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Article

Is Maternal Selenium Status Associated with Pregnancy Outcomes in Physiological and Complicated Pregnancy?

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Abstract: Selenium is essential for the synthesis and function of various selenoenzymes, such as glutathione peroxidases, selenoprotein P, and thioredoxin reductase, which play an important role in both antioxidant defense and limiting oxidative damage. Associations between serum selenium concentration and obstetric complications as well as pregnancy outcomes has been reported in many studies. The aim of this study was to determine whether the dietary intake of selenium, its concentration in serum and the activity of glutathione peroxidase in subsequent trimesters of pregnancy affect the birth condition of newborns assessed on the basis of the APGAR score in the 1st and 5th minute of life, birth weight, body length and head and chest circumference in physiological and complicated pregnancy course. Twenty-seven pregnant women at a mean age 29.6 ± 4.8 years from the Lower Silesia region of Poland were recruited to the study, 55% of studied group had pregnancy complications. The mean reported Se intake and serum selenium content for Polish pregnant women was in the first trimester – $56.53 \mu g/day$ and $43.75 \mu g/l$, the second trimester – $61.79 \mu g/day$ and 41.77μg/l and the third trimester – 58.37 μg/day and 42.13 μg/l, respectively. In the subgroup of pregnant women with a physiological pregnancy course, a weak, although statistically significant, positive correlation was found in the first trimester between Se intake and the length (R=0.48, p=0.019) and birth weight of newborns (R=0.472, p=0.022), and in the second trimester with the APGAR score at 1 (R=0.680, p=0.005) and 5 minutes (R=0.55, p=0.033), as well as in the third trimester with th APGAR score at 1 minut (R=0.658, p=0.019). The GPX value had a strong positive correlation with the APGAR score at 1 min. (R=0.650, p=0.008) in the second trimester and with the birth weight of the newborns (R=0.598, p=0.039) in the third trimester. There was no correlation between newborns' birth measurements and serum selenium concentration. In the subgroup of pregnant women with pregnancy complications, a strong, statistically significant, negative correlation was found between Se intake in the second trimester and gestational age (R=-0.618, p=0.032), and in the third trimester, a positive correlation between Se concentration in serum and head circumference (R=0.587, p=0.021). The obtained results indicate that there is a relationship between the maternal selenium status during pregnancy, both in terms of the intake of this element, its serum concentration as well as the glutathione peroxidase activity, and the anthropometric parameters of the newborn, such as birth weight, length and APGAR score, especially in the group with physiological course of pregnancy, but when pregnancy complications occur, these relationships lose their importance.

Keywords: selenium; GPX; pregnancy; pregnancy complications; pregnancy outcomes

1. Introduction

An adequate supply of macro- and microelements is necessary for the proper functioning of the human body. It becomes particularly important for pregnant women when a properly balanced diet has a significant impact on the course of pregnancy, the development of the fetus, the health of the

child, and also the health of the pregnant woman herself. Along with food, the mother's body receives all nutrients, including trace elements, which are then transported across the blood-placenta barrier and reach the fetus. Selenium is essential for the synthesis and function of various selenoenzymes, such as glutathione peroxidases, selenoprotein P, and thioredoxin reductase, which play an important role in both antioxidant defense and limiting oxidative damage. This element inhibits the activation of carcinogens, prevents the accumulation of DNA damage, lipid peroxidation, and inhibits the induction of pro-inflammatory cytokines [1–3]. Previous research results suggest that plasma Se concentrations and glutathione peroxidase activity decrease during pregnancy, partly due to the increasing mass of erythrocytes in the developing fetus [4,5].

The optimal concentration of this trace element may contribute to reducing the risk of complications both in the pregnant woman and the fetus, such as miscarriages, thyroid dysfunction, preeclampsia, premature birth and gestational diabetes [6]. Selenium deficiency in pregnant women may lead to dysfunction in the nervous system of the developing fetus. The oxidative stress deeply affects gestational parameters, and leads to intrauterine growth retardation and abnormal development of tissues, which is related to endocrine metabolic imbalance. As research shows, Se low intake is also associated with the risk of giving birth to an infant with low birth weight or small for gestational age. In Poland, the selenium content in the soil is relatively low, which translates into its concentration in food. Filipowicz et al. research [7] has shown that the intake of Se in the Polish pregnant women diet is lower than in other European countries.

So far, no research has been conducted on the influence of the selenium status, as Se intake, its serum concentration and GPX activity, in the pregnant woman's body throughout pregnancy and the birth condition of the newborn. The undertaken research will allow for the verification of previous scientific reports regarding the topic of the presented research task.

