Journal of Trace Elements in Medicine and Biology 54 (2019) 110–117

Contents lists available at ScienceDirect

Journal of Trace Elements in Medicine and Biology

journal homepage: www.elsevier.com/locate/jtemb

Nutrition

# Is maternal dietary selenium intake related to antioxidant status and the occurrence of pregnancy complications?

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ARTICLE INFO

*Keywords:*
Selenium
Pregnancy
Antioxidant status
Pregnancy complications

ABSTRACT

Selenium (Se) is a trace element essential for the appropriate course of vital processes in the human body. It is also a constituent of the active center of glutathione peroxidase and other antioxidant compounds which play an important role in red-ox processes. Associations between lower blood selenium concentration and obstetric complications has been reported in many studies. The aim of this study was to determine the dietary selenium intake and serum selenium content in pregnant Polish women and relate this to antioxidant status as whole blood glutathione peroxidase (GPX) activity, serum uric acid (UA) content and serum total antioxidant status (TAS) and pregnancy complications occurrence. Ninety-four pregnant women at a mean age 30.6 ± 5.4 years from the Lower Silesia region of Poland were recruited to the study, 37% of studied group had pregnancy complications. The mean reported Se intake and serum selenium content for Polish pregnant women was in the first trimester – 53.99 μg/day and 44.36 μg/l, the second trimester – 58.93 μg/day and 43.16 μg/l and the third trimester – 62.89 μg/day and 40.97 μg/l, respectively. Selenium intake below or above recommended value hadn't significant effect on GPX activity, TAS and UA levels. There were no statistical differences in selenium intake, serum selenium content, GPX activity and TAS and UA level between physiological and complicated pregnancy, but a positive correlation between Se intake and serum selenium content was observed during all period of gestation as well as in the second trimester of pregnancy between Se intake and GPX activity in group with physiological pregnancy where selenium intake was below the recommended level. Selenium intake above the recommended level was positively correlated also with serum UA level in first and second trimester of pregnancy. Despite weak, positive correlations in the first two trimesters of pregnancy between selenium supply and GPX activity and UA concentration we concluded that selenium intake does not significantly affect during pregnancy, both: markers of the antioxidant status of pregnant women and the occurrence of pregnancy complications.

## 1. Introduction

Many of the determinants of obstetric complications are related to maternal suboptimal nutrition and an infant's deficiency of some essential trace elements such as copper (Cu), iron (Fe), manganese (Mn), selenium (Se) and zinc (Zn). All these trace elements, but particularly selenium, play a critical role in antioxidant defense. As a component of enzymes, Se impairs adverse processes of lipids peroxidation and protects cells against damage to genetic material. The protective role of selenium results from its presence in glutathione peroxidase (GPX) and thioredoxin reductase (TrxRs), namely in the active center of antioxidative enzymes [1]. Dietary selenium intake in Poland, as in some other European countries, is often below the recommended nutrient intake (50 μg/day for pregnant women in Poland) [2–4], and associations between lower blood selenium concentration and obstetric complications have been reported [5–7]. Maternal selenium status may contribute to the incidence of the preeclamptic state (EPH gestosis). Significantly lower levels of selenoenzymes such as glutathione peroxidase and thioredoxin reductase have been found in serum, plasma and placenta samples from preeclamptic women than in those from

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https://doi.org/10.1016/j.jtemb.2019.04.010
Received 6 November 2018; Received in revised form 2 April 2019; Accepted 18 April 2019

matched healthy controls [8–10]. It is speculated to be a consequence of the action of mechanisms protecting the body against the occurrence of oxidative stress. Circulating lipid peroxides may lead to damage of the placenta, which causes retardation of fetus growth. They additionally lead to an increased content of thromboxane, a reduced content of prostacyclins, and damage of vascular endothelium cells, resulting in an improper blood flow in the placenta [11]. The pregnant women with cholestasis were also characterized by a lower selenium concentration in the blood and by a lower activity of GPX in erythrocytes than the healthy pregnant women. In patients with intrahepatic cholestasis of pregnancy, this may lead to the formation of free radicals, which could damage the hepatocytes and reduce excretion of bile [7,12]. Selenium is also speculated to be essential for proper glucose uptake, the regulation of the cellular absorption of glucose and reduction of insulin resistance. Contrary to recent epidemiological and intervention studies with non-pregnant women, several studies have reported that blood selenium level was reduced in gestational diabetes mellitus GDM [6,13]. This trace element plays an important role in the regulation of thyroid gland function under physiological conditions and in the case of disease. In particular, pregnant women with autoimmune thyroiditis (thyroid-peroxidase-antibody positive) are prone to develop hypothyroxinemia during pregnancy and thyroid dysfunction after delivery [14].

