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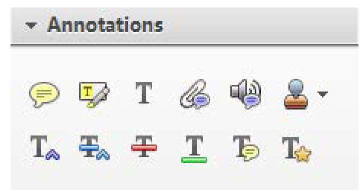

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The pattern of serum zinc and its contributing factors among third trimester pregnant women in Urmia, Iran, 2018

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Abstract

Purpose – The deficiency or excess of serum zinc in pregnancy may threaten the health of the mother and the fetus. The purpose of this study is to determine the pattern of serum zinc in pregnant women covered by Urmia urban health centers and its association with some nutritional and clinical determinants in the third trimester, from July to December 2018.

Design/methodology/approach – In this analytic cross-sectional study, of six selected health centers in Urmia, 400 pregnant women subjects who were in their third trimester were recruited in a simple random manner. The nutritional, demographic, clinical data as well as fasting blood samples were taken from each of the subjects. The data were analyzed using chi-square, independent t-test and logistic regression tests.

AQ: 1

Findings – The study revealed that about 3 per cent of pregnant women had zinc deficiency, 70.2 per cent were normal and 26.8 per cent had high serum zinc levels. In 388 pregnant women (72.4 per cent with normal serum zinc and 27.6 per cent with high serum zinc), binary logistic regression model showed that high concentration of serum zinc was directly associated with dietary intake zinc (OR: 2.252; 95 per cent CI: 1.85-2.74), supplement zinc (OR: 7.823; 95 per cent CI: 3.676-16.649) and total intake magnesium (OR: 1.005; 95 per cent CI: 1.000-1.01) and inversely associated with frequent reproductive cycling (OR: 0.739; 95 per cent CI: 0.569-0.959).

This study was extracted from an MS dissertation with license code of IR.UMSU.REC.1397.130 obtained from the ethics committee of the research center at Urmia University of Medical Sciences. This work was funded by the research committee of Urmia University of Medical Sciences. Funding agency had no role in the design, analysis and writing this article. Hereby, we appreciate all who participated in this study.

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Conflict of Interest: The authors declare no conflict of interest.

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Originality/value – Pregnant women in Urmia probably have high concentrations of serum zinc, and it is likely related to consumption of the zinc supplementation. Supplementation programs need to be scaled up for pregnant women that take inadequate dietary zinc.

Keywords Nutrition, Zinc, Epidemiology, Pregnancy, Clinical assessment

Paper type Research paper

1. Introduction

Zinc is a micronutrient, which has catalytic, regulatory and constructive roles in many enzymes, the gene transcription system, hormonal receptors, and signaling pathways that are essential for human metabolism, growth and reproduction (Shen *et al.*, 2015; Aggett and Comerford, 1995). Despite the importance of dietary zinc in maintaining health, adverse effects could also occur in case of excessive consumption or deficiency (Maret and Sandstead, 2006). The deficiency of serum zinc, perhaps, has a negative effect on maternal health and consequently on pregnancy outcomes, including gestational diabetes, preeclampsia and intrauterine growth restriction, increased risk of abortion, neural tube defects, low birth weight neonates, congenital heart malformations, preterm labor and prolonged pregnancy (Dickinson *et al.*, 2014; Dickinson *et al.*, 2009; Shen *et al.*, 2015). High levels of serum zinc can cause teratogenic and fatal effects during embryonic development (Maret and Sandstead, 2006).

In 2007, the World Health Organization (WHO), United Nations Children's Emergency Fund (UNICEF), International Atomic Energy Agency (IAEA), and International Zinc Nutrition Consultative Group (IZINCG) promptly announced the need to identify and determine the status of zinc around the world as a necessity (Benoist *et al.*, 2007). Approximately 1/4 of Iranian households suffer from Zn deficiency (Houshiar-rad *et al.*, 2013). In 2014, Tabrizi and his colleagues conducted a longitudinal study on 162 Iranian pregnant women. Their result indicated that 42 per cent of pregnant women had zinc deficiency (Tabrizi and Pakdel, 2014).

Urmia with a population of 679995 people in 2017 is one of the greatest border towns in the province of West Azerbaijan located in the northwest of Iran.

