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Trace Element Supplementation and Serum Levels in Pregnant Women: A Randomized Double-Blind Trial in Kisangani, Democratic Republic of the Congo

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Abstract

Introduction: The evolution of pregnancy demands increased energy and an enhanced supply of nutrients to support optimal fetal growth. This study aims to investigate the effects of trace element supplementation on the concentrations and fluctuations of these elements in the serum of pregnant women in Kisangani, Democratic Republic of the Congo. **Methods:** This was a double-blind, randomized controlled trial that compared two regimens of supplementation in pregnant women with deficiencies in micronutrients such as calcium, selenium, and zinc. The study evaluated a supplement containing calcium, selenium, and zinc against a placebo. Research was conducted in Kisangani from January 10, 2024, to October 10, 2024. All statistical analyses were performed using R software, version 4.3.0. **Results:** The mean age of pregnant women was 28.1 ± 5.6 years versus 24.5 ± 5.7 years; and the mean BMI was 26.3 ± 3.2 kg/m^2 versus 25.1 ± 3.4 kg/m^2, in the control group and in the intervention group, respectively. In terms of trace element concentrations, there was an increase in the supplementation group, whereas a decrease was observed in the control group. Notably, the selenium concentration in the intervention group was elevated at 0.8 micromol/L, compared to a stable concentration of 0.4 micromol/L in the control group. **Conclusion:** Supplementation with micronutrients deficiency during pregnancy is a simple alternative to use in deficient pregnant women, which is very useful for increasing their concentrations, which are necessary for a good evolution of pregnancy and the fight against certain morbidities that can hinder the proper evolution and favorable outcome of pregnancy.

Keywords

Trace Element, Zinc, Calcium, Selenium, Pregnant Woman, Concentrations, Fluctuations

1. Introduction

Immediately after conception, physiological changes in the maternal body begin and affect the body systems, including the endocrine, cardiovascular, hematological, gastrointestinal, skeletal, and respiratory systems [1], leading to changes in maternal nutritional needs. During pregnancy, these physiological changes are summarized as usual adaptations intended to prepare the fetus for growth and the mother for normal labor [2].

Pregnancy requires an increased intake of energy and nutrients from the maternal body to support optimal fetal growth [3]. Micronutrients, including essential vitamins and minerals, play an important role in the health of pregnant women and the growing fetus [4]. Trace minerals can be used as cofactors and coenzymes for nutrient metabolism and are useful in preventing different diseases in pregnant women [5]. The need for trace minerals increases more than dietary energy needs increase during pregnancy [6]. Micronutrients deficiencies are common among pregnant women in low- and middle-income countries, particularly in sub-Saharan Africa, due to a lack of dietary diversity and food fortification [7].

Insufficient intake of micronutrients during pregnancy can lead to deficiencies that result in anemia, hypertension, various complications during labor, maternal death, stillbirth, premature delivery, intrauterine growth restriction, birth defects, decreased immune capacity, and fetal hypotrophy [8].

Maternal undernutrition is a common public health problem and a key driver of poor perinatal outcomes in sub-Saharan Africa [9]. Pregnant women are primarily vulnerable to the effects of trace element deficiency due to the high needs of the growing fetus, placenta, and maternal tissues [10]. Failure to meet these increased needs has potentially harmful consequences for both the mother and the fetus [11].

In low- and middle-income countries, many women have poor diets and lack nutrients and micronutrients essential for good health, leading to multiple micronutrient deficiencies [12]. During pregnancy, these women are at increased risk of multiple deficiencies and often suffer from greater deficiencies. These deficiencies are exacerbated due to the increased needs of the growing fetus, the placenta and maternal tissues. Failure to meet increased needs/demands leads to potentially adverse effects on both mother and fetus [13].

Currently, there are insufficient clinical studies assessing the effectiveness of trace element supplementation on the fluctuations of various trace elements during pregnancy. Most previous research has been conducted after the 20-week mark and often focuses on just one or two trace minerals at most [14]. Supplementation with trace elements initiated early, between 8 and 14 weeks of gestation, may have better results in the prevention of adverse pregnancy outcomes than that administered late.

Due to the limited research on micronutrient supplementation in sub-Saharan Africa, we found it appropriate to conduct this study in the city of Kisangani, in order to evaluate the effects of micronutrient supplementation on micronutrient concentrations in pregnant women with a low concentration.