Reactive oxygen species (ROS) play a physiological role in gestation, but in excess, they might perturb the antioxidant systems and lead to oxidative damage. Under physiological conditions, high levels of ROS during embryonic, fetal and placental development are a feature of pregnancy. This state is associated with an activity increase of the main endogenous antioxidants -superoxide dismutases, catalase, glutathione and glutathione peroxidase [15,16]. However, if there is an inadequate production of antioxidants, oxidative balance is lost. In this case oxidative stress has emerged as a likely promoter of several pregnancy-related disorders, such as spontaneous abortions, embryopathies, pre-eclampsia, fetal growth restriction, preterm labor and low birth weight [17,18]. Antioxidant status is also speculated to be associated with inhibition of bacterial adhesion in urine [19]. Urinary tract infections (UTI) are common during pregnancy, and the most common causative organism is *Escherichia coli*. Asymptomatic bacteriuria can lead to the development of cystitis or pyelonephritis and is associated with an increased risk of intrauterine growth retardation and low birthweight infants [20]. In the study of Mazor-Dray et al. [21], pregnant women with UTI had significantly higher rates of intra-uterine growth restriction (IUGR), pre-eclampsia, caesarean deliveries (CD) and pre-term deliveries.

In order to protect against the harmful effects of free radicals, the human organism has developed a variety of defense mechanisms in which chemical compounds belonging to three groups take part: preventive antioxidants, non-enzymatic scavengers of free radicals and antioxidant enzymes. Even though their action is well known, the possibilities of laboratory assessment of the intensity of oxidative stress and the efficiency of antioxidant mechanisms are limited and based on the evaluation of individual enzyme antioxidants or the overall antioxidant potential created by non-enzymatic antioxidants.

The aim of this study was to determine the dietary selenium intake and serum selenium content in pregnant Polish women and relate this to antioxidant status as whole blood glutathione peroxidase (GPX) activity, serum uric acid (UA) content and serum total antioxidant status (TAS) and pregnancy complications occurrence.

## 2. Material and methods

### 2.1. Participants

Ninety-four eligible women were recruited to the study between November 2013 and February 2017 at several obstetric private clinics in the Lower Silesia region of Poland. Women were excluded if they have a multiple pregnancy, preexisting hypertension, diabetes mellitus, pregestational hypothyroidism, autoimmune diseases, recurrent cystitis or present or previous cardiovascular disease. All participants provided informed written consent under ethical approval granted from Wroclaw Medical University Bioethics Committee KB-884/2012. The women were followed up at the obstetric private clinics until delivery and the development of severe or minor maternal complications was recorded. Severe complications included gestational diabetes (glucose levels over 140 mg/dl in the oral glucose tolerance test), gestational hypothyroidism as well as gestational hypertension (SBP ≥ 140 mm Hg or DBP ≥ 90 mm Hg during or after the 20th week of pregnancy, without features of preeclampsia). Minor complications included urinary tract infections and anemia. Differences in the number of participants in groups result from the fact that only 32 women participated in the study from first to third trimester, the remaining participants either joined later in the study or resigned from participation in the study before the third trimester. All participants of the study used mineral and vitamin supplements with or without selenium dedicated to pregnant women from the first trimester throughout the whole period of pregnancy. Characteristics of the studied group are shown in Table 1.

**Table 1**
Baseline characteristics of pregnant women.

| Demographics | T I | T II | T III |
|---|---|---|---|
| | Pregnancy complications n (% of group) | | |
| No | 57 (86.4%) | 34 (54.8%) | 21 (42.0%) |
| Yes | 9 (13.6%) | 28 (45.2%) | 29 (58.0%) |
| Hypothyroidism* | 4 (6.0%) | 9 (14.5%) | 9 (18.0%) |
| Gestational diabetes mellitus | 3 (4,5%) | 3 (4.8%) | 6 (12.0%) |
| Urinary tract infections** | 2 (3.1%) | 12 (19.3%) | 6 (12.0%) |
| Hypertension*** | – | 1 (1.6%) | 2 (4.0%) |
| Anemia**** | – | 3 (4.8%) | 8 (16.0%) |
| Weight (kg) | 63.12 ± 11.04 | 69.32 ± 12.06 | 75.28 ± 12.09 |
| Pregnancy (weeks) | 10.98 ± 2.97 | 22.24 ± 3.45 | 33.97 ± 2.46 |
| | Mean age (year) 30.6 ± 5.4 | | |
| | Education n (% of group) | | |
| Elementary school | 2 (1.7%) | | |
| High school | 20 (17%) | | |
| Academic | 93 (81.3%) | | |
| | Place of residence n (% of group) | | |
| Urban | 88 (93.6%) | | |
| Rural | 6 (6.4%) | | |
| | Smoking cigarettes n (% of group) | | |
| Current smoker | 4 (4.3%) | | |
| Quit smoking | 28 (29.8%) | | |
| Never smoked | | | |
| | Using supplements with Se n (% of group) | | |
| Yes | 26 (27.7%) | | |
| No | 68 (72.3%) | | |

* Subjects received medication (levothyroxine).
** Subjects received medication (nitrofurantoin/ furazidin).
*** Subjects received anti-hypertensive medication (methyldopa and/or labetalol).
**** Subjects received iron supplementation.

