Comparison of Maternal Serum Level of Calcium, Copper, Zinc, and Selenium between Assisted and Spontaneous Pregnancy

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Abstract

Background: Pregnant women should get enough calcium (Ca), copper (Cu), zinc (Zn), and selenium (Se). The point of this study was to establish the levels of these elements in the serum of pregnant women with assisted pregnancy with respect to maternal age and body mass index (BMI) compared with spontaneous pregnancy. **Objectives:** Determine the levels of serum Ca, Cu, Zn, and Se between assisted and spontaneous pregnancy. **Materials and Methods:** The case groups consisted of 150 pregnancies in the first trimester, including 50 women with in vitro fertilization (IVF), 50 women with intrauterine insemination (IUI), 50 women with spontaneous pregnant (SP), and 50 apparently healthy nonpregnant women. Minerals were detected by using the conventional wet acid digestion method. **Results:** The present study showed a significant decrease in serum Ca and Se levels between groups of SP, IVF, and IUI with nonpregnant the mean are 9.02 ± 0.52, 9.018 ± 0.52, 9.014 ± 0.52, and 9.29 ± 0.31; 88.752 ± 4.87, 89.264 ± 4.43, 89.15 ± 5.71; and 91.224 ± 4.46, respectively. The serum Cu and Zn showed a nonsignificant change. A nonsignificant difference was seen between the different pregnant groups with age groups and the BMI, but the serum Se level showed a significant decrease with BMI ($P < 0.05$). **Conclusion:** Statistical analysis showed Se and Ca were at a significant decrease in serum levels in the 1st trimester between pregnant and nonpregnant women. The serum Cu showed a nonsignificant increase in the first trimester of pregnancy. There was no significant difference in these elements between different groups of pregnant women.

Keywords: Copper, in vitro fertilization, intrauterine insemination, selenium

Introduction

In pregnancy, the period of increased metabolic demand with a change in the woman's body physiology occurs due to the necessity of growing the fetus. During this time, inadequate intake of micronutrients or inadequate stores can have adverse effects on the mother and the fetus.[1] Calcium (Ca) is the most prevalent mineral in the human body and is necessary for numerous vital processes such as hormone and enzyme production, muscle contraction, bone development, and muscular contraction.[2] Due to hemodilution, total serum concentrations decrease during pregnancy. The homeostatic control system maintains the consistent Ca levels in the circulation.[3] Copper (Co) is important for the function of several cuproenzymes. Its deficiency can lead to a defect in adenosine triphosphate production; hormone activation, lipid peroxidation, angiogenesis, abnormalities of the skeleton, vasculature, and lung,[4,5] liver diseases,[6] hypochromic anemia, intrauterine growth retardation, and spontaneous abortion. Wilson's illness and Fenton's reagent can be brought on by hypercupremia, which can also increase the risk of preterm birth, low birth weight, and gestational diabetes.[7] Zinc is considered a cofactor of more than 300 enzymes, which adjust the different cellular processes and are essential for some cell divisions, cell differentiation, and organ growth. Zn can regulate the reproduction, development of the fetus, stability of membrane, digestion of nutrients, wound recovery,

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and the homeostasis of the central nervous system. Zn is also participating in bone mineralization and in the development of collagen makeup in the bone.[8,9] Selenium is a micronutrient element with antioxidant characteristics and is essential for the synthesis of different selenoenzymes like glutathione peroxidases, thioredoxin reductase, and selenoproteins (P), which can limit the oxidative damage.[10] During pregnancy, the maternal oxygen demand increases, and this increases the formation of reactive oxygen species, which is associated with the occurrence of adverse outcomes like gestational diabetes and intrauterine growth restriction.[11] Many researchers found that the concentrations of various trace elements like Ca, Cu, Zn, and Se vary during pregnancy; however, the majority of those studied the serological analysis of one micronutrient[12,13] or in women with different durations of pregnancy.[14,15] An essential component of maternal and fetal physiology during pregnancy is calcium homeostasis, and new research suggests that changes to calcium metabolism may contribute to the pathogenesis of pregnancy-related hypertension.[16]

Materials and Methods

Study design and selection criteria

The current prospective study was carried out at Taiba Centre for Infertility Treatment (IVF & ICSI) in Babylon/Iraq, from November 2022 to February 2023. This study was approved by the University/College of Babylon via the Medicine Ethical Committee. Consent was obtained from all pregnant and non-pregnant participants before the data were collected.

