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Original article

The Pattern of Serum Copper and Magnesium in Pregnant Women Covered by Urmia Urban Health Centers and Its Clinical and Nutritional Determinants in the Third Trimester of Pregnancy, 2018

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Abstract

Background: Copper and Magnesium are essential for development of the fetus and maternal health. The aim of this study was to determine the pattern of serum copper in pregnant women in Urmia and its association with some clinical and nutritional factors in the third trimester of pregnancy. ***Materials and method:*** In this analytic cross-sectional study, 400 pregnant women in the third trimester were randomly selected from the women who referred to 6 selected health centers for their routine care. It was investigated demographic, nutritional and clinical factors and fasting blood samples were obtained. The data were analyzed using Chi-square, Independent T-test and logistic Regression tests using SPSS 21 software. ***Results:*** The serum analysis showed that Magnesium and copper deficiency among studied population were not prevalent but high serum levels of magnesium and copper were seen in 24% and 13% of them respectively. Based on binary logistic regression model outputs, the development of excessive serum magnesium levels was directly correlated with dietary magnesium intake, magnesium supplementation and dietary fiber intake (OR: 1.109; 95% CI: 1.008-1.219) and inversely correlated with total dietary intake of calcium. The high concentration of serum copper was directly associated with dietary intake of copper and negatively associated with total intake of dietary magnesium, iron deficiency anemia (OR: 0.369; 95% CI: 0.166-0.819) and pre-pregnancy BMI. ***Conclusion:*** Pregnant women in Urmia probably have high concentrations of serum magnesium in comparison to other parts of the country. It is likely related to consumption of the Mg supplementation.

Keywords: ***Nutritional assessment, Copper, Magnesium, epidemiology, pregnancy.***

Introduction

Copper and magnesium are known as essential elements for human well-being [1]. These two elements have prominent effects on the health of pregnant women and fetal development [2,3].

Copper plays an important role in biological processes such as antioxidant defense, mitochondrial respiration and iron homeostasis [4]. Either low or high serum levels of copper could exert adverse effects on health and wellbeing [5,6]. High levels of Copper in maternal serum could cause cerebral disorders in the fetus and might induce abortion [3]. Copper deficiency during embryonic and