### 2.2. Blood samples

Blood samples from pregnant women were collected at three different time points across gestation, i.e. 8–14 weeks of gestation (T I), 18–24 weeks of gestation (T II) and 31–36 weeks of gestation (T III). Blood samples were collected from 8:00 to 9:00 a.m. by venipuncture in S-Monovette® tubes following the protocols established by the medical staff in charge. One sample containing lithium heparin was used to assess glutathione peroxidase activity. A second sample was obtained in S-Monovette® tubes containing separation gel. From this blood sample, serum was obtained by centrifugation (2300 g, 15 min at 4 °C) within a maximum of 2 h after extraction. Thereafter, it was immediately aliquoted and stored at -80 °C for use in Total Antioxidant Status (TAS) and uric acid (UA) and selenium concentration measurement.

**Table 2**
Selenium intake, serum selenium concentration and antioxidant status during pregnancy (mean ± SD).

| | T I N = 32 | T II N = 32 | T III N = 32 | p-value |
|---|---|---|---|---|
| Se intake [μg/day] | 53.99 ± 25.14 | 58.93 ± 28.25 | 62.89 ± 33.19 | NS |
| Se serum [μg/L] | 44.36 ± 8.58[a] | 43.16 ± 8.47 | 40.97 ± 7.50[a] | 0.001 |
| GPX [U/L] | 230.56 ± 43.73 | 227.18 ± 43.52 | 236.34 ± 44.06 | NS |
| TAS [mmol/L of Trolox] | 1.43 ± 0.19 | 1.44 ± 0.17 | 1.48 ± 0.22 | NS |
| UA [mg/dL] | 3.51 ± 0.50[a] | 3.73 ± 0.42 | 4.54 ± 0.70[a] | 0.000 |

Differences between groups were assessed using Friedman's ANOVA, $p < 0.05$.
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; TAS – total antioxidant status, UA – uric acid.

### 2.3. Biochemical measurements

#### 2.3.1. Glutathione peroxidase

Whole blood GPX activity was analyzed with the use of the RANSEL Randox® kit (Randox Laboratories, Ltd, Crumlin, UK) using auto-analyzer Konelab 20i (ThermoScientfic,Vantaa, Finland). In applied method GPX catalyses the oxidation of glutathione by cumene hydroperoxide. In the presence of glutathione reductase and NADPH, the oxidized glutathione is immediately converted to its reduced form with a concomitant oxidation of NADPH to NADP + . The decrease in absorbance at 340 nm was expressed as units per liter of the hemolysate.

#### 2.3.2. Total antioxidant status (TAS)

Plasma total antioxidant status (TAS) was analyzed with the use of the TAS Randox® kit (Randox Laboratories, Ltd, Crumlin, UK) using autoanalyzer Konelab 20i (ThermoScientfic,Vantaa, Finland). Measured in this method total plasma antioxidant capacity is constituted mainly by non-enzymatic compounds like uric acid, free sulfhydryl groups of proteins, vitamin C and bilirubin. Results were expressed in mM of Trolox equivalents. The linearity of calibration extends to 2.5 mmol/L of Trolox. The reference range for human blood plasma is given by the manufacturer as 1.30–1.77 mmol/L.

#### 2.3.3. Uric acid (UA)

Uric acid was analyzed with the use of the Uric Acid (AOX) Thermo Fisher Scientific kit (Thermo Fisher Scientific Oy, Vantaa, Finland) using autoanalyzer Konelab 20i (ThermoScientfic,Vantaa, Finland). Uric acid is oxidized to allantoin by uricase. The generated hydrogen peroxide reacts with 4-aminoantipyrine (4-AAP) and N-ethyl-N-(hydroxy-3-sulfopropyl)-m-toluidin (TOOS) to a blue violet dye. The absorbance of the formed colour is measured at 540 nm. The reference range for female serum/ plasma is given by the manufacturer as 150–350 μmol/l (2.6–6.0 mg/dl).