The aim of the research task was to demonstrate whether the dietary intake of selenium, its concentration in serum and the activity of glutathione peroxidase in individual trimesters of pregnancy affect the birth condition of newborns assessed on the basis of the Apgar score in the 1st and 5th minute of life, birth weight, body length and head and chest circumference in physiological and complicated pregnancy course.

2. Material and Methods

2.1. Participants

The research was conducted from November 2013 to February 2017 at the Department of Food Science and Dietetics of Wroclaw Medical University. 94 pregnant women recruited from several private maternity clinics in Lower Silesia were qualified for it. The exclusion criteria were: multiple pregnancy; pre-pregnancy: hypothyroidism, hypertension, diabetes and autoimmune diseases, current or past cardiovascular disease and recurrent cystitis. All qualified pregnant women gave informed, written consent to participate in the research on the basis of the ethical consent issued by the Bioethics Committee of the Medical University of Wrocław KB-884/2012. Obstetric supervision of study participants was carried out in private maternity clinics until delivery, where pregnancy complications were recorded in the medical records.

In the studied group of pregnant women, serious pregnancy complications were recorded, such as gestational hypothyroidism and gestational diabetes, as well as minor complications such as anemia and urinary tract infections. Of a total of ninety-four pregnant women recruited, only thirty-two subjects participated throughout all three trimesters of pregnancy, of which only twenty-seven provided documentation of the anthropomeric parameters of their offspring. All pregnant women declared taking mineral and vitamin supplements containing or not containing selenium throughout their pregnancy. The characteristics of the study group are presented in Table 1.

 Table 1. Baseline characteristics of study particiants.

Demographics	TI	T II	T III					
Pregnancy complications n (% of group)								
No	23 (85.2%) 15 (55.6%) 12 (44.4%)							
Yes	4 (14.8%) 12 (44.4%) 15 (55.6%)							
Hypothyroidism	2 (7.4%) 4 (14.8%) 5 (18.5%)							
Gestational diabetes mellitus	1 (3.7%)	3.7%) 1 (3.7%) 3 (11.1%						
Urinary tract infections	1 (3.7%)	5 (18.5%)	3 (11.1%)					
Anemia	-	2 (7.4%)	4 (14.8%)					
Weight (kg)	62.82±10.54	68.92±11.96	74.48±11.79					
Pregnancy (weeks)	10.95 ± 2.87 22.32 ± 3.48 34.07 ± 2.1							
Mean age (year) 29.6±4.8								
	Delivery n	(% of group)						
Term delivery	26 (96.3%)							
Preterm delivery	1 (3.7%)							
	Birth	weight						
<2500g	1 (3.7%)							
>2500g	26 (96.3%)							
	Education n	(% of group)						
Elementary school	ool 1 (3.7%)							
High school	1 (3.7%)							
Academic	25 (92.6%)							
	Place of residen	ce n (% of group)						
Urban	26 (96.3%)							
Rural	1 (3.7%)							
	Smoking cigaret	tes n (% of group)						
Current smoker		0 (0%)						
Quit smoking		6 (22.2%)						
Never smoked	Never smoked 21 (77.8%)							
	Pre-pregnancy B	MI n (% of group)						

BMI < 18,5	4 (14.8%)					
BMI 18,6-24,9	15 (55.6%)					
BMI >25	8 (29.6%)					
	Prenatal vitamin/mineral intake n (% of group)					
Vitamin/mineral supplements without Se	19 (70.4%)					
Vitamin/mineral supplements with Se	8 (29.6%)					

2.2. Blood Samples

Blood was collected from study participants once in each trimester, i.e. 8–14 weeks of pregnancy (T I), 18–24 weeks of pregnancy (T II) and 31–36 weeks of pregnancy (T III). Under the supervision of medical staff, in accordance with established protocols, fasting blood was collected in the morning by venipuncture into S-Monovette® tubes.

2.3. Biochemical Measurements

2.3.1. Glutathione Peroxidase

The assessment of GPX activity in whole blood was performed using the RANSEL Randox® kit (Randox Laboratories, Ltd, Crumlin, UK) on the Konelab 20i autoanalyzer (ThermoScientfic, Vantaa, Finland).

2.4. Selenium Intake

The assessment of selenium intake was based on measurements using electrothermal atomic spectrometry with Zeeman's background correction (AAS Z-5000 Hitachi, Japan) in reconstituted food rations. Once in each trimester of pregnancy, study participants provided a three-day food diary, along with samples of the food they consumed and dietary supplements they took, a week before blood collection. To assess the accuracy of the method, a certified reference material was used - simulated diet D (LivsmedelsVerked National Food Administration, Sweden). The estimated selenium intake for each study participant was presented as an average over three days.