The objectives of this study are to assess the effects of micronutrient supplementation on the serum concentrations of these trace elements in pregnant women in Kisangani, Democratic Republic of the Congo. Additionally, we aim to examine the fluctuations in these micronutrient concentrations throughout pregnancy.

2. Materials and Methods

2.1. Type and Terrain of the Study

This study was a double-blind, randomized controlled trial that compared two types of supplements in pregnant women with micronutrient deficiencies, specifically in calcium, selenium, and zinc. The two groups were given either supplements containing calcium, selenium, and zinc or placebo supplements. The investigators and the pregnant women did not know which treatment (supplementations) each of the participants was receiving.

The participants were recruited from eight health facilities located in Kisangani, Democratic Republic of the Congo. These facilities included the Makiso-Kisangani General Referral Hospital, Kabondo General Referral Hospital, Mangobo General Referral Hospital, Lubunga General Referral Hospital, Matete Referral Health Center, Saint Joseph Referral Health Center, Social Foyer Referral Health Center, and Kisangani University Clinics.

2.2. 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 in order to participate in the study.

Based on the research of Gunabalasingam *et al.* [15], the minimum sample size was calculated with 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. It was 88 individuals. To compensate for an anticipated 10% attrition rate (approximately 8 participants), the total sample size was adjusted to 96 participants, with 48 allocated to each arm. The study was therefore designed with two groups: one arm comprising 48 pregnant women supplemented with trace elements (calcium, selenium, and zinc) and the other arm comprising 48 pregnant women receiving a placebo.

2.3. Selection Criteria

2.3.1. 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 and not being on any other form of micronutrient supplementation.

2.3.2. Non-Inclusion Criteria

Pregnant beyond the first trimester of pregnancy and not having consented to participate in the study, pregnant with chronic high blood pressure, or pregnant and on other forms of micronutrient supplementation.

2.3.3. Exclusion Criteria

Pregnant women who have experienced intolerable side effects during supplementation, pregnant women who have personally decided to leave the research with or without a valid reason, and women who received other forms of supplementation during the study. The criteria for Discontinuation of Supplementation (Treatment) are:

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

2.4. Flow Chart of Study Design and Enrolment of Pregnant Women

Out of a total of 196 pregnant women selected, 94 were excluded because they did not meet the inclusion criteria or did not consent to participate in this research; 102 others were included. A total of 102 pregnant women were recruited for the study and randomly assigned to two groups: 51 women received micronutrient supplementation (the intervention group), while the other 51 received a placebo (the control group). Throughout the follow-up period, none of the participants experienced any severe side effects. In the intervention group, 3 pregnant women were removed from the analyses due to being lost to follow-up, compared to 2 women from the control group (**Figure 1**).

2.5. 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), one health facility representative, one doctor, one nurse, one medical biologist, and one community liaison. 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.