### 2.4. Selenium intake

Dietary intake of selenium by pregnant women was estimated using the 3-day record method, including food and supplements, in each trimester of pregnancy one week before blood sample collection. At the same time pregnant women collected food samples in accordance with the consumption record. On the basis of the daily record of the menu and the food samples collected, a full-day ration was restored and homogenized. To determine the selenium content, 4 g samples of a homogenous meal were taken in two replications. The meal samples were weighed into digestion vessels, to which were added 5 ml 70% HNO3 (Baker, Instra-Analyzed for trace elements U.S.A). They were subjected to mineralization in a microwave unit Milestone mls 1200 mega. Parallel blanks were prepared, containing the reagents in amounts given above. We determined the food selenium content by electrothermal atomic absorption spectrometry with Zeeman background correction (AAS Z-5000 Hitachi, Japan). A certified reference material – Simulated diet D (LivsmedelsVerked National Food Administration, Sweden) - was used to assess the accuracy of the method. The average daily intake of selenium was calculated as the average of three days in which the selenium intake was estimated for each subject.

The amount of selenium supplied with the supplements has been included in the calculation of the daily intake of this element. The supplements selenium content varied in range from 20 to 60 μg/daily dose. Recommended daily selenium intake for pregnant women in Poland is 50 μg [22]. This value was the cut-off point taken into account when dividing the studied group into the subgroups "Se intake below the recommended level" (< 50 μg Se/day) and "Se intake above the recommended level" (> 50 μg Se/day).

### 2.5. Serum selenium determination

The selenium content was directly determined in serum by electrothermal atomic absorption spectrometry with Zeeman background correction (AAS Z-5000 Hitachi, Japan). Samples were diluted (1 + 2) with a 0.2% Triton X-IOO. Samples were atomised from a L'vov platform in a pyrolytically-coated electrographite tube and peak area signals were measured. The accuracy of the analysis was checked against reference material: Seronorm Trace Element Serum L-1 (Nycomed AS, Oslo, Norway).

### 2.6. Statistical analysis

Due to the small number of participants in groups for individual maternal complications in subsequent trimesters of pregnancy (Table 1), it was not possible to perform reliable statistical analyses, therefore all complications were included as one group. The normality of variables distributions in the quotient / interval scales was evaluated by three different statistical tests: the Kolmogorow-Smirnow test, the Lillefors test and the Shapiro-Wilk test. To compare TAS and UA levels, GPX activity, serum selenium content and Se daily intake between trimesters we used nonparametric analysis of variance with the post-hoc Friedman's test for dependent variables. In the case of statistically significant differences, post-hoc comparisons NIR and RIR Tukey for unequal numbers were used. The homogeneity of variances was evaluated using Levene and Brown-Forsyth tests. Mann–Whitney U tests were used to compare the concentrations/activity between physiological and complicated pregnancy groups, and "below the recommendation" and "above the recommendation" subgroups in selenium intake context. Correlations were analyzed by Spearman's rank correlation test. For all tests a confidence level of $\alpha = 0.05$ was taken as being statistically significant.

## 3. Results

### 3.1. Participant baseline characteristics (Table 1)

The maternal age of most of the participants (50.7%) was in the range of 25–30 years, the mean age being 30.6 ± 5.4 years. The mean weight during the first, second and third trimesters was 63.12, 69.32 and 75.28 kg, respectively. Along with the duration of the pregnancy,

**Table 3**
Antioxidant status and serum selenium concentration during pregnancy according to selenium intake (mean ± SD).

| | T I | | T II | | T III | | p-value |
|---|---|---|---|---|---|---|---|
| | below the recommendations N = 44 | above the recommendations N = 22 | below the recommendations N = 33 | above the recommendations N = 29 | below the recommendations N = 24 | above the recommendations N = 26 | |
| Se intake [μg/day] | 33.14 ± 9.87[a] | 79.47 ± 22.56[a] | 34.58 ± 9.77[b] | 76.87 ± 22.40[b] | 35.98 ± 8.309[c] | 84.41 ± 32.04[c] | [a]0.0000 [b]0.0000 [c]0.0000 |
| Se serum [μg/L] | 41.87 ± 7.74 | 43.49 ± 7.01 | 40.42 ± 8.72 | 42.25 ± 7.06 | 39.58 ± 7.31 | 41.98 ± 7.81 | NS |
| GPX [U/L] | 219.97 ± 30.89 | 225.81 ± 48.13 | 219.3 ± 33.97 | 230.44 ± 41.94 | 221.04 ± 41.85 | 237.19 ± 32.18 | NS |
| TAS [mmol/L of Trolox] | 1.45 ± 0.18 | 1.46 ± 0.19 | 1.40 ± 0.21 | 1.46 ± 0.17 | 1.58 ± 0.51 | 1.55 ± 0.23 | NS |
| UA [mg/dL] | 3.45 ± 0.41 | 3.42 ± 0.43 | 3.75 ± 0.36 | 3.64 ± 0.43 | 4.57 ± 0.87 | 4.60 ± 0.67 | NS |

Differences between groups were assessed using U-Mann Whitney test [a,b,c] – $p < 0.05$.
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; TAS – total antioxidant status, UA -uric acid.

the percentage of complicated pregnancies increased from 13.6% at first trimester to 58.3% at third trimester. The vast majority of study participants had a higher education, lived in urban areas and never smoked cigarettes. All women were taking multivitamin and minerals supplements routinely used during pregnancy, but only 44% of the group were taking supplements containing selenium.