This study included 200 female selected healthy pregnant women with uncomplicated pregnancy, which were divided into four groups:

1. Fifty women with spontaneous pregnancy (SP).
2. Fifty women with intrauterine insemination (IUI).
3. Fifty women with in vitro fertilization (IVF).

These three groups had singleton pregnancies with live babies in the first trimester of pregnancy.

4. In addition, 50 apparently healthy nonpregnant women as a control group (NP).

Pregnant and nonpregnant participants who had past or present history of chronic diseases, infections, liver or kidney diseases, immunological disorders, alcohol, or smoking were excluded from the study.

Serum assay

Blood was aspirated from the Vein by using disposable syringes, which are left from 10 to 20 min at room temperature for clotting, and then put in a centrifuge at 3000 RPM for 20 min. A labeled Eppendorf is used to collect supernatant (serum) and then storage until usage in deep freeze at –20°C. The extraction and assay procedures for the studied minerals were done by adding a freshly made mixture of strong nitric acid and hydrogen peroxide (HNO_3–H_2O_2) to the traditional wet acid digesting process using flame atomic absorption spectrophotometry.[17]

Gestational age was calculated from the first day of the last menstrual cycle, and body mass index (BMI) was calculated using the formula weight/height^2.[18]

Statistical analysis

Analysis was carried out using SPSS statistical software version 23 (IBM). Descriptive statistics were drawn for all studied parameters. Assessment of normality was performed using the Kolmogorov–Smirnov test. Data were described as percentages and mean with standard deviation (SD). The level of significance between pregnant and nonpregnant women was analyzed using an independent *t*-test and Mann–Whitney *U* test for parametric and nonparametric variables, respectively. The age and BMI were analyzed using a one-way analysis of variance. Statistical significance was assumed at a *P*-value of <0.05.

Ethical approval

The study was carried out in conformity with the ethical standards set forth in the Helsinki Declaration. According to document number 11-1, a local ethics committee evaluated and approved the study protocol, subject information, and permission form on April 27, 2023.

Results

Biochemical parameters

Sample distribution

A total of 150 pregnant women in the first trimester of pregnancy with a mean age of 28.90 ± 5.97 years (P = 0.069) and 50 apparently healthy non-pregnant women with a mean age of 27.26 ± 6.84 years participated in the study. The highest number of pregnant and nonpregnant participants were seen within the age group (26–33) years. Regarding the BMI, the highest percentage of women with IVF were seen as obese, while the highest percentage of pregnant women with SP, IUI, or nonpregnant women were seen over overweight. No one of the participants was seen as underweight [Table 1].

Statistical analysis also showed nonsignificant differences between the pregnant groups of age and BMI.

Serological analysis results

Regarding the relation of the serum levels of Ca, Cu, Zn, and Se between the different pregnant and NP groups, statistical analysis showed that the serum Ca level showed a slight but significant decrease in pregnant in comparison with the NP group (P < 0.05).

The present study showed that the serum Cu and Zn showed a nonsignificant change in pregnant serum in comparison with NP. The serum Se showed a significant decrease in pregnancy in comparison with NP. There was a nonsignificant difference present among the different pregnant groups ($P < 0.05$) regarding the serum level of Ca, Cu, Zn, and Se, as shown in Table 2.