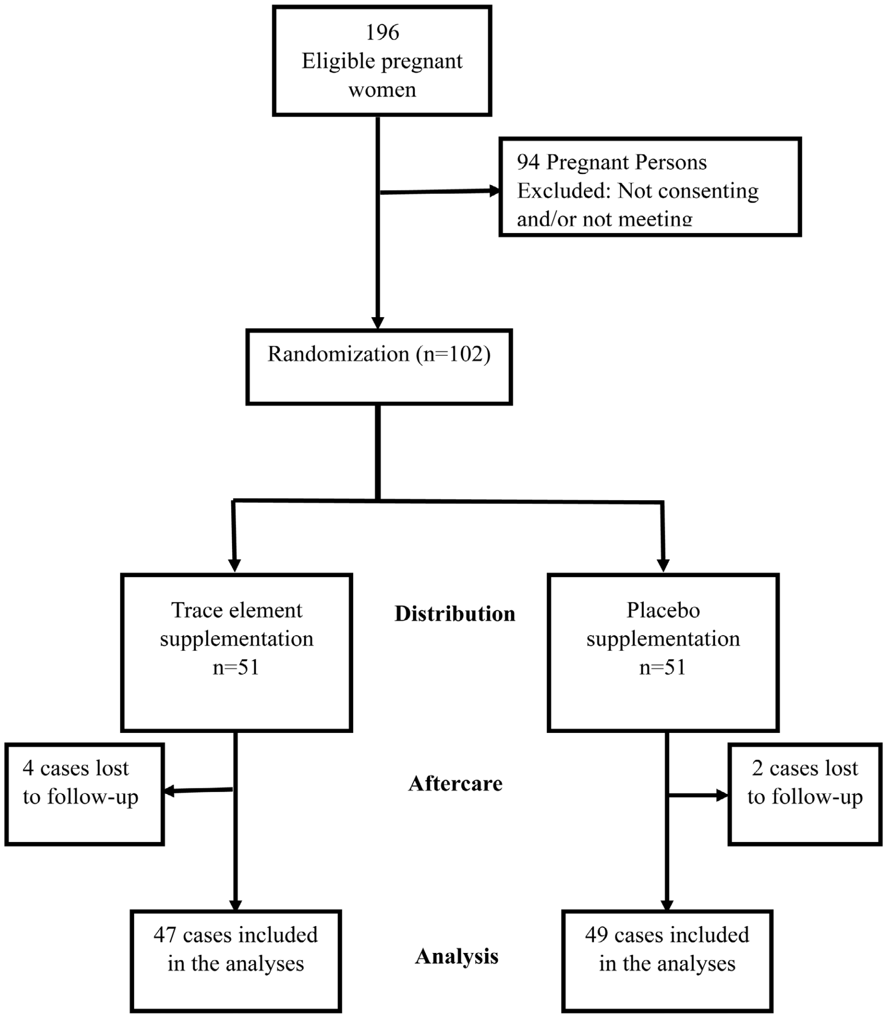


Figure 1. Flow chart of study design and Enrolment of pregnant women.

Upon admission, personal data was collected alongside measurements of trace element concentrations in all consenting pregnant women. This approach effectively identified women with trace element deficiencies, allowing for their integration into further research. In addition to collecting socio-demographic data, the medical history also included the date of the last menstrual period and inquiries about previous pregnancies to assess any history 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/m^2) and age (<30 years vs. ≥30 years). These randomization blocks were established on the basis of 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 600 mg/day), selenium tablets 65 μg (organic selenium 65 mg) and zinc tablets 15 mg. In the control group, participants received three placebo tablets: two white tablets for calcium and zinc, and a red tablet for selenium, all made from 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 health workers visited the selected pregnant women every seven days to ensure they were taking their medication by counting the remaining tablets. A follow-up appointment was scheduled after four weeks for clinical evaluation, monitoring of any adverse drug reactions, and conducting necessary paraclinical tests. At each prenatal consultation appointment, pregnant women brought the medication envelopes from their previous visit. This allowed the doctor and nurse to verify their compliance with the prescribed medication. After assessing the situation, the pregnant woman would receive a second envelope containing the same code as the first one.

All the 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 characteristics of the medicinal products used in this research are presented in **Table 1**.

2.6. 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 were informed about the adverse effects of the trace elements in the study and asked to report any issues. 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 conducted each time respondents reported a side effect. This information was gathered when pregnant women attended antenatal consultations and picked up their next batch of supplementation.

Table 1. Characteristics of the drugs used in this research.

Drug	Trade Name	Dosage Form	Manufacturer	Batch No.	Expiry Date
Calcium carbonate	Caltrate	600 mg film-coated tablet, 30 tablets/box	Pfizer Consumer Manufacturing, Italy	488R	January 2025
Selenium	Organic yeast selenium 65 µg	65 µg capsule, 30 capsules/box	Granions Laboratory, France	SE338J	December 2026
Zinc	Zinc 15 mg	15 mg capsule, 30 capsules/box	Granions Laboratory, France	CO20	October 2026
Placebo	Placebo	100 mg tablet	Granions Laboratory, France	PX356S	November 2025

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. Pregnant women who experienced mild to moderate adverse effects were required to be monitored on an outpatient basis. Those with severe symptoms needed to be hospitalized at one of the facilities involved in the research, preferably close to their residence. At the midpoint of the study, data on any adverse effects had to be reported to the ethics committees of the University of Kisangani and the health committee to obtain approval for the continuation of the trial.

2.7. Laboratory Examination

Serum micronutrient assays were conducted using Agilent 7700X inductively coupled plasma mass spectrometry (ICP-MS). Measurements were taken at baseline (13 weeks of amenorrhea), at 23 and 33 weeks, and at the time of preeclampsia diagnosis.

2.8. Expected Results

The primary outcomes targeted in this research were 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.

2.9. 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 assign pregnant women to specific groups, a sequence was generated using Excel software.