### *3.2. Selenium intake, serum selenium concentration and antioxidant status during pregnancy (Table 2)*

Whole blood GPX activity and total antioxidant status as well as selenium intake were the highest in the third trimester, but significant differences were not observed between values for these parameters in particular trimesters. Serum selenium concentration was the highest in the first trimester and the lowest in the third trimester, while the concentration of UA was the lowest in the first and the highest in the third trimester of pregnancy and the differences were statistically significant in both cases.

### *3.3. Antioxidant status and serum selenium concentration during pregnancy according to selenium intake (Table 3)*

The cut-off point taken into account when dividing the studied group into subgroups “below recommendation” and subgroup “above recommendation” was 50 μg Se/day. These Se intake above the recommended level results were reflected in higher daily Se intake - differences were statistically significant in each trimester, and higher serum selenium concentration, whole blood GPX activity and TAS level, but differences were not statistically significant between subgroups in particular trimesters. The serum uric acid in first and second trimester in the subgroup “above recommendation” was lower than in the subgroup “below recommendation”, however, the differences were not statistically significant.

### *3.4. Selenium intake, serum selenium concentration and antioxidant status during physiological and complicated pregnancy (Table 4)*

During the first two trimesters, women with a complicated pregnancy had higher selenium daily intake and lower serum selenium concentration compared to women with physiological pregnancy, but differences in any of the trimesters were not statistically significant. Regardless of the trimester of pregnancy, lower GPX activity and TAS level were observed in women with physiological course of pregnancy; and higher serum UA concentration, however, the differences were not statistically significant.

### *3.5. Correlations between selenium intake and antioxidant status parameters during pregnancy according to occurrence of pregnancy complication and selenium intake below or above the recommended level (Fig. 1)*

Daily Se intake was significantly, albeit weakly, correlated with the whole blood GPX activity (Spearman’s $\rho = 0.25$, $p < 0.05$) when results were taken overall during pregnancy, however, the correlation between these two parameters in particular trimesters of pregnancy was not observed. In the group of pregnant women who had Se intake above the recommended level, a significant positive correlation between selenium intake and serum UA concentration was recorded in the first and second trimester. Considering the occurrence of pregnancy complications, only in the group of pregnant women with the proper course of pregnancy, which had Se intake below recommended level, a significant positive correlation between Se intake and GPX activity was demonstrated in the second trimester. Statistical analysis did not show a statistically significant correlation between selenium intake and TAS level during pregnancy, similarly to serum Se concentration and particular markers of antioxidant status.

**Table 4**
Selenium intake, serum selenium concentration and antioxidant status during physiological and complicated pregnancy.

| | T I | | T II | | T III | | p-value |
|---|---|---|---|---|---|---|---|
| | Physiological pregnancy N = 57 | Pregnancy complications N = 9 | Physiological pregnancy N = 34 | Pregnancy complications N = 28 | Physiological pregnancy N = 21 | Pregnancy complications N = 29 | |
| Se intake [μg/day] | 47.93 ± 26.06 | 52.70 ± 31.97 | 51.79 ± 26.73 | 57.48 ± 27.65 | 62.36 ± 37.01 | 60.22 ± 31.98 | NS |
| Se serum [μg/L] | 42.01 ± 6.26 | 44.95 ± 13.14 | 42.17 ± 7.29 | 40.51 ± 8.81 | 41.90 ± 8.17 | 39.72 ± 7.09 | NS |
| GPX [U/L] | 217.21 ± 31.33 | 251.75 ± 56.93 | 218.78 ± 30.55 | 234.17 ± 40.32 | 216.45 ± 31.25 | 233.64 ± 43.93 | NS |
| TAS [mmol/L of Trolox] | 1.45 ± 0.18 | 1.49 ± 0.19 | 1.42 ± 0.21 | 1.43 ± 0.17 | 1.52 ± 0.22 | 1.61 ± 0.48 | NS |
| UA [mg/dL] | 3.45 ± 0.44 | 3.41 ± 0.21 | 3.76 ± 0.41 | 3.63 ± 0.38 | 4.46 ± 0.62 | 4.54 ± 0.83 | NS |

Differences between groups were assessed using U Mann- Whitney test $p < 0.05$.
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; TAS – total antioxidant status, UA – uric acid.