White flour and white rice are considered to be the main food in Iran. The zinc intake in this type of diet usually reaches 15 mg per day (Shams *et al.*, 2016). The zinc bioavailability is weaker than all cereal-based diet due to the presence of insoluble fiber and phytate factors (Gibson *et al.*, 2010; Lonnerdal, 2000). Respectively, bread, rice, and red meat are the major food sources of zinc in Iran (Houshiar-rad *et al.*, 2013).

The previous epidemiological studies indicated that the serum zinc status is influenced by many physiological and dietary factors, such as age, gender, ethnicity, soil, geographical location, seasonal changes, food preparation, pollution, body composition, individual pathophysiologic conditions (hormone therapy, pregnancy or inflammatory status), iron supplementation, and lifestyle (tobacco and cigarette) (Freeland-Graves *et al.*, 2015; Shen *et al.*, 2015; Lopes *et al.*, 2004; King, 2000).

Understanding the epidemiology of zinc status is critical to understand what intervention strategies will work best under different conditions (Bailey *et al.*, 2015). Assessment of pregnant women in the third trimester is necessary because it is a period of rapid growth for the fetus (McCarthy *et al.*, 2016). Consequently, it is a period when both mother and fetus are very susceptible to alterations in dietary supply, especially of nutrients which are marginal under normal circumstances (Tabrizi and Pakdel, 2014). The demand for zinc in a normal pregnancy, especially during the third trimester, imposes considerable systemic oxidative, metabolic and inflammatory stresses that play an important role in many diseases and adverse pregnancy outcomes such as miscarriages, preeclampsia, gestational diabetes mellitus, and intrauterine growth restriction (Choi *et al.*, 2016a). However, few community-based studies have investigated the prevalence of zinc status in the pregnancy of the Iranian women, and serum zinc status during pregnancy in the women in Urmia is not understood. Understanding the pattern of serum zinc in pregnant women helps public health programs to guide women during their pregnancy about intake of zinc, and to minimize the occurrence of adverse pregnancy outcome. Therefore, this study was conducted to determine the pattern of serum zinc in pregnant women covered by Urmia urban health centers and its association with some nutritional and clinical factors in the third trimester in 2018.

2. Method

2.1 Study subjects

This descriptive-analytical cross-sectional study was conducted in six selected urban health centers and their subset health stations, Urmia, Iran. The protocol of this study was approved by the research and ethics committee of Urmia University of Medical Sciences. According to a study that zinc deficiency was reported in 42 per cent of pregnant women (Tabrizi and Pakdel, 2014); sample size of the current study was calculated based on the formula for cross-sectional studies: $n = [(Z^2 a_{/2} P\ (1\_P)]/d^2$; where P and d were the prevalence of zinc deficiency and accuracy, respectively. Given the $Z\ a_{/2} = 1.96$, $d = 0.05$ and $P = 42$ per cent, the calculated sample size was 375 subjects. In total, to increase the accuracy of the results of the study, 400 pregnant women in the third trimester entered the study.

Health centers include a maternal and child health care provider (midwife and health technician), a family physician, dentist, dietitian, psychologist, nurse, and many laboratory technicians. Each of these health centers has 3 to 5 subset health stations that only have a health care provider. Regarding to the health center reports, around 790 pregnant women have been enrolled for routine antenatal care during their third trimester of pregnancy ($\geq$28 weeks of pregnancy) from July to December 2018.

According to the number of pregnant women covered by each center, subjects were recruited in a simple random manner from pregnant women who came to attend a routine follow up at urban health centers during their third trimester of pregnancy. All selected subjects were explained about the purpose of the study and if they agreed to participate, they were included in the study. After written informed consent was obtained, 400 subjects were included in this study of 790 pregnant women. Subjects were asked to come to health houses or health centers on the appointed day for blood sampling, and then demographic, clinical, and nutritional information from each subject was taken by the interviewer.