The Pearson χ^2 test at the significance level of $p < 0.05$ was calculated to compare proportions. The Fisher's 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, a t-Student test was conducted. We tested the homogeneity of variances between the two assignment groups. A difference was considered significant when the P-value was less than 0.001. To account for confounding factors, we performed a multivariate logistic regression analysis. All statistical analyses were carried out using R software version 4.3.0.

2.10. Ethical Considerations

This study was approved by the Ethics Committee of the University of Kisangani, UNIKIS/CER/024/2023 on the 7th of June 2023, and the Ethics Committee of the School of Public Health at the University of Kinshasa: ESP/CE/43/2024.

2.11. 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[15] and the ESPEN Micronutrient guideline [16].

2.12. Expression of Interest

We have no conflicts of interest to declare for this work

3. Results

3.1. Socio-Demographic Characteristics of the Respondents

The Placebo group and the Micronutrients group are the two randomization groups that are compared in the data in Table 2. These groups were evaluated according to a number of criteria, such as the pregnant women's age, place of residence, education, marital status, employment, parity, height, weight, and body mass index (BMI).

In the intervention group, which was supplemented with trace elements, the average age of pregnant women was 24.5 ± 5.7 years, whereas in the control group, which was given a placebo, the average age was 28.1 ± 5.6 years. The control group's mean BMI was 26.3 ± 3.2 kg/m^2, while the intervention group's was 25.1 ± 3.4 kg/m^2.

Table 2. Socio-demographic characteristics of pregnant women.

Characteristic	Placebo N = 49	Supplementation N = 47	Total N = 96
Age (years)			
<30 years	31 (63.3%)	38 (80.9%)	69 (71.9%)
≥30 years	18 (36.7%)	9 (19.1%)	27 (28.1%)
Residence			
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%)
Education level			
Primary	4 (8.2%)	8 (17.0%)	12 (12.5%)
Secondary	34 (69.4%)	35 (74.5%)	69 (71.9%)
Higher/University	11 (22.4%)	4 (8.5%)	15 (15.6%)
Marital status			
Single	1 (2.0%)	7 (14.9%)	8 (8.3%)
Married	48 (98.0%)	40 (85.1%)	88 (91.7%)
Occupation			
Civil servant	2 (4.1%)	2 (4.3%)	4 (4.2%)
Trader	10 (20.4%)	4 (8.5%)	14 (14.6%)
Seamstress	1 (2.0%)	3 (6.4%)	4 (4.2%)
Farmer	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			
Grand 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%)

Continued

Primiparous	14 (28.6%)	16 (34.0%)	30 (31.3%)
Secundiparous	12 (24.5%)	11 (23.4%)	23 (24.0%)
Weight (Kg), mean (SD)	66.8 (7.8)	64.0 (8.4)	65.4 (8.2)
Height (cm), mean (SD)	159.4 (6.5)	159.7 (5.8)	159.6 (6.1)
BMI (Kg/m^2)			
<25	19 (38.8%)	27 (57.4%)	46 (47.9%)
≥25	30 (61.2%)	20 (42.6%)	50 (52.1%)

3.2. Averages of Trace Elements During Pregnancy

The various study groups' average trace element concentrations during pregnancy are displayed in Table 3. This table's analysis demonstrates that the supplementation group's mean micronutrient concentrations varied in a direction of rise, whereas the control group's concentrations varied in a direction of decline. From the second trimester forward, the difference was statistically significant for all averages.

Table 3. Average trace element concentrations during pregnancy in both groups.