## 4. Discussion

The maintenance of the oxidation-reduction balance is a process dependent on many endo- and exogenous factors. The disturbance of this equilibrium may be reflected in the change in the values of laboratory parameters related to the body's antioxidant system. In our study, we evaluated the GPX activity as enzymatic and TAS and UA as a non-enzymatic component of the antioxidant defense of pregnant women's blood to assess the relationship between the prevalence of pregnancy complications with regarding to selenium intake and serum selenium concentration. GPX plays a critical role in the reduction of lipid and hydrogen peroxides and its enzymatic activity strongly depends on the availability of selenium [1]. Selenium is absorbed from food in the form of inorganic compounds like selenites (Me2SeO3) and selenates (Me2SeO4) or organic links – Se-methionine (SeMet) and Se-cysteine (SeCys). The absorption of selenium from organic compounds reaches 90–95%, whereas from inorganic links, it is lower by ca. 10%. Its bioavailability increases when a diet is rich in low molecular weight proteins, vitamins (mainly A, C and E), and it decreases if a diet contains an increased concentration of heavy metals (cadmium, lead, arsenic and mercury) [23]. For humans, a source of this microelement is foodstuff of both plant and animal origin, and marginally – drinking water. High quantities of selenium are provided by, among others, cereal products, seafood, haslets, eggs, yeast, tomatoes, asparagus, garlic, broccoli, nuts (especially Brazilian nuts), and turnip cabbage. Selenium compounds with confirmed red-ox potential are ebselen, Se-methionine, Se-cystine, diselenodipropanoic acide and others [24,25].

## 5. Dietary selenium intake and serum selenium concentration

Dietary selenium intake in Poland, as in some other European countries, is below the recommended nutrient intake level [2–4], however, in our study, the mean daily Se intake in particular trimesters was on the same level and covered the recommended value for Polish pregnant women. This fact may result from taking dietary supplements containing Se by a part of subjects, however, it should be noted that approximately 50% of pregnant women in each of the trimesters had a Se intake below the recommendations (Table 2). There is no data concerning dietary Se intake in European pregnant women, but our results are comparable with the intake of selenium among non-pregnant women from other European countries – 43 μg/d (United Kingdom); 74 μg/d (Spain) [2]. Dietary selenium intake has a decisive influence on the concentration of this element in the blood. We also noted this dependence in our study (Fig. 1). In each of the trimesters pregnant women consuming selenium in quantities above the recommendation were characterized by a higher serum Se concentration in comparison with pregnant women consuming Se in insufficient amounts. During pregnancy, the concentration of selenium in the blood decreases significantly [26,27]. In the case of our study, it was a decrease from 44.36 μg/L in the first trimester to 40.97 μg/L in the third trimester. Serum Se concentrations obtained in our study are comparable to the results of other authors –35 μg/L (Poland [28]); 58 μg/L(UK [5]); 52 μg/L (Ukraine [29]).

## 6. Selenium intake and glutathione peroxidase activity

Consumption of food rich in selenium, e.g Brazil nuts or Se-enriched foods, effectively raises plasma selenium concentration and GPX activity [30–32]. Plasma selenium reflects short-term changes in tissue selenium concentrations, whereas plasma and whole blood GPX activities are functional indexes of selenium status. According to the WHO, the plasma selenium concentration required to optimize plasma GPX activity is 6316 μg/L [33]. In our study we observed higher whole blood GPX activity in the subgroups “above recommendations” in each trimester of gestation comparing with the subgroups “below recommendations”, however, the differences were not statistically important. This is probably related to the low serum Se concentration of the studied pregnant women. We also showed a weak positive correlation between selenium intake and GPX activity during pregnancy, especially in the second trimester. The relationship between selenium intake and GPX activity is difficult to interpret as this biomarker is affected by dietary and other factors, such as the chemical nature of selenium ingested, baseline selenium status or the presence of certain diseases or gen polymorphisms [34].

In our study, we observed GPX activity was slightly decreased between first and third trimester. Uotila and colleagues [35] present reverse results, although in their study, GPX activity in erythrocytes was measured. In the study of Mihailovic and colleagues [36] selenium blood concentration and the activity of whole blood GPX in pregnant women in particular trimesters of pregnancy were assessed. A significant decrease in the level of selenium was noted in the second and third trimesters of pregnancy and during delivery. Concurrently, a decline was observed in the activity of GPX in the first trimester, and during the two subsequent trimesters, it maintained a similar level of activity as in the first trimester, whereas during delivery, it slightly increased.