2.2 Data collection and anthropometric measurements

Information about social-demographic characteristics (including age, the number of family members, the level of education, home status, smoking, alcohol consumption during pregnancy and during 4 weeks prior to the last menstrual period, occupational status, place of residence, addiction, and background the prison during pregnancy), obstetrical and gynecological histories, including gestation (number of pregnancy), parity (number of deliveries) and gestational week were obtained from health center medical records.

Clinical information on subjects including pre-pregnancy diabetes, stillborn and abortion history, anemia during pregnancy, coagulation disorders, edema, autoimmune disease, metabolic bone disease, liver and kidney failure, adrenal and thyroid dysfunction, parathyroid gland diseases, dyslipidemia, gastrointestinal disease, including malabsorption or hepatic disorders, cardiovascular disease, cancer, infection, chronic inflammatory disease, obesity, drug used for weight loss, antidepressants and anti-inflammatory drugs, and hormone therapy during the last 6 months and twin pregnancy had been extracted through health records of pregnant women.

A trained research assistant recorded anthropometric measurements in each participant. Maternal weight and height were measured at the time of blood sampling, with the subjects wearing light clothing and no footwear. Each participant's weight was measured using a calibrated digital weighing scale at a precision of 0.1 kg (Seca 813; Germany). The height in all subjects was measured at a precision of 0.1 cm with a meter strip (behind the foot, the buttocks, the scapula, and behind the head was abutted on the wall). The pre-pregnancy BMI was calculated as weight in kilograms divided by height in meters squared based on pre-pregnancy weight.

The dietary intakes were estimated from three days 24-hour dietary recall method and other nutritional information, including the breastfeeding during pregnancy, weight gain during pregnancy, alcohol intake, dietary supplementation, specific diet was obtained through the health center medical records of pregnant women.

2.3 Dietary assessment

Food consumption data were collected through pregnant women interviews using 24-hour recall method for three days and it was converted into certain nutrient intake, including zinc, copper, magnesium, calcium, iron, and fiber using the Nutritionist IV software (version 7.0; N-Squared Computing, Salem, OR, USA) which was modified for Iranian food items (Abdollahi *et al.*, 2016). The first 24-hour dietary recall was done using a private in-person interviews, whereas the second and third interviews were conducted by the researcher through a phone call on a holiday and non-holiday day (Bogle *et al.*, 2001). The adequacy of nutrients zinc and fiber were determined by using the recommended dietary allowances (RDAs) (Mahan and Janice, 2016a).

2.4 Laboratory tests

Blood samples were taken from all individuals by a trained person. To measure levels of serum zinc, 3 ml venous blood sample was taken from pregnant women after ten hours of fasting in the third trimester between about 8:00 a.m. and 9:00 a.m. and poured into an acid-washed test tube. Peripheral blood samples were obtained by venipuncture. Blood samples were allowed to clot at room temperature nd were centrifuged for 10 min at 3,000 rpm and serum was separated from the clot (Kilinc *et al.*, 2010). The serum was poured into metal-free plastic polyethylene tubes using a sampler and cap. The test tubes were labeled with an identification number, and serum was then stored at $-20\ ^3$C before transportation. All serum samples were collected and placed in a cold box over dry ice, and transported to the biochemical analysis laboratory of the nutritional science department in the Urmia medical college within 20 to 30 min. They were kept on -80^3C prior to analysis. The maternal serum was assessed in nutritional science department laboratory. Zinc concentration of the samples was determined by using a standard kit (Dialab, Australia) and the BT-1500 auto analyzer (Biotechnical, Rome, Italy) (Vafaei *et al.*, 2015; Johnsen and Eliasson, 1987). Serum levels of 50-77 μg/dl were considered as the normal ranges (Mahan and Janice, 2016b).