Statistical analysis also showed a nonsignificant difference present between the different age groups regarding the serum levels of all studied trace elements [Table 3]. The serum levels of Ca, Cu, and Zn showed a nonsignificant relation with the BMI, but the serum Se level showed a significant relation with the BMI, and it decreased significantly as the BMI increased [Table 4].

Discussion

Concentrations of different trace elements change during pregnancy, response to the needs of the growing fetus, and changes in the mother's physiological state.

The present study showed that the serum Ca decreased slightly but significantly ($P < 0.05$) in the 1st trimester of pregnancy in comparison with that of nonpregnant. Baig *et al.*[19] and Liu *et al.*[3] found the same result regarding the first trimester. The decrease could be a result of the mother's hemodilution and the increased requirement for calcium and inorganic phosphate during fetal growth.[20] According to additional research, the serum Ca level remained constant throughout pregnancy.[21] These results may be due to different socioeconomic status and nutritional intake or due to different pregnancy-associated hormones such as estrogen, progesterone, and placental lactogen.[2] Hypercalcemia in pregnancy is very rare, and most cases are associated with a newly diagnosed primary hyperparathyroidism.[22]

Regarding the relation of serum levels of Ca, Cu, Zn, and Se between the different studied groups with assisted pregnancy, the present study showed a nonsignificant difference present with that of the SP group. Grossi *et al.*[23] found that the values of the serum Ca do not

Table 1: Distribution of pregnant women according to the age groups and the body mass index (BMI)

Mean ± SD	(SP) No. 50	(IUI) No. 50	(IVF) No. 50	*P* value
Age	28.18±6.30	30.0±5.80	30.08±5.59	0.222
BMI	28.03±4.14	26.96±3.80	29.014±5.39	0.079
Age (years) and BMI (kg/m^2) groups		Pregnant (no. and %)		Total pregnant (no. and %)
	(SP)	(IUI)	(IVF)	
18–25	15 (30%)	12 (24%)	12 (24%)	39 (26.0%)
26–33	21 (42%)	21 (42%)	22 (44%)	64 (42.7%)
34–44	14 (28%)	17 (34%)	16 (32%)	47 (31.3%)
Total (no. and %)	50 (100%)	50 (100%)	50 (100%)	150 (100%)
Underweight (≤19.9)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Normal weight (20–24.9)	14 (28%)	18 (36%)	13 (26%)	45 (30%)
Overweight (25–29.9)	24 (48%)	20 (40%)	17 (34%)	61 (40.7%)
Obese (30 or more)	12 (24%)	12 (24%)	20 (40%)	44 (29.3%)
Total (no. and %)	50 (100%)	50 (100%)	50 (100%)	150 (100%)

*Significant at $P < 0.05$

Table 2: The relation of serum levels of calcium, copper, zinc, and selenium between the different studied groups

Group	Ca (mg/dL) mean ± SD	*P* value	Free Cu (μg/dL) mean ± SD	*P* value	Zn (μg/dL) mean ± SD	*P* value	Se (μg/L) mean ± SD	*P* value
NP	9.29±0.31	0.002*	1.652±0.02	0.081	94.117±10.41	0.452	91.224±4.46	0.018*
SP	9.02±0.52		1.701±0.24		91.795±18.87		88.752±4.87	
NP	9.29±0.31	0.002*	1.652±0.02	0.072	94.117±10.41	0.242	91.224±4.46	0.048*
IUI	9.018±0.52		1.694±0.19		87.564±17.55		89.15±5.71	
NP	9.29±0.31	0.002*	1.652±0.02	0.076	94.117±10.41	0.533	91.224±4.46	0.031*
IVF	9.014±0.52		1.691±0.18		89.837±11.16		89.264±4.43	
SP	9.02±0.52	0.98	1.701±0.240	0.435	91.795±18.87	0.252	88.752±4.87	0.696
IUI	9.018±0.52		1.694±0.19		87.564±17.55		89.15±5.71	
SP	9.02±0.52	0.95	1.701±0.240	0.411	91.795±18.87	0.533	88.752±4.87	0.575
IVF	9.014±0.52		1.691±0.18		89.837±11.16		89.264±4.43	
IUI	9.018±0.52	0.96	1.694±0.19	0.473	87.564±17.55	0.446	89.15±5.71	0.932
IVF	9.014±0.52		1.691±0.18		89.837±11.16		89.264±4.43	