The results of the present study clearly show that selenium intake and GPX were elevated in women with pregnancy complications, but we have not observed differences between physiological and complicated pregnancy GPX activity statistically significant (Table 4). We noted that women with pregnancy complications cared more about their diet by eating more eggs, cereals and vegetables at the expense of meat and fruit than women with physiological pregnancy (unpublished data). These food product groups are also a good source of selenium, which may explain the observed, although not significantly, higher Se daily intake in the group of women with complications. In addition, this group of pregnant women more often used supplements containing Se. The difference in GPX activity between physiological and complicated

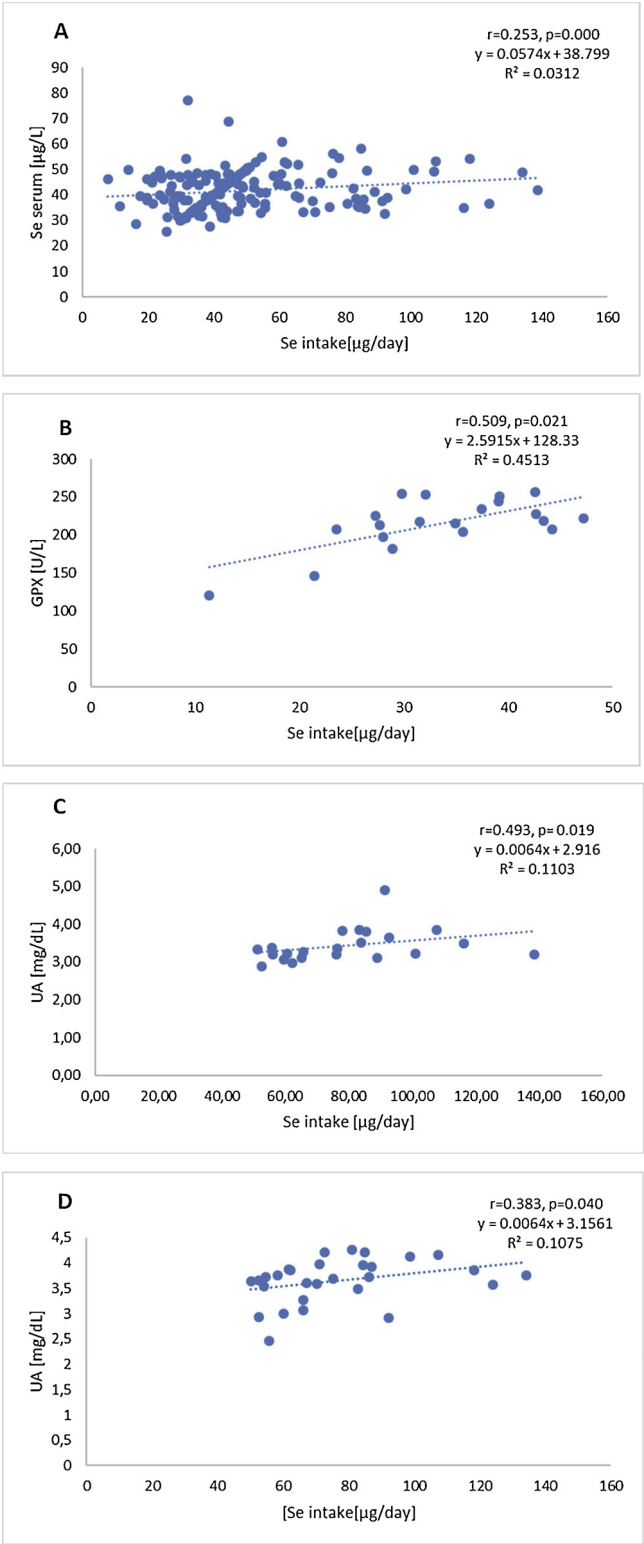


**Fig. 1.** Scatter plot with regression line showing correlation (A) between the Se intake and Se selenium concentration overall during pregnancy, (B) between the Se intake and GPX activity in subgroup with physiological pregnancy and Se intake below recommendations at second trimester, between the Se intake and serum UA concentration in subgroup with Se intake above recommendations at first (C) and second (D) trimester.

pregnancy has also been reported by other authors [37,38]. GPX, an oxidative stress inducible enzyme plays a significant role in the peroxyl scavenging mechanism and in maintaining functional integration of the cell membranes [39]. The increase in the GPX activity could be an adaptive response to elevated levels of oxidative stress in pregnancy complicated group connected with disturbances occurrence, higher Se intake and/or caring more about diet in this group.