2.5 Statistical analysis

Prevalence data were reported as percentages and confidence intervals. Distribution of normality for quantitative data was evaluated by Kolmogorov–Smirnov test. Data with normal distribution was summarized by mean, standard deviations and minimum-maximum values for data with abnormal distribution. Categorical variables are presented as frequency and percentage. The chi-squared test was used to compare categorical variables and Fisher's exact tests were performed for categorical variables if necessary. The means of quantitative variables were compared with the independent sample *t*-test and one-way ANOVA. A *p* value of less than 0.05 was considered statistically significant in the single variable analysis. Logistic regression with 95 per cent confidence intervals was used to calculate odds ratios (OR) for effective factors between various patterns of serum zinc concentration. Variables with a *p* value of less than 0.05 in the single variable analysis were included in the multivariable analysis. The classification of nutrient intake on the criteria of the Institute of Medicine and RDA for zinc. The data were analyzed by statistical package for the social sciences (SPSS) version 21.

3. Results

In the present study, out of 400 enrolled subjects, only 12 pregnant women (3 per cent) showed zinc concentrations lower than 50 μg/dl (95 per cent CI, 1.33 per cent to 4.67 per cent), 107 pregnant women (26.8 per cent) presented zinc concentrations higher than 77 μg/dl (95 per cent CI, 26.75 per cent to 26.84 per cent) and 281 pregnant women (70.2 per cent) had normal serum zinc levels.

Serum zinc deficiency in the studied population is very low; therefore, we omitted pregnant women with serum zinc deficiency. Our study analyzed the relationships between excessive and normal serum zinc with clinical, nutritional, demographic and socioeconomic factors.

The mean serum zinc level in the pregnant women was between the normal ranges of 50 to 77 μg/dl, but 27.6 per cent of the 388 pregnant women in the third trimester had serum zinc values above 77 μg/dl. Among 388 pregnant women with excessive and normal serum zinc level, the mean (SD) and range of age, gestational week, BMI, weight gain and serum zinc concentrations were 27.15 (6.66), 14-44 years, 32.4(2,73), 28-40 weeks, 26.01 (4.84), 15.4-45 kg/m2, 7.8 (4.1), _4-25 kg and 73.7(17.1), 50-185 μg/dl, respectively. The statistical
T1 significance between normal and excessive serum zinc groups was shown in Tables I, II and III. We found that about 13.5 per cent of the pregnant women in Urmia city take zinc supplements. Also, the dietary zinc intake by 92.3 per cent of pregnant women was adequate
AQ: 2 according to the RDA (Table I).

Pregnant women with excessive serum zinc were more likely to have a higher mean
T2 income (Table I). As shown in Table II, excessive serum zinc has been more prevalent in pregnant women with interval since last live birth more than 154 weeks (Serum zinc concentrations were lower in women with closely spaced pregnancies). No associations were found between maternal serum zinc concentration and gestational age (28-32, 33-35, 36-
F1 40 weeks) (Figure 1).

The food intake of zinc, zinc supplementation, total zinc intakes, folic acid supplementation, magnesium supplementation and total magnesium intakes (diet and supplement) were higher in the excessive serum zinc group compared with the normal serum zinc group; but frequent reproductive cycling (maternal gravidity), food intake of iron, iron supplementation and total iron intakes in pregnant women with excessive serum
T3 zinc were lower than pregnant women with normal serum zinc levels (Table III).

Since several variables affect, the excess of serum zinc, the logistic regression model was used by selecting the LR method with PE = 0.05, PR = 0.1 to estimate the coefficients of effectiveness variables as predictors of multiplier excessive serum zinc. Multivariate studies with binary logistic regression showed a strong association between the zinc supplementation and excessive serum zinc. (OR: 7.823; 95 per cent CI: 3.676-16.649). Also, excessive serum zinc was directly associated with food intake of zinc (OR: 2.252; 95 per cent