The daily intake of selenium takes into account the amount of this element supplied with supplements. The supplements contained selenium in amounts ranging from 20 to $60 \mu g/day$.

2.5. Serum Selenium Determination

Selenium concentration was determined directly in serum by electrothermal atomic spectrometry with Zeeman background correction (AAS Z-5000 Hitachi, Japan). The accuracy of the method was assessed on the reference material: Seronorm Trace Element Serum L-1 (Nycomed AS, Oslo, Norway).

2.6. Pregnancy Outcome Data

Measures describing pregnancy course, obstetric complications, and neonatal outcome status were obtained from either the medical records or through subject self-report. Based on the medical records provided by mothers after delivery the following data were obtained regarding: gestational age at birth, APGAR score at 1 and 5 minutes after birth, birth weight, body length, head circumference and chest circumference.

2.7. Statistical Analysis

Due to the small number of participants in groups for individual maternal complications in subsequent trimesters of pregnancy (Tables 1 and 3), it was not possible to perform reliable statistical analyses, therefore all complications were included as one group. Similarly, too low a number of pregnant women with complications in the first trimester did not allow for a correlation analysis to be performed (Table 4). The normality of variable distributions was assessed using three different statistical tests: the Kolmogorov-Smirnov test, the Lillefors test and the Shapiro-Wilk test. Nonparametric analysis of variance with the Friedman post-hoc test for dependent variables was used to compare between trimesters GPX activity, serum selenium content, and Se intake. Mann-Whitney U tests were used to compare concentrations/neonatal outcomes in the physiological and complicated pregnancy groups. The Spearman rank correlation test was used to assess correlations between selenium status and anthropometric parameters of newborns. For all tests, the confidence level of $\alpha = 0.05$ was considered statistically significant.

3. Results

3.1. Participant Baseline Characteristics (Table 1)

Mean maternal age was 29.6±4.8 years, most of the study participants (74.1%) was in range 26-34 years. With each subsequent trimester of pregnancy, the rate of pregnancy complications increased from 14.8% in the first trimester to 55.6% in the third trimester. There was only one case of premature birth and low birth weight among study participants. Almost all surveyed pregnant women declared education on academic level, lived on urban area and never smoked cigarettes. All study participants used vitamin, mineral or mixed supplements dedicated to pregnant women, but only almost 30% of the group took supplements containing selenium. Mean pre-pregnancy BMI value was 22.09, however, four study participants were malnourished and 8 were overweight, and no pregnant women were obese before pregnancy.

3.2. Selenium Status during Gestation (Table 2)

In the second trimester of pregnancy, the highest selenium intake (61.79 $\mu g/day$) and the highest GPX value (231.07 U/l), as opposed to the serum Se concentration (41.77 $\mu g/l$), were observed, however significant differences were not observed between values for all parameters at particular trimesters.

,	TI	T II	T III	p-value
	N=27	N=27	N=27	•
Se intake [µg/day]	56.53±25.32	61.79±25.71	58.37±21.29	NS
Se serum [µg/l]	43.75±6.06	41.77±7.96	42.13±6.60	NS
GPX [U/l]	225.70±44.65	231.07±40.62	229.77±48.51	NS

Table 2. Selenium status during pregnancy (mean ± SD).

NS - non-significant; T I – the first trimester of pregnancy; T II – the second trimester of pregnancy; T III-the third trimester of pregnancy; Se – selenium; GPX –glutathione peroxidase;.

3.3. Mean Values of Neonatal Outcome Measurements and Selenium Status in Normal and Complicated Pregnancy (Table 3)

Pregnant women with pregnancy complications were characterized by statistically significantly lower serum selenium concentration (40.99 vs 44.5 μ g/l , p=0.029) and higher gestational age of the newborns (40.0 vs 38.66 weeks, p=0.005) compared to healthy pregnant women.

Table 3. Mean values of neonatal outcome measurements and selenium status in physiological and complicated pregnancy.

	Physiological pregnancy N=12	Pregnancy complications N=15	
Se intake [μg/day]	52.93±16.36	63.67±27.94	NS
Se serum [μg/l]	44.50±6.71	40.99±6.70	0.029
GPX [U/l]	217.52±33.81	237.91±49.55	NS
Body length[cm]	53.08±3.20	53.80±2.62	NS
Chest circumference [cm]	32.91±2.15	33.53±1.50	NS
Head circumference [cm]	32.83±1.26	33.40±1.24	NS
Birth weight [g]	3231.60±619.50	3513.06±410.30	NS
APGAR score at 1 minutes	8.53±3.08	9.66±0.61	NS
APGAR score at 5 minutes	9.5±1.24	9.8±0.56	NS
Gestational age at birth [weeks]	38.66±1.30	40.0±1.51	0.005

NS - non-significant; T I – the first trimester of pregnancy; T II – the second trimester of pregnancy; T III-the third trimester of pregnancy; Se – selenium; GPX –glutathione peroxidase.