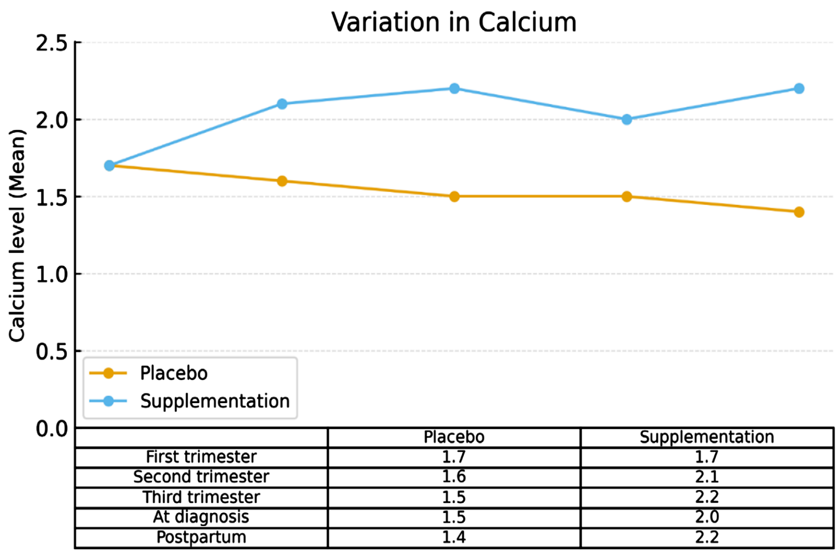
Characteristic	Placebo (N = 491)	Supplementation (N = 471)	p-value[2]
	Calcium		
First trimester	1.7 (0.2)	1.7 (0.2)	0.3
Second trimester	1.6 (0.3)	2.1 (0.2)	<0.001
Third trimester	1.5 (0.4)	2.2 (0.3)	<0.001
At diagnosis	1.5 (0.3)	2.0 (0.4)	<0.001
Postpartum	1.4 (0.3)	2.2 (0.3)	<0.001
	Selenium		
First trimester	0.5 (0.1)	0.5 (0.1)	0.7
Second trimester	0.4 (0.1)	0.7 (0.1)	<0.001
Third trimester	0.4 (0.2)	0.8 (0.2)	<0.001
At diagnosis	0.4 (0.1)	0.6 (0.2)	<0.001
Postpartum	0.4 (0.1)	0.7 (0.2)	<0.001
	Zinc		
First trimester	7.8 (0.9)	8.0 (0.9)	0.4
Second trimester	7.7 (1.6)	10.5 (1.1)	<0.001
Third trimester	7.8 (2.5)	12.1 (2.0)	<0.001
At diagnosis	7.4 (1.6)	10.5 (2.2)	<0.001
Postpartum	7.4 (2.2)	12.1 (2.0)	<0.001

[1]Mean (SD), [2]Student's *t*-test.

3.3. Serum Fluctuations of the Different Trace Elements

3.3.1. Serum Calcium Fluctuation

Pregnant women's fluctuations in blood calcium levels are seen in Figure 2. According to this figure, the third trimester and postpartum periods in the intervention group had the greatest calcium content (2.2 mmol/L), whereas the postpartum period had the lowest value in the control group.

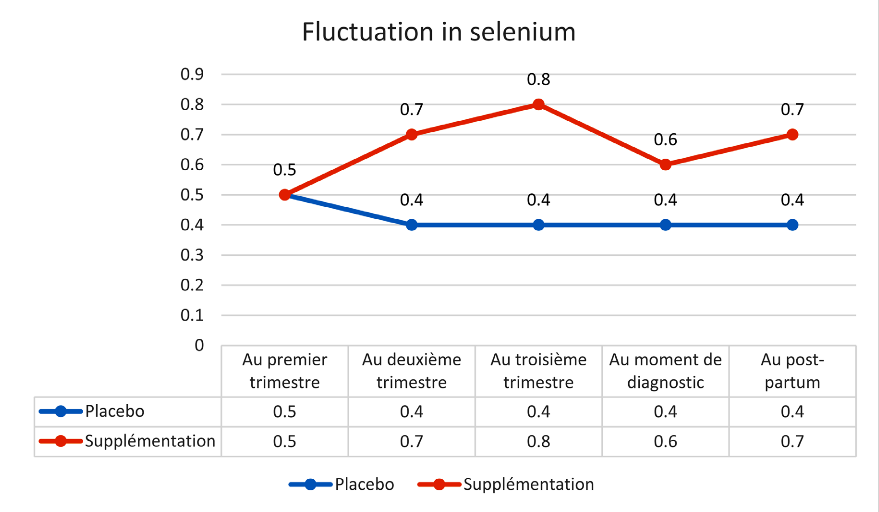


	Placebo	Supplementation
First trimester	1.7	1.7
Second trimester	1.6	2.1
Third trimester	1.5	2.2
At diagnosis	1.5	2.0
Postpartum	1.4	2.2

Figure 2. Change in calcium concentration in the two groups.

3.3.2. Serum Fluctuation of Selenium Concentration

Variations in pregnant women's serum selenium concentrations are seen in Figure 3. The selenium level in the control group was constant from the second trimester to the postpartum period, at 0.4 micromol/l, whereas the intervention group's high concentration of selenium was recorded in the third trimester of pregnancy, at 0.8 micromol/l.