* Significant $P < 0.05$

Table 3: Means ± SD of serum levels of calcium, copper, zinc, and selenium in the different pregnant groups according to the age

Biochemical test	Age group (year)	(SP) Mean ± SD	*P* value	(IUI) Mean ± SD	*P* value	(IVF) Mean ± SD	*P* value
Ca (mg/dL)	18–25	9.114±0.52	0 .71	9.121±0.51	0.61	8.862±0.41	0.75
	26–33	9.00±0.49		9.014±0.51		8.909±0.53	
	34–44	8.953±0.53		8.926±0.58		9.016±0.70	
Cu (μg/dL)	18–25	1.698±0.24	0.941	1.630±0.22	0.149	1.582±0.19	0.15
	26–33	1.690±0.27		1.655±0.23		1.652±0.21	
	Above 34	1.72±0.20		1.755±0.08		1.725±0.14	
Zn (μg/dL)	18–25	95.542±5.18	0.471	88.376±19.59	.510	93.002±11.27	0.329
	26–33	93.313±27.9		87.061±19.8		90.370±10.68	
	Above 34	87.486±12.97		81.196±15.08		86.754±11.84	
Se (μg/L)	18–25	87.437±4.53	0.487	86.9±4.08	0.31	88.875±5.02	0.142
	26–33	89.345±5.26		89.023±5.15		86.690±4.57	
	Above 34	88.05±4.57		90.4±7.87		89.343±3.22	

Table 4: Means ± SD of serum levels of calcium, copper, zinc, and selenium in the different pregnant groups according to the BMI

Biochemical test	BMI	(SP) Mean ± SD	*P* value	(IUI) Mean ± SD	*P* value	IVF mean ± SD	*P* value
Ca (mg/dL)	Normal weight	9.20±0.55	0.42	9.075±0.55	0.90	9.3±0.50	0.08
	Overweight	9.024±0.53		9.00±0.51		9.0±0.55	
	Obese	8.846±0.46		8.988±0.55		8.922±0.48	
Cu (μg/dL)	Normal weight	1.785±0.18	0.38	1.944±1.53	0.66	1.731±0.14	0.07
	Overweight	1.687±0.24		1.786±0.04		1.683±0.19	
	Obese	1.667±0.26		1.685±0.22		1.592±0.17	
Zn (μg/dL)	Normal weight	92.668±25.72	0.596	90.632±16.97	0.88	90.016±11.29	0.937
	Overweight	86.746±12.5		89.1369±14		89.937±11.53	
	Obese	86.733±11.45		87.798±14.88		88.690±11.89	
Se (μg/L)	Normal weight	91.021±5.07	0.019*	89.916±5.53	0.018*	89.776±6.80	0.036*
	Overweight	87.458±4.48		86.44±4.15		87.035±4.58	
	Obese	86.025±2.05		84.483±6.13		84.925±4.17	