In all studied neonatal outcome measurments: birth weight, body length, head circumference and chest circumference, APGAR score at 1 and 5 minutes after birth, results were slightly higher in women with complicated than with normal pregnancy but differences were not statistically significant.

3.4. Correlations Observed between Selenium Status Parameters and Neonatal Outcome Measurements during Normal and Complicated Pregnancy (Table 4)

In the subgroup of pregnant women with a physiological pregnancy course, a weak, although statistically significant, positive correlation was found in the first trimester between Se intake and the length (R=0.48, p=0.019) and birth weight of newborns (R=0.472, p=0.022), and in the second trimester with the APGAR score at 1 (R=0.680, p=0.005) and 5 minutes (R=0.55, p=0.033), as well as in the third trimester with the APGAR score at 1 minut (R=0.658, p=0.019). The GPX value had a strong positive correlation with the APGAR score at 1 min. (R=0.650, p=0.008) in the second trimester and with the birth weight of the newborns (R=0.598, p=0.039) in the third trimester. There was no correlation between newborns' birth measurements and serum selenium concentration.

Table 4. Correlations observed between selenium status parameters and neonatal outcome measurements during physiological and complicated pregnancy.

	_		-			
Correlations	ΤI	-	T II	•	T III	
	R	p-value	R	p-value	R	p-value
P	hysiologi	cal pregnar	ісу			
Se intake vs body length	0.481	0.019	0.090	0.748	0.047	0.884
Se intake vs birth weight	0.472	0.022	0.017	0.949	0.316	0.315
Se intake vs chest circumference	0.379	0.074	-0.060	0.830	-0.071	0.825
Se intake vs head circumference	0.247	0.255	-0.247	0.374	0.111	0.730
Se intake vs APGAR score at 1min.	0.090	0.680	0.680	0.005	0.658	0.019
Se intake vs APGAR score at 5 min.	0.119	0.586	0.551	0.033	0.573	0.051
Se intake vs gestational age	0.093	0.671	-0.153	0.584	-0.279	0.379