	Group 1 High serum zinc Frequency (%)	Group 2 Normal serum zinc Frequency (%)	Total(n = 388) Frequency (%)	p-value
Age				
<18	8 (7.5)	23 (8.2)	31 (8.2)	0.17
18-19.9	8 (7.5)	18 (6.4)	26 (6.7)	
20-24.9	23 (21.5)	63 (22.4)	86 (22.2)	
25-29.9	37 (34.6)	75 (26.7)	112 (28.2)	
30-35	26 (24.3)	63 (22.4)	89 (22.7)	
>35	5 (4.6)	39 (13.9)	44 (11.3)	
Season				
Summer	46 (43)	139 (49.5)	185 (47.7)	0.25
Fall	61 (57)	142 (50.5)	203 (52.3)	
Educational status				
Guidance sch.	33 (30.8)	91 (32.4)	124 (32)	0.32
High school	42 (39.3)	125 (44.5)	167 (43)	
Bachelor	27 (25.2)	48 (17.1)	75 (19.3)	
Msc and higher	5 (4.7)	17 (6)	22 (5.7)	
Residence				
Good	32 (29.9)	67 (23.8)	99 (25.5)	0.25
Average	44 (41.1)	109 (38.8)	153 (39.4)	
Poor	31 (30)	105 (37.4)	136 (35.1)	
Income				
More than expenses	38 (35.5)	70 (24.9)	108 (27.8)	0.020
Equal	61 (57)	164 (58.4)	225 (58)	
Less than expenses	8 (7.5)	47 (16.7)	55 (14.2)	
House area				
<100	58 (54.2)	158 (56.2)	216 (55.7)	0.031
100-200	38 (35.5)	113 (40.2)	151 (38.9)	
>200	11 (10.3)	10 (3.6)	21 (5.4)	
Mother's occupation				
Employed	9 (8.4)	20 (7.1)	29 (7.5)	0.66
Housewife	98 (91.6)	261 (92.9)	359 (92.5)	
Housing status				
Householder	75 (70)	180 (64.1)	255 (65.7)	0.26
Rental house	32 (30)	101 (35.9)	133 (34.3)	
Smoking				
Yes	1 (0.1)	3 (1.1)	4 (1)	0.91
No	106 (99.1)	278 (98.9)	384 (99)	
Intake food Zn (RDA)				
Inadequate	3 (2.8)	27 (9.6)	30 (7.7)	0.025
Adequate	104 (97.2)	254 (90.4)	358 (92.3)	
Zn supplementation				
No	70 (65.4)	266 (94.7)	336 (86.5)	<0.001
Yes	37 (34.6)	15 (5.3)	52 (13.5)	
Intake fiber (RDA)				
Inadequate	94 (87.9)	243 (86.5)	337 (88.9)	0.72
Adequate	13 (12.1)	38 (13.5)	51 (13.1)	

Notes: Abbreviations: Zn, zinc; RDA, Recommended dietary allowance; p-value; for a comparison of frequencies, chi-square test was used; Differences between Groups 1 and 2 are statistically significant; $p < 0.05$

Table I.
Frequency distribution of demographic and nutritional data in normal and excessive serum zinc groups

	Group 1 (n = 107) high serum zinc Frequency (%)	Group 2 (n = 281) normal serum zinc Frequency (%)	In total (n = 388) Frequency (%)	p-value
BMI *				
<18.5	2 (1.8)	15 (5.4)	17 (4.4)	0.41
18.5-24.9	40 (37.4)	116 (41.3)	156 (40.2)	
25-29.9	40 (37.4)	94 (33.4)	134 (34.5)	
30-34.9	19 (17.8)	47 (16.7)	66 (17)	
≥35	6 (5.6)	9 (3.2)	15 (3.9)	
IOM recommendations *				
Inadequate WG	18 (16.8)	55 (19.6)	73 (18.8)	0.82
Adequate WG	82 (76.7)	208 (74)	290 (74.8)	
Excessive WG	7 (6.5)	18 (6.4)	25 (6.4)	
Gestational age $^{\alpha}$ *wk* *				
28-32	64 (59.8)	173 (61.6)	237 (61.1)	0.42
33-35	31 (29)	66 (23.5)	97 (25)	
36-40	12 (11.2)	42 (14.9)	54 (13.9)	
Lactation with pregnancy **				
Yes	0 (0)	8 (2.8)	8 (2.1)	0.07
No	107 (100)	273 (97.2)	380 (97.9)	
Anemia *				
Yes	16 (15)	44 (15.7)	60 (15.5)	0.86
No	91 (85)	237 (84.3)	328 (85.5)	
Heartburn *				
Yes	11 (10.3)	34 (12.1)	45 (11.6)	0.62
No	96 (89.7)	247 (87.9)	343 (88.4)	
Twin pregnancy *				
Yes	3 (2.8)	4 (1.4)	7 (1.8)	0.26
No	104 (97.2)	277 (98.6)	381 (98.2)	
Stillborn history *				
Yes	1 (0.5)	9 (4.5)	10 (3.7)	0.21
No	70 (98.5)	189 (95.5)	259 (96.3)	
Abortion history *				
No	49 (69)	143 (72.2)	192 (71.4)	0.61
Yes	22 (31)	55 (27.8)	77 (28.6)	
Birth interval (week) *				
≤154	6 (10)	34 (18.9)	38 (15.8)	0.025
≥155	54 (90)	146 (81.1)	202 (84.2)	