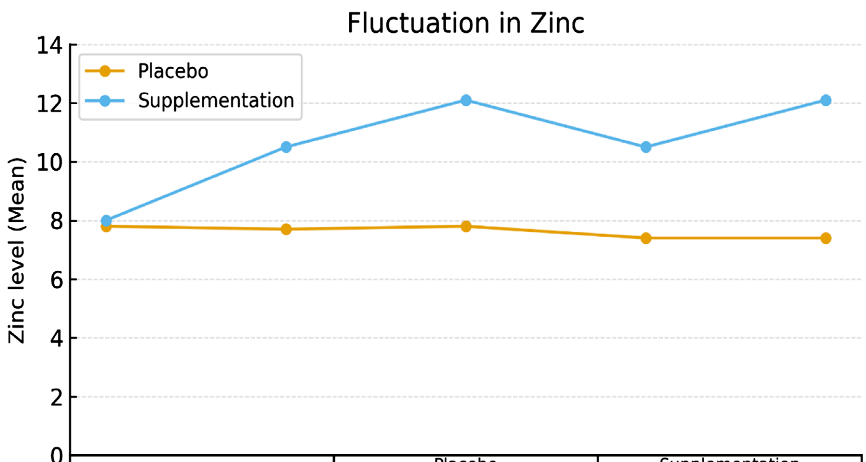


	Au premier trimestre	Au deuxième trimestre	Au troisième trimestre	Au moment de diagnostic	Au post-partum
Placebo	0.5	0.4	0.4	0.4	0.4
Supplémentation	0.5	0.7	0.8	0.6	0.7

Figure 3. Oscillation of serum selenium concentration in pregnant women.

3.3.3. Serum Fluctuations in Zinc Concentration in Pregnant Women

Analysis of this figure reveals that the intervention group's highest serum zinc concentration, 12.1 micromole/l, was recorded during the third trimester of pregnancy and the postpartum period, while the control group's zinc concentration was low during the preeclampsia diagnosis and the postpartum period, 7.4 micromole/day.



	Placebo	Supplementation
First trimester	7.8	8.0
Second trimester	7.7	10.5
Third trimester	7.8	12.1
At diagnosis	7.4	10.5
Postpartum	7.4	12.1

Figure 4. Oscillation of serum zinc concentration in the 2 groups.

4. Discussion

The current research evaluated the effects of supplementation of deficient micronutrients (calcium, selenium and zinc) in pregnant women in two groups, one of which received placebo and the other micronutrients, on the variation of micronutrients in pregnant women's serums. According to **Table 2** and **Table 3**, the two randomization groups had similar clinical, biochemical, and sociodemographic characteristics. According to the observed data, pregnant women who took micronutrient supplements showed a greater variation of trace elements than those who got a placebo.

During pregnancy, the demand for trace elements increases to meet or cover maternal needs for pregnancy maintenance and fetal growth to term. The values or concentrations of trace elements therefore vary in both directions (decrease and/or increase), which can lead to nutritional deficiencies if the dietary or supplement intake does not cover this deficit. This study revealed that the two groups' serum micronutrient concentrations varied in both directions. Micronutrient concentrations in the micronutrient supplementation group rose during the trimesters to normal levels before falling while staying within the lower bounds of normalcy. Additionally, all trace elements in supplements fall within this category (**Figures 2-4**). However, in the control group, micronutrient concentrations decreased over time with no tendency to return to the values recorded at the beginning of pregnancy. Nevertheless, the low selenium concentration had stabilized at this value for quite some time in the pregnant women in the control group (**Figures 2-4**). These two phenomena in both groups would be justified by the increase in the metabolism of the gravid organism for the balance of pregnancy and fetal growth, thus leading to an increased consumption or demand for trace elements. This would explain why these different trace elements are not maintained at stable or uniform values, regardless of the group evaluated.

The research of Rihwa C. *et al.* [17] was notable for the oscillations of micronutrient concentrations during pregnancy. They observed that the bioavailability of trace elements was affected by the season of sampling (seasonal variations), with higher levels in spring, summer, and autumn compared to winter, in addition to variations over the trimesters of pregnancy. This observation led them to believe that a seasonal diet (consumption of rice, vegetables, fruits, and seafood) [18] was a factor in addition. Certain demographic and behavioral factors, such as age, body mass index (BMI), education level, intake of iron or multivitamin supplements, and passive exposure to tobacco, have been associated with changes in micronutrient levels [17] [18]. The examination of the concentration levels of trace elements throughout our investigation did not properly account for these various parameters or the meteorological seasons.