Se serum vs birth weight 0.033 0.878 0.078 0.779 0.239 0.453 Se serum vs chest circumference -0.018 0.931 -0.027 0.922 0.203 0.524 Se serum vs head circumference 0.216 0.321 -0.122 0.663 0.200 0.532 Se serum vs APGAR score at 1 min. 0.150 0.494 0.212 0.447 0.496 0.100 Se serum vs APGAR score at 5 min. 0.122 0.578 -0.133 0.635 0.286 0.365 Se serum vs gestational age -0.108 0.622 -0.035 0.900 -0.213 0.504 GPX vs body length 0.318 0.138 0.243 0.381 0.231 0.469 GPX vs beat circumference -0.008 0.970 -0.022 0.936 0.225 0.481 GPX vs head circumference 0.0132 0.545 0.650 0.008 0.055 0.863 GPX vs APGAR score at 5 min. -0.033 0.880 0.497 0.058 -0.108 0.737							
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Se serum vs head circumference 0.216 0.321 -0.122 0.663 0.200 0.532 Se serum vs APGAR score at 1 min. 0.150 0.494 0.212 0.447 0.496 0.100 Se serum vs APGAR score at 5 min. 0.122 0.578 -0.133 0.635 0.286 0.365 Se serum vs gestational age -0.108 0.622 -0.035 0.900 -0.213 0.504 GPX vs body length 0.318 0.138 0.243 0.381 0.231 0.469 GPX vs birth weight 0.155 0.478 0.334 0.222 0.598 0.039 GPX vs chest circumference -0.008 0.970 -0.022 0.936 0.225 0.481 GPX vs head circumference 0.212 0.329 0.173 0.537 0.155 0.628 GPX vs APGAR score at 5 min. -0.032 0.880 0.497 0.058 -0.108 0.737 GPX vs gestational age -0.182 0.404 -0.116 0.679 0.025 0.937 C	serum vs birth weight	0.033	0.878	0.078	0.779	0.239	0.453
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GPX vs head circumference 0.212 0.329 0.173 0.537 0.155 0.628 GPX vs APGAR score at 1min. 0.132 0.545 0.650 0.008 0.055 0.863 GPX vs APGAR score at 5 min. -0.033 0.880 0.497 0.058 -0.108 0.737 GPX vs gestational age -0.182 0.404 -0.116 0.679 0.025 0.937 Complicated pregnancy Se intake vs body length x x -0.281 0.375 -0.133 0.634 Se intake vs birth weight x x -0.394 0.204 -0.322 0.240 Se intake vs chest circumference x x -0.400 0.197 -0.134 0.633 Se intake vs head circumference x x -0.102 0.752 -0.168 0.548 Se intake vs APGAR score at 1min. x x -0.091 0.777 -0.012 0.965	GPX vs birth weight	0.155	0.478	0.334	0.222	0.598	0.039
GPX vs APGAR score at 1min. 0.132 0.545 0.650 0.008 0.055 0.863 GPX vs APGAR score at 5 min. -0.033 0.880 0.497 0.058 -0.108 0.737 GPX vs gestational age -0.182 0.404 -0.116 0.679 0.025 0.937 Complicated pregnancy Se intake vs body length x x -0.281 0.375 -0.133 0.634 Se intake vs birth weight x x -0.394 0.204 -0.322 0.240 Se intake vs chest circumference x x -0.400 0.197 -0.134 0.633 Se intake vs head circumference x x -0.102 0.752 -0.168 0.548 Se intake vs APGAR score at 1min. x x -0.091 0.777 -0.012 0.965	X vs chest circumference	-0.008	0.970	-0.022	0.936	0.225	0.481
GPX vs APGAR score at 5 min. -0.033 0.880 0.497 0.058 -0.108 0.737 GPX vs gestational age -0.182 0.404 -0.116 0.679 0.025 0.937 Complicated pregnancy Se intake vs body length x x -0.281 0.375 -0.133 0.634 Se intake vs birth weight x x -0.394 0.204 -0.322 0.240 Se intake vs chest circumference x x -0.400 0.197 -0.134 0.633 Se intake vs head circumference x x -0.102 0.752 -0.168 0.548 Se intake vs APGAR score at 1min. x x -0.142 0.658 0.142 0.611 Se intake vs APGAR score at 5 min. x x -0.091 0.777 -0.012 0.965	K vs head circumference	0.212	0.329	0.173	0.537	0.155	0.628
GPX vs gestational age -0.182 0.404 -0.116 0.679 0.025 0.937 Complicated pregnancy Se intake vs body length x x -0.281 0.375 -0.133 0.634 Se intake vs birth weight x x -0.394 0.204 -0.322 0.240 Se intake vs chest circumference x x -0.400 0.197 -0.134 0.633 Se intake vs head circumference x x -0.102 0.752 -0.168 0.548 Se intake vs APGAR score at 1min. x x -0.142 0.658 0.142 0.611 Se intake vs APGAR score at 5 min. x x -0.091 0.777 -0.012 0.965	vs APGAR score at 1min.	0.132	0.545	0.650	0.008	0.055	0.863