Notes: Abbreviations: BMI, body mass index; IOM, Institute of Medicine; WG, weight gain. $^{\alpha}$Gestational week at blood drawing time; $^{*}p$ value; for a comparison of frequencies, chi-square test was used; $^{**}p$ value; for a comparison of frequencies, fishers exact test was used; Stillborn and abortion history was assessed for subjects with at least one gestational history. Birth interval was assessed for subjects with at least one parity; Differences between Groups 1 and 2 are statistically significant; $p < 0.05$

Table II. Frequency distribution of clinical variables in normal and excessive serum zinc groups

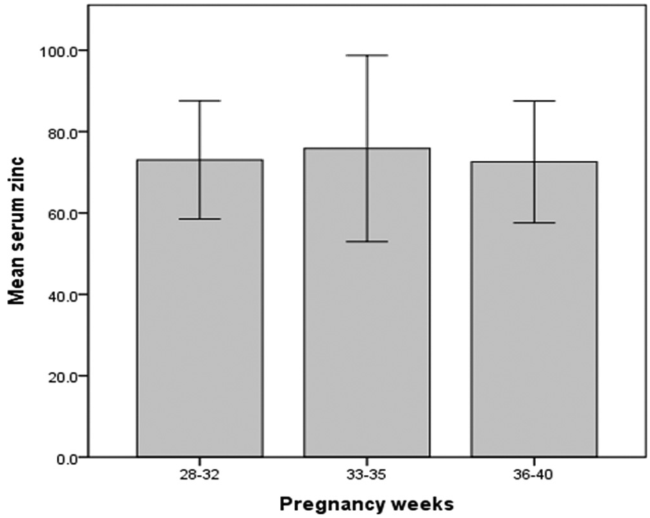

Figure 1.
Serum zinc concentrations during the third trimester of pregnancy

Note: No associations were found between maternal serum zinc concentration by gestational age. One-way ANOVA P-value for gestational age = 0.346

CI: 1.85-2.74) and total magnesium intake (OR: 1.005; 95 per cent CI: 1.000-1.01), and inversely associated with frequent reproductive cycling (OR: 0.739; 95 per cent CI: 0.569-0.959) (Table IV). T4

4. Discussion

In this study, which included a large number of pregnant women in the third trimester from different socioeconomic areas of the Urmia, we found that the frequency of zinc deficiency was not noticeable while the frequencies of the excessive serum zinc was remarkable. Excessive serum zinc was associated with food intake of zinc, supplement zinc, total intake magnesium. Additionally, we observed an inverse association between maternal serum zinc concentration and frequent reproductive cycling or number of pregnancy.

Based on a systematic review study conducted in 2017, it had been concluded that 46-76 per cent of pregnant women have a serum zinc deficiency, and inadequate dietary zinc has been reported to be 84 per cent in South African pregnant women (Harika *et al.*, 2017). In the present study, we found that only 3 per cent of the pregnant women had a serum zinc deficiency and 26.8 per cent had high concentrations of serum zinc and about 92.3 per cent of the subjects have adequate dietary intake of zinc. Adequate intake of micronutrients and subsequent adequate levels of zinc in the blood stream are influenced by culture, environment and demographic variables. Our study was conducted in urban health centers and subjects were selected from different socioeconomic conditions. While Harika *et al.* reviews included 65 surveys and studies from Ethiopia, Kenya, Nigeria and South Africa that have low socioeconomic populations (undeveloped countries), and mostly at rural level, that nutrition intervention and public health programs, such as dietary diversification, micronutrient fortification and supplementation are not developed.