## 7. Selenium intake and total antioxidant status

Total antioxidant status slightly increased during pregnancy, and we have not noted a significant difference in values between trimesters (Table 2). There is very little information in the literature regarding the total antioxidant status in the course of physiological pregnancy. As in our study, Hung and colleague [40] observed the highest TAS values in the third trimester of pregnancy. However, Belo and colleague [41] observed a gradual decrease in the level of TAS in the subsequent trimesters of pregnancy and they showed a significant difference between the first and second trimester and the first and third trimester. The TAS values obtained in our study are comparable to those provided by Karacay and colleague [42] and Belo and colleague [41]. We also noted a no significant correlation between selenium intake and TAS level regardless of the occurrence of pregnancy complications and the amount of selenium consumed. Perhaps selenium intake was too low among studied subjects and the TAS level was influenced by the intake of other food components such as vitamins C and E, phenolic compounds, carotenoids and protein-related compounds. All these antioxidant compounds are naturally occurring mainly in plant sources. With the development of pregnancy, we observed an increase in the consumption of vegetables and fruits as well as fish and eggs among pregnant subjects (unpublished data). The successively higher intake of fruit and vegetables, as a source of antioxidants other than selenium compounds, could have contributed to the increase in TAS level.

The occurrence of pregnancy complications are not significantly related to the TAS value in our study (Table 4). Studies carried out so far in which TAS was determined have concerned pregnant women with preeclampsia and gestational diabetes. The results of these studies indicate that in both preeclampsia and gestational diabetes, TAS values are lower in relation to physiological pregnancy [42,43]. However, Mert and colleague [44] obtained the opposite results. In pregnant women with preeclampsia and intrauterine growth restriction, they noted a higher TAS level than in physiological pregnancy.

## 8. Selenium intake and serum uric acid concentration

Uric acid is the major product of the catabolism of the purine nucleosides, adenosine and guanosine. Purines from catabolism of dietary nucleic acid are converted to uric acid directly. Uric acid accounts for roughly half the antioxidant ability of plasma. It has important antioxidant properties in vitro, by scavenging free radicals and chelating iron, the latter preventing iron-catalyzed oxidation. There is a strong correlation between the concentration of UA in biologic fluids and demonstrable antioxidant activity [45].

The serum UA concentration in each subsequent trimester of pregnancy gradually increased (Table 2), although this increase was lower in pregnant women with optimal selenium intake (Table 3) as well as in those with pregnancy complications (Table 4). Interestingly, we also showed a significant positive correlation between selenium intake and serum UA concentration in the first and second trimester in the group of pregnant women with the optimal selenium intake (Fig. 1). The placenta in physiological pregnancy is an abundant source of purines because of its high cell turnover, resulting in a higher production of uric acid at each subsequent trimester of pregnancy. The gradual increase in UA concentration along with the development of the pregnancy is also confirmed by the studies of other authors [46]. Among pregnancy complications affecting the level of serum UA, the ones that are most commonly mentioned are gestational hypertension and pre-eclampsia. In these cases, the concentration of UA is higher than in normal pregnancy [47,48]. Among the pregnant subjects we examined, only 2

patients had hypertension and none pre-eclampsia. This is probably why we did not show statistically significant differences between the group with physiological pregnancy and the group with complicated pregnancies. A positive correlation between selenium intake and serum UA concentration in the first and second trimester in the group of pregnant women with the optimal selenium intake, probably resulted from the successively increased intake of whole grain products and eggs as a source of selenium and meat, dairy products and fish as a source of purines in this period of pregnancy (unpublished data).

The lack of significant differences in TAS, UA and GPX values among pregnant women with physiological and complicated pregnancy may be due to the fact that only 6 pregnant women had gestational diabetes and 2 hypertension, where the correlation between complications and values of these parameters was proven. In other cases of complications, such relationships have not been shown in previous research or have been overcome by pharmacotherapy.

## 9. Limitation of the study

High homogeneity of the studied group (education, place of residence and age) and small numbers in the subgroups are the major limitations of our study.

## 10. Conclusions

Despite weak, positive correlations in the first two trimesters of pregnancy between selenium intake and GPX activity and UA concentration, we can conclude that selenium intake does not significantly affect during pregnancy, both: markers of the antioxidant status of pregnant women and the occurrence of pregnancy complications. Trends in the relationship between selenium intake and the values of antioxidant status markers and the occurrence of pregnancy complications require re-testing on more numerous group of pregnant women, in particular with complicated pregnancy.

## Conflict of interest

The authors declare that there are no conflicts of interest.

## Acknowledgements

The authors are extremely grateful to all the women who took part in the study and the team at the Department of Professional Training in Clinical Chemistry from Wroclaw Medical University, especially Lilla Pawlik-Sobecka and Izabela Kokot, for the blood samples collecting and laboratory analysis.

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