Complicated pregnancy Se intake vs body length x x -0.281 0.375 -0.133 0.634 Se intake vs birth weight x x -0.394 0.204 -0.322 0.240 Se intake vs chest circumference x x -0.400 0.197 -0.134 0.633 Se intake vs head circumference x x -0.102 0.752 -0.168 0.548 Se intake vs APGAR score at 1min. x x -0.142 0.658 0.142 0.611 Se intake vs APGAR score at 5 min. x x -0.091 0.777 -0.012 0.965	es APGAR score at 5 min.	-0.033	0.880	0.497	0.058	-0.108	0.737
Se intake vs body length x x -0.281 0.375 -0.133 0.634 Se intake vs birth weight x x -0.394 0.204 -0.322 0.240 Se intake vs chest circumference x x -0.400 0.197 -0.134 0.633 Se intake vs head circumference x x -0.102 0.752 -0.168 0.548 Se intake vs APGAR score at 1min. x x -0.142 0.658 0.142 0.611 Se intake vs APGAR score at 5 min. x x -0.091 0.777 -0.012 0.965	PX vs gestational age	-0.182	0.404	-0.116	0.679	0.025	0.937
Se intake vs birth weight x x -0.394 0.204 -0.322 0.240 Se intake vs chest circumference x x -0.400 0.197 -0.134 0.633 Se intake vs head circumference x x -0.102 0.752 -0.168 0.548 Se intake vs APGAR score at 1min. x x -0.142 0.658 0.142 0.611 Se intake vs APGAR score at 5 min. x x -0.091 0.777 -0.012 0.965	Со	mplicate	d pregnan	ісу			
Se intake vs chest circumference x x -0.400 0.197 -0.134 0.633 Se intake vs head circumference x x -0.102 0.752 -0.168 0.548 Se intake vs APGAR score at 1min. x x -0.142 0.658 0.142 0.611 Se intake vs APGAR score at 5 min. x x -0.091 0.777 -0.012 0.965	intake vs body length	X	x	-0.281	0.375	-0.133	0.634
Se intake vs head circumference x x -0.102 0.752 -0.168 0.548 Se intake vs APGAR score at 1min. x x -0.142 0.658 0.142 0.611 Se intake vs APGAR score at 5 min. x x -0.091 0.777 -0.012 0.965	intake vs birth weight	X	x	-0.394	0.204	-0.322	0.240
Se intake vs APGAR score at 1min. x x -0.142 0.658 0.142 0.611 Se intake vs APGAR score at 5 min. x x -0.091 0.777 -0.012 0.965	ike vs chest circumference	X	x	-0.400	0.197	-0.134	0.633
Se intake vs APGAR score at 5 min. x x -0.091 0.777 -0.012 0.965	ake vs head circumference	X	x	-0.102	0.752	-0.168	0.548
	e vs APGAR score at 1min.	X	x	-0.142	0.658	0.142	0.611
	vs APGAR score at 5 min.	x	x	-0.091	0.777	-0.012	0.965
Se intake vs gestational age x x -0.618 0.032 -0.083 0.766	ntake vs gestational age	X	x	-0.618	0.032	-0.083	0.766
Se serum vs body length x x 0.060 0.851 -0.045 0.871	serum vs body length	X	x	0.060	0.851	-0.045	0.871
Se serum vs birth weight x x 0.309 0.327 0.039 0.889	serum vs birth weight	X	x	0.309	0.327	0.039	0.889
Se serum vs chest circumference x x 0.392 0.206 0.272 0.326	ım vs chest circumference	X	x	0.392	0.206	0.272	0.326
Se serum vs head circumference x x 0.510 0.089 0.587 0.021	um vs head circumference	X	x	0.510	0.089	0.587	0.021
Se serum vs APGAR score at 1min. x x 0.046 0.887 -0.096 0.731	n vs APGAR score at 1min.	x	x	0.046	0.887	-0.096	0.731
Se serum vs APGAR score at 5 min. x x 0.252 0.428 0.211 0.449	ı vs APGAR score at 5 min.	X	x	0.252	0.428	0.211	0.449
Se serum vs gestational age x x 0.058 0.857 0.142 0.612	erum vs gestational age	x	x	0.058	0.857	0.142	0.612
GPX vs body length x x 0.068 0.833 0.004 0.987	GPX vs body length	X	x	0.068	0.833	0.004	0.987
GPX vs birth weight x x -0.078 0.809 -0.053 0.848	GPX vs birth weight	x	x	-0.078	0.809	-0.053	0.848
GPX vs chest circumference x x 0.056 0.861 0.051 0.855	X vs chest circumference	X	X	0.056	0.861	0.051	0.855
GPX vs head circumference x x 0.051 0.873 0.225 0.418	ζ vs head circumference	X	X	0.051	0.873	0.225	0.418
GPX vs APGAR score at 1min. x x -0.194 0.544 -0.108 0.700	vs APGAR score at 1min.	X	X	-0.194	0.544	-0.108	0.700
GPX vs APGAR score at 5 min. x x -0.092 0.776 -0.145 0.606	os APGAR score at 5 min.	x	x	-0.092	0.776	-0.145	0.606
GPX vs gestational age x x 0.066 0.837 0.395 0.144	PX vs gestational age	x	X	0.066	0.837	0.395	0.144