Table III. The concentration of serum zinc related to the clinical and nutritional variables, stratified by zinc status in the examined pregnant women (mean ± SD)

	Group 1 (n = 107) Excessive serum zinc[a] (n = 107)	Group 2 (n = 281) Normal serum zinc[a] (n = 281)	Total[a] (n = 388)	p-value
Serum Zn	93.9 ± 19.2	65.9 ± 6.7	73.7 ± 17.1	<0.001
Diet Zn (mg)	14.4 ± 1.6	12.4 ± 1.4	12.9 ± 1.73	<0.001
Supplement Zn (mg)	9.2 ± 13.4	1.3 ± 5.6	3.5 ± 9.2	<0.001
Diet Mg (mg)	380.4 ± 49.6	373.3 ± 45.9	375.2 ± 47.1	0.18
Supplement Mg (mg)	94.4 ± 27.4	85.2 ± 34.9	87.8 ± 33.2	0.007
Total Mg intake (mg)	474.8 ± 57.3	458.5 ± 58.9	462.9 ± 58.8	0.015
Diet Fe (mg)	19.9 ± 3.3	21.3 ± 2.6	20.9 ± 2.9	0.003
Supplement Fe (mg)	55 ± 23.3	63.4 ± 20.9	61 ± 21.1	0.001
Total Fe intake (mg)	74.9 ± 23.5	84.7 ± 21.2	81.9 ± 22.3	0.001
Diet Ca (mg)	871.6 ± 123.4	890.1 ± 119.6	884.9 ± 120.8	0.18
Supplement Ca (mg)	200.3 ± 181.7	193.1 ± 193	195.1 ± 189.7	0.73
Total Ca intake (mg)	1071.9 ± 230.8	1082.2 ± 226.9	1080 ± 227.8	0.66
Diet Cu(gr)	1.6 ± 0.5	1.5 ± 0.5	1.5 ± 0.5	0.09
Diet fiber	23.6 ± 3.1	22.9 ± 3.1	23.1 ± 3.1	0.16
Supplement folic acid	0.5 ± 0.2	0.3 ± 0.2	0.4 ± 0.19	0.002
Supplement vit D	382.1 ± 121.9	376 ± 153.6	378.8 ± 145.4	0.49
Weight gain during pregnancy(kg)	8.3 ± 3.8	7.9 ± 4.2	7.9 ± 4.1	0.30
Maternal gravidity	2.1 ± 1.0	2.3 ± 1.2	2.25 ± 1.18	0.026
Maternal parity	0.9 ± 0.9	1.1 ± 1.1	1.0 ± 1	0.072

Notes: Abbreviations: Cu, Copper; Zn, Zinc; Mg, Magnesium; Fe, Iron; Ca, Calcium. [a]Mean ± standard deviation (X±SD); Maternal gravidity (number of pregnancy or frequent reproductive cycling), including number of abortions, stillborn, and child birth. Maternal parity including number of stillborn and child birth; Comparison between excessive serum zinc and normal serum zinc groups were performed with independent t test for continuous variables; Differences between Groups 1 and 2 are statistically significant; $p < 0.05$

Table IV. Binary logistic regression model for excessive serum zinc

Significant explanatory variables	OR	Lower–upper 95 % CI	p-value
Total intake of Mg	<1.01	1.00-1.01	0.039*
Maternal gravidity	0.74	0.57-0.96	0.023*
Supplement Zn			
Yes	7.82	3.68-16.65	<0.001*
No	Reference	–	
Food intake of Zn	2.25	1.9-2.7	<0.001*

Notes: Abbreviations: Mg, magnesium; Zn, zinc; CI, confidence interval; OR, odds ratio. *Statistically significant p value

Based on a prospective study conducted in 2016, it had been concluded that the concentrations of serum zinc varied significantly during the three trimesters and serum zinc concentrations decreased during the course of pregnancy (Choi *et al.*, 2016a), but in our study, serum zinc concentration was not significantly different during the third trimester of pregnancy. The serum zinc concentration progressively decreases from early gestation until week 22, after which this concentration remains constant (Tamura *et al.*, 2000).