Several factors, such as age, place of residence, anthropometric status, and stage of pregnancy, allow a precise and contextualized interpretation of the results on fluctuations in micronutrient concentrations in pregnant women. These variations are likely related to physiological changes during pregnancy, environmental exposure, or differences in the nutrition and lifestyle of pregnant women [19] [20].

Another important piece of information that emerged from this study is related to the side effects observed during supplementation or excessive intake of micronutrients. No side effects were reported by the respondents, let alone by the research team. We believe that this phenomenon could be explained by the dose of trace elements administered. This is in line with the data in the literature on the rarity of side effects when the recommended dosages are adhered to in a state of deficiency or deficiency of the trace element concerned [21] [22].

5. Limitations of the Study

Among the weaknesses of this research, we note that the evaluation of the diet of pregnant women had not been carried out. This did not make it possible to determine the effects of daily micronutrient intakes on micronutrient concentrations in pregnant women.

6. Conclusion

Supplementation with micronutrients in pregnant women can be used safely to improve their concentrations in the resource-limited environment, especially when initiated early in pregnancy. The effectiveness of this supplementation will be significantly greater than in cases where trace elements were previously found in trace amounts.

Conflicts of Interest

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

References

[1] Soma-Pillay, P., Nelson-Piercy, C., Tolppanen, H. and Mebazaa, A. (2016) Physiological Changes in Pregnancy. *Cardiovascular Journal of Africa*, **27**, 89-94. https://doi.org/10.5830/cvja-2016-021

[2] Meo, S.A. and Hassain, A. (2016) Metabolic Physiology in Pregnancy. *Journal of the Pakistan Medical Association*, **66**, S8-S10.

[3] Lowensohn, R.I., Stadler, D.D. and Naze, C. (2016) Current Concepts of Maternal Nutrition. *Obstetrical & Gynecological Survey*, **71**, 413-426. https://doi.org/10.1097/ogx.0000000000000329

[4] Black, R.E. (2001) Micronutrients in Pregnancy. *British Journal of Nutrition*, **85**, S193-S197. https://doi.org/10.1079/bjn2000314

[5] Shonibare, M.T., Oyinloye, B.E. and Ajiboye, B.O. (2021) Roles of Micronutrients in Pregnancy. *Letters in Applied NanoBioScience*, **10**, 2605-2613.

[6] Marangoni, F., Cetin, I., Verduci, E., Canzone, G., Giovannini, M., Scollo, P., *et al*. (2016) Maternal Diet and Nutrient Requirements in Pregnancy and Breastfeeding. An Italian Consensus Document. *Nutrients*, **8**, Article No. 629. https://doi.org/10.3390/nu8100629

[7] Black, R.E., Victora, C.G., Walker, S.P., Bhutta, Z.A., Christian, P., de Onis, M., *et al*. (2013) Maternal and Child Undernutrition and Overweight in Low-Income and Middle-Income Countries. *The Lancet*, **382**, 427-451. https://doi.org/10.1016/s0140-6736(13)60937-x

[8] Ramakrishnan, U., Manjrekar, R., Rivera, J., Gonzáles-Cossío, T. and Martorell, R. (1999) Micronutrients and Pregnancy Outcome: A Review of the Literature. *Nutrition Research*, **19**, 103-159. https://doi.org/10.1016/s0271-5317(98)00178-x

[9] Tang, A.M., Chung, M., Dong, K.R., Bahwere, P., Bose, K., Chakraborty, R., *et al*. (2020) Determining a Global Mid-Upper Arm Circumference Cut-Off to Assess Underweight in Adults (Men and Non-Pregnant Women). *Public Health Nutrition*, **23**, 3104-3113. https://doi.org/10.1017/s1368980020000397

[10] Keats, E.C., Das, J.K., Salam, R.A., Lassi, Z.S., Imdad, A., Black, R.E., *et al*. (2021) Effective Interventions to Address Maternal and Child Malnutrition: An Update of the Evidence. *The Lancet Child & Adolescent Health*, **5**, 367-384. https://doi.org/10.1016/s2352-4642(20)30274-1