T I – the first trimester of pregnancy; T II – the second trimester of pregnancy; T III-the third trimester of pregnancy; Se – selenium; GPX –glutathione peroxidase; p< 0.05.

In the subgroup of pregnant women with pregnancy complications, a strong, statistically significant, negative correlation was found between Se intake in the second trimester and gestational age (R=-0.618, p=0.032), and in the third trimester, a positive correlation between Se concentration in serum and head circumference (R=0.587, p=0.021).

In the remaining analyses, both for selenium intake, its concentration in serum and the GPX value, there was no correlation with the newborns' birth measurements.

4. Discussion

The aim of the was to demonstrate whether the dietary intake of selenium, its concentration in serum and the activity of glutathione peroxidase in individual trimesters of pregnancy affect the birth condition of newborns assessed on the basis of the Apgar score in the 1st and 5th minute of life, birth weight, body length and head and chest circumference in physiological and complicated pregnancy course.

The recommended Se intake for the Polish pregnant population is 50 µg/d. Pregnant women participating in our study covered the recommended dietary intake in each trimester of pregnancy -56.53 μg/d in T I; 61.79 μg/d in T II and 58.37 µg/d in T III (Table 2). Similar results were obtained by Modzelewska et al. [8] (53 ug/d) for pregnant women in Norway, however, in the population of Chinese pregnant women, the selenium intake was estimated at 30 ug/d [9]. It should be remembered that the Se intake is strictly dependent on the content of this element in the soil, which translates into its amount in food, and China is a region with a particularly low Se content in the soil [10,11]. Dietary selenium intake has a decisive influence on the concentration of this element in the serum and GPX Both the concentration of Se in the serum and the activity of GPX depend on the activity [12,13]. dietary intake of this element [12,13]. A marker of short-term changes in selenium concentration in tissues is the amount of this element in serum, while GPx activity in plasma and whole blood is a functional indicator of selenium level. According to the World Health Organization (WHO), in healthy adults, the optimal mean serum selenium concentration ranges from 39.5 to 194.5 µg/L, but to obtain maximum glutathione peroxidase activity, the optimal Se concentration is 70–90 µg/L [14].

As research results indicate, the concentration of selenium in the blood decreases significantly with subsequent trimesters of pregnancy [6,15]. In the participants of our study, a decrease in Se concentration was observed from 43.75 μ g/L in the first trimester to 42.13 μ g/L in the third trimester (Table 2). Serum Se concentrations obtained in our study are comparable to the results of other authors –40.5 μ g/L (Hungary [16]); 38.21 μ g/L (Turkey [17]); 51 μ g/L (Yugoslavia [18]). The obtained GPX values in individual trimesters of pregnancy were also comparable to those presented by other authors [4].

Despite a slightly higher dietary Se intake, pregnant women with complicated pregnancies in our study had significantly lower serum Se concentrations compared to pregnant women with a physiological pregnancy (Table 3). Higher selenium consumption in this subgroup may be related to greater attention to the quality of the diet (higher consumption of eggs and whole grain products as a good source of this element) and the use of vitamin and mineral supplements containing Se - six out of eight taking such preparations belonged to this subgroup. Perhaps in response to the increased redox processes accompanying pregnancy complications, the body of pregnant women increased the synthesis of GPX (a statistically insignificant increase in GPX concentration in this group compared to physiological pregnancies - Table 3) using selenium circulating in the bloodstream for this purpose.

The results of anthropometric measurements of newborns, as well as the APGAR score at 1 and 5 minutes, did not differ significantly between the groups with a physiological and complicated pregnancy course (Table 3). The obtained results are consistent with data from other European populations [19–22]. According to the WHO centile charts [23], the body length of the newborns we examined was between the 75th and 90th percentile, the body weight was between the 50th and 75th percentile, but the head circumference was only between the 10th and 25th percentile.

The length of pregnancy differed statistically significantly between the groups with physiological and complicated pregnancy (38.66 vs. 40.0 weeks). This observation may be related to the higher selenium intake in the group with complicated pregnancy than in physiological (64 vs. $53 \mu g/day$). Research by Barman et al. [24] on a large population of Norwegian pregnant women (72,025 women) showed that Se intake from the mother's diet in the first half of pregnancy was significantly associated with a reduced risk of preterm birth and also influenced the duration of pregnancy.

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The correlation analysis in our study showed statistically significant relationships between selenium intake in the first trimester of pregnancy and the weight (R=0.472, p=0.022) and body length of newborns (R=0.48, p=0.019) in the group of pregnant women with a physiological course of pregnancy (Table 4). The proper development of the fetus depends on genetic factors, fetal-placental circulation, environmental factors and the nutritional status of the mother [25-27]. Among these factors, oxidative stress seems to play an important role in the development of the placenta and disorders of its functionality [27,28]. Selenium as a component of selenoproteins, which include strong antioxidant enzymes also present in the placenta (glutathione peroxidase-GPx and thioredoxin reductase-ThRedx), influences redox processes in the body [27,29]. In the early stages of pregnancy, the invasion of trophoblasts through the wall of the spiral artery increases placental blood flow, which increases oxidative stress. During this time, trophoblast cells are protected by antioxidant enzymes against the harmful effects of free radicals [27,28]. As research indicates, the antioxidant activity of GPX depends on the Se concentration in the blood, which translates into effective protection of trophoblast cells and protection of the placenta and fetus against oxidative stress [27,29]. This element is involved not only in ensuring oxidative balance, but also in immune reactions, inflammatory processes as well as cell apoptosis, which take place in the early development of the placenta [29]. Studies in animal models indicate that the main effect of Se in the embryonic phase is related to the antioxidant activity of GPx in various tissues, as well as its important role in fetal development, related to growth and metabolic endocrine function [30]. In this context, Se improves duodenal function and influences the hormonal secretion of various hormones significantly related to fetal development in early pregnancy, such as thyroid hormones (TH), insulin-like growth factor (IGF) and insulin [31-33]. Few studies have correlated Se concentration in blood in early pregnancy with birth weight and the risk of low birth weight. Bogden et al. [34] in a group of 126 pregnant women who gave birth to full-term babies showed a statistically significant positive correlation between the Se concentration in the mother's serum at the 15th week of pregnancy and the newborn's birth weight. In another study, Lewandowska et al. [35] on a cohort of 750 pregnant women showed that the Se concentration in the serum at 10-14 weeks of pregnancy was significantly lower in pregnant women who gave birth to small for gestational age (SGA) newborns compared to pregnant women giving birth to newborns with a weight adjusted to the gestational age. In the same study, the authors showed that pregnant women with serum Se concentrations in quartile Q1 had a threefold higher risk of delivering an SGA neonate than those with Se concentrations in quartile Q4. Also, Mistry et al. [36], in a study involving 126 teenagers, found statistically lower levels of Se in the plasma of mothers in the middle stage of pregnancy giving birth to SGA infants compared to pregnant women giving birth to newborns weighing appropriate for gestational age (AGA).