* Significant $P < 0.05$

alter significantly in ovarian-stimulated women following stimulation with gonadotropins. The present study also found a nonsignificant relation among the serum Ca level with the maternal age, and BMI. Kocyłowski *et al.*[24] observed that the Ca concentration in the maternal serum was significantly decreased in relation to the maternal age only after birth ($P = 0.03$). Other research found that significantly decreased calcium blood serum values were found in both underweight and overweight women.[25] The serum Cu showed a nonsignificant change in the first 3 months of pregnancy in comparison with non-pregnant. Iwueke *et al.*'s[26] study also revealed the Cu level in pregnant women and non-pregnant controls did not differ significantly. Other researchers found that Cu values for a healthy pregnancy were much higher than those for nonpregnancies, and considerably raised throughout the course of pregnancy before returning to normal upon birth.[27-29] The creation of ceruloplasmin, a key protein that binds Cu, as an effect of elevated levels of maternal estrogen may be partially responsible for the increase in Cu with the course of pregnancy.[4] Vukelić *et al.*[30] suggest that there were not many pregnant who had a copper deficit. Cu deficiency is connected with some pathological conditions and impacts a number of cuproenzymes. This results in anomalies in angiogenesis, lipid peroxidation, hormone activation, deficiencies in ATP generation, and vasculature.[31] Matsubayashi *et al.*'s[32] study found that high serum copper concentrations are a risk factor for implantation failure, and the copper concentrations were significantly higher in nonpregnant than in the pregnant group with assisted reproductive techniques.

The present study also found a nonsignificant relation between the serum Cu level and the maternal age and BMI. Alvarez *et al.*[15] observed that the maternal age did not influence serum levels of cu. Lewicka *et al.*[26] revealed women who were overweight or obese had significantly lower copper concentrations. Regarding the Zn serum level, the present result showed a nonsignificant change in its serum level in the first trimester of pregnancy in comparison with nonpregnant. Other studies found that there was a nonsignificance increase at early pregnancy but there is a decrease in serum Zn levels as pregnancy develops.[2,15,33] Some studies noted that a high concentration of iron or a high plasma folate concentration, when given as a supplement, could interfere with zinc absorption.[34,35] Tabrizi *et al.*[36] found the increase in plasma volume and the transfer from mother to fetus as the explanations for the reduction in blood zinc levels from the first to third trimesters. Wang *et al.*[37] found Zn blood concentrations and the probability of IVF failure were found to be statistically associated, indicating that Zn plays a key role in female reproductive health.

The present study also found a nonsignificant relation between the serum Zn level and the maternal age and BMI. Alvarez *et al.*[15] observed that the maternal age did not influence serum levels of Zn. Liu *et al.*[38] observed that serum zinc concentration increased nonsignificantly with increased age of pregnant women. A nonsignificant difference in Zn serum level between the normal weight and the overweight groups (P = 0.246) was seen in Martadiansyah *et al.*'s study.[39] The present result showed a significant decrease in the Se serum level in the first trimester of pregnancy in comparison with nonpregnant, but nonsignificant differences were seen between the different pregnant groups. For fetal growth, there is an increased requirement for Se during pregnancy. This results in lower levels of selenium in maternal blood. Navarro *et al.*[40] observed a nonsignificant difference in the selenium serum levels present between pregnant and nonpregnant women.

In the present study, a nonsignificant relation between the serum Se level and the maternal age was seen, but a significant relation with the BMI was observed. Other studies also found that nonsignificant differences were observed regarding the age of pregnant women. Lewandowska *et al.*,[41] evaluate the serum Se level in pregnant with 10–14th gestational week in comparison to women whose prepregnancy BMI was within the normal value, those whose prepregnancy BMI was 25 kg/m^2 had lower average Se levels (60.27 vs. 62.23 g/L; P = 0.0007). Se is found in the thyroid gland and catalyzes the conversion of the inactive thyroid T4 to the active form T3. Because the thyroid controls basal metabolism, there seems to be a connection between thyroid function and body weight. Suggesting the importance of thyroid hormones in body weight regulation and metabolism.[42]

Conclusion

In conclusion, there was a significant decrease in serum selenium and calcium levels in 1st trimester of pregnant women compared to the nonpregnant women, which means that during pregnancy, the necessity of these elements increases to meet the demand for fetus growth. Preeclampsia, hypertension, and miscarriage can all result from a decrease in the mother's selenium levels during pregnancy. The serum Cu showed a nonsignificant increase in the first trimester of pregnancy. There was no significant different in these elements between different groups of pregnant.

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Conflicts of interest

There are no conflicts of interest.

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