20]. Selenium works synergistically with calcium and zinc to stabilize mitochondrial membranes that are targets of oxidative damage for the release of toxic forms of oxygen. This association potentiates antioxidant and immune defenses, particularly in a deficient population [22,23].

In Iran, in a double-blind, randomized controlled trial, Ziba Zahiri S. *et al.,* observed that the incidence of preeclampsia was 4.8% in the micronutrient supplemented group and 4.1% in the nonsupplemented group. And the difference between the two groups was not statistically significant (p=0.835); The cases of preterm delivery and in utero death were similar in the two groups [24]. Compared to our research, in this study, the authors had mentioned a lack of strict verification of compliance with home supplementation (a limitation in the direct assessment of treatment adherence). The absence of placebo was also noted in the control group. And here, supplementation started from 16 weeks of amenorrhea, whereas in our case, it was from 13 weeks

of amenorrhea on average, in addition to the low or low serum concentration of trace elements in the respondents.

Sen Chena *et al.,*[25], in a randomized, double-blind, three-arm controlled clinical trial comparing supplementations of one, two, and multiple trace minerals for the prevention of preeclampsia; they observed an overall incidence per group of 7.1%; 6.3% and 6.3%; with a reduction of this incidence by 18% in pregnant women who received supplementation with several (multiple) trace elements: ORa of 0.81 (95% CI: 0.67-0.96). This research was only conducted in pregnant women from rural areas of northern China, of normal weight, without anemia with sometimes a lack of data on proteinuria, which would have influenced the diagnosis of preeclampsia justifying these low incidences of preeclampsia. This selection of pregnant women limits the generalization of the results to urban populations or women with different clinical profiles.

The particularity of our study lies in the selection of cases considering the low concentration of trace elements and the early start of supplementation, especially in trace elements that are deficient or at low concentrations. Micronutrients have often been implicated in favorable pregnancy outcomes [26,27], which justifies the reduction of several morbidities in pregnant women in the intervention group than in the control group. This observation is in line with the data in the literature which stipulates that selective supplementation with trace elements is most often associated with a reduction in the risks of preeclampsia, inflammation, oxidative stress and maternal-fetal complications. The benefits appear to be more pronounced in pregnant women at risk or deficient [28-30].

Limitations of the study

One of the strengths of the present study is that it compared supplementation with deficiency trace elements in a well-identified population to a placebo. Although there is an abundant literature on micronutrient supplementation during pregnancy; Most of them are made up of one or two trace elements [24,25,31,32-37], and often the deficit or deficiency of these elements is not determined from the outset in order to hope for an expected effect [38-41], which is necessary especially for our environments with limited resources. The other strength is related to the methodology used. First, the selected cases had a low concentration of trace elements, the "double-blind" randomization limits the influence of the investigators on the results of the study. In addition, the fact of comparing two homogeneous groups of pregnant women, whose socio-demographic and clinical characteristics were similar, and whose low or low concentration of trace elements (calcium, selenium and zinc) was the only indication for supplementation, makes it possible to attribute the results obtained to the effects of these trace elements. The evaluation of the serum concentration of these trace elements in the monitoring of pregnant animals is a simple, practical and easy way to carry out even in developing countries. Among the weaknesses of this research, the evaluation of the diet of pregnant women had not been carried out. This did not make it possible to determine the daily intake of trace elements in addition to supplementation.

CONCLUSION

Deficiency micronutrient supplementation in pregnant women can be safely used in the fight against preeclampsia in resource-limited settings. Early supplementation with trace elements has shown a remarkable reduction in the risk or incidence of preeclampsia in pregnant women with deficiency, thus minimizing some complications related to the occurrence of this morbid entity.

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