[11] Berti, C., Biesalski, H.K., Gärtner, R., Lapillonne, A., Pietrzik, K., Poston, L., *et al*. (2011) Micronutrients in Pregnancy: Current Knowledge and Unresolved Questions. *Clinical Nutrition*, **30**, 689-701. https://doi.org/10.1016/j.clnu.2011.08.004

[12] Leal, L.F., Grandi, S.M., Miranda, V.I.A., Dal Pizzol, T.d.S., Platt, R.W., Silveira, M.F.d., *et al*. (2020) Hypertensive Disorders of Pregnancy and Medication Use in the 2015 Pelotas (Brazil) Birth Cohort Study. *International Journal of Environmental Research and Public Health*, **17**, Article No. 8541. https://doi.org/10.3390/ijerph17228541

[13] Wang, Y., Arvizu, M., Rich-Edwards, J.W., Wang, L., Rosner, B., Stuart, J.J., *et al*. (2021) Hypertensive Disorders of Pregnancy and Subsequent Risk of Premature Mor-

tality. *Journal of the American College of Cardiology*, **77**, 1302-1312. https://doi.org/10.1016/j.jacc.2021.01.018

[14] Beazley, D., Ahokas, R., Livingston, J., Griggs, M. and Sibai, B.M. (2005) Vitamin C and E Supplementation in Women at High Risk for Preeclampsia: A Double-Blind, Placebo-Controlled Trial. *American Journal of Obstetrics and Gynecology*, **192**, 520-521. https://doi.org/10.1016/j.ajog.2004.09.005

[15] Gunabalasingam, S., De Almeida Lima Slizys, D., Quotah, O., Magee, L., White, S.L., Rigutto-Farebrother, J., *et al*. (2022) Micronutrient Supplementation Interventions in Preconception and Pregnant Women at Increased Risk of Developing Pre-Eclampsia: A Systematic Review and Meta-Analysis. *European Journal of Clinical Nutrition*, **77**, 710-730. https://doi.org/10.1038/s41430-022-01232-0

[16] Alexander, S.P.H., Mathie, A., Peters, J.A., Veale, E.L., Striessnig, J., Kelly, E., *et al*. (2021) The Concise Guide to Pharmacology 2021/22: Ion Channels. *British Journal of Pharmacology*, **178**, S157-S245. https://doi.org/10.1111/bph.15539

[17] Choi, R., Sun, J., Yoo, H., Kim, S., Cho, Y., Kim, H., *et al*. (2016) A Prospective Study of Serum Trace Elements in Healthy Korean Pregnant Women. *Nutrients*, **8**, Article No. 749. https://doi.org/10.3390/nu8110749

[18] Liang, C., Wu, X., Huang, K., Yan, S., Li, Z., Xia, X., *et al*. (2019) Trace Element Profiles in Pregnant Women's Sera and Umbilical Cord Sera and Influencing Factors: Repeated Measurements. *Chemosphere*, **218**, 869-878. https://doi.org/10.1016/j.chemosphere.2018.11.115

[19] Liu, X., Zhang, Y., Piao, J., Mao, D., Li, Y., Li, W., *et al*. (2017) Reference Values of 14 Serum Trace Elements for Pregnant Chinese Women: A Cross-Sectional Study in the China Nutrition and Health Survey 2010-2012. *Nutrients*, **9**, Article No. 309. https://doi.org/10.3390/nu9030309

[20] Santander Ballestín, S., Giménez Campos, M.I., Ballestín Ballestín, J. and Luesma Bartolomé, M.J. (2021) Is Supplementation with Micronutrients Still Necessary during Pregnancy? A Review. *Nutrients*, **13**, Article No. 3134. https://doi.org/10.3390/nu13093134

[21] Cheftel, H. and Truffert, L. (1972) Oligo-éléments et leur toxicité dans l'alimentation de l'homme. *Annales de la nutrition et de l'alimentation*, **26**, B521-B561.

[22] Stojsavljević, A., Rovčanin, M., Rovčanin, B., Miković, Ž., Jeremić, A., Perović, M., *et al*. (2021) Human Biomonitoring of Essential, Nonessential, Rare Earth, and Noble Elements in Placental Tissues. *Chemosphere*, **285**, Article ID: 131518. https://doi.org/10.1016/j.chemosphere.2021.131518