In the present study, we found that there was a significant positive relation between excessive serum zinc and zinc intake from food or zinc supplements. Our finding is supported by the results of another study reported that the population means serum zinc concentrations increase consistently during zinc supplementation (Hess *et al.*, 2007). Zinc supplement is the major factor determining toxicity(Maret and Sandstead, 2006). Increased concentrations of heavy metals in the serum result from the environmental exposure of the organism, including dietary intake, and the degree of environmental pollution in the place of residence(Padilla *et al.*, 2010). We found that about 13.5 per cent and 92.3 per cent of the pregnant women in Urmia city take zinc supplements and adequate dietary zinc, respectively. It should be noted that since a large amount of zinc is required for pancreatic islet β-cells, zinc suddenly released under certain conditions might affect the function or survival of islet cells, and cause paracrine effects of the endogenous zinc on β-cell death. Therefore, zinc supplementation in pregnant women with adequate dietary intake zinc may be toxic to the pancreas (Zheng *et al.*, 2008).

In our study, excessive serum zinc has been more prevalent in pregnant women with less frequent reproductive cycling. Gibson and his colleagues reported that the number of pregnancies was an etiological factor influencing the biochemical zinc status of pregnant women. Nulliparous women had the highest hair zinc concentrations and concentration of hair zinc decreased due to the increase in the number of pregnancy, but such a trend was not apparent for plasma zinc concentrations. Pregnant women with a more frequent reproductive cycling consumed diets of poorly available zinc compared to women with less frequent reproductive cycling (Gibson and Huddle, 1998).

Human studies suggest that folic acid causes an inhibitory effect on zinc uptake (Tupe *et al.*, 2007). However, increasing the intake of folic acid through supplementation or fortification is generally considered safe (Hansen *et al.*, 2001). In the present study, we found that there was a significant positive relation between serum zinc levels and folic acid supplementation, and we revealed the negative effect of consumption of iron on serum zinc levels. Because folic acid supplements have an effect on zinc excretion patterns and reduce the urinary zinc excretion (Milne *et al.*, 1984).

The present study revealed a negative association between consumption of iron and excessive serum zinc. Oral iron supplementation impairs zinc absorption in pregnant women (Liu *et al.*, 2010). Iron may interfere with zinc absorption because of similar physicochemical properties and shared absorption pathways. Fractional iron absorption is strongly dose dependent, and an intraluminal interaction may occur between zinc and iron (Choi *et al.*, 2016b; Ackland and Michalczyk, 2016).

The study's limitation is that this study was carried out only in the urban areas of Urmia and did not investigate the serum zinc status in the villages of the province. The techniques used for trace element analyses in human biological fluids and tissues, such as flame atomic absorption spectrometry (AAS), graphite furnace AAS, inductively coupled plasma (ICP) atomic emission spectrometry, and inductively coupled plasma-mass spectrometry (ICP-MS) were not used due to lack of facilities.

5. Conclusion

The present study showed that zinc deficiency among the studied population was not prevalent, but high serum levels of zinc were seen in 26.8 of them. Our study also indicates that the excessive serum zinc is predicted by dietary intake zinc, supplement zinc, total intake magnesium and less frequent reproductive cycling. Research to date has not identified an effective zinc supplementation strategy to combat the adverse perinatal effects associated with suboptimal maternal diet; indeed, supplementation strategies may only be beneficial when a deficiency is observed. Thus, pregnant women should maintain nutritional balance; have regular medical examinations, serum trace elements should also be investigated, thereby reducing adverse pregnancy outcomes. A complete understanding of the underlying dietary profile is warranted to avoid needless supplementation where no deficiency exists. The recommendations of our study are to examine the amount of zinc in the soil and study the use of fertilizers in agricultural lands in this province.

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