In the second trimester of pregnancy, our study showed statistically significant correlations between selenium supply and the GPX value and the APGAR score at 1 and 5 minutes (Table 4). During this period of pregnancy, there is intensive development of the nervous system and myelination of nerve fibers, as well as an intensive increase in the weight of developed organs. At the same time, there is an increased concentration of lipid peroxidation products in the mother's blood, which may decrease later in pregnancy [37]. Lipid peroxides are also produced in the placenta, but their uncontrolled production can cause oxidative stress with significant damage to cell integrity [38]. In response to oxidative stress, larger amounts of antioxidant enzymes, including GPX, are activated. The undisturbed course of developmental processes and antioxidant protection translates into proper reflexes and the functioning of key systems such as the respiratory and circulatory systems immediately after birth. These are the parameters assessed as part of the APGAR scoring.

Also in the third trimester, a statistically significant positive relationship was noted between GPX activity and the newborn's birth weight (Table 4). Similarly, other authors have shown in their studies that the antioxidant status, including GPX activity, correlates with birth weight in a group of newborns weighing appropriate for gestational age [39,40].

Significantly fewer correlations between Se status and birth parameters were found in the subgroup of women with complicated pregnancies. In this subgroup, there was a significant negative correlation between Se intake and gestational age in the second trimester of pregnancy, and a positive

correlation between serum Se concentration and head circumference in the third trimester of pregnancy (Table 4).

Similar results were obtained by Lozano et al. [41] in a group of 1,249 Spanish mother-newborn pairs, where a negative correlation was shown between the serum Se concentration and the length of pregnancy and a positive correlation between the serum Se concentration and head circumference, but only in the group of pregnant women. whose serum mercury content was found to be above 15µg/L. Unfortunately, the authors of the study did not specify whether any pregnancy complications occurred in the study group of pregnant women. The impact of selenium intake on the duration of pregnancy in the case of pregnancy complications has not been the subject of research so far, and the vast majority of studies refer to the concentration of selenium in serum or whole blood - however, a meta-analysis of such studies indicates a positive relationship between Se concentration and the duration of pregnancy [24,42].

5. Strengths and Limitations

The study conducted has both its strengths and limitations. Its strength is the study design. The results were based solely on data obtained from pregnant women participating in the study from the first trimester of pregnancy to delivery. During this period, not only blood and urine samples, medical data on the newborn's birth parameters, 24-hour nutritional interviews from the next 7 days, but also food samples corresponding to the entries in the food diaries were collected three times (once in each trimester). This unique approach allowed for the assessment of actual selenium intake, unlike studies based only on estimated data from the FFQ. This meant we could get a true reflection of the changes in selenium status that occur during pregnancy.

The limitation of the study, however, is the low number of study participants, which could have translated into the results of statistical analyses and high homogeneity of the studied group (education, place of residence and age).

6. Conclusions

The obtained results indicate that there is a relationship between the maternal selenium status during pregnancy, both in terms of the intake of this element, its serum concentration as well as the glutathione peroxidase activity, and the anthropometric parameters of the newborn, such as birth weight, length and APGAR score, especially in the group with physiological course of pregnancy, but when pregnancy complications occur, these relationships lose their importance.

Author Contributions: Conceptualization, J.P.; Data curation, S.P.; Formal analysis, S.P. Investigation, R.S.; Methodology, J.P. and H.G.; Resources, R.S.; Software, S.P.; Supervision, H.G.; writing—original draft, J.P. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest: The authors declare that there are no conflicts of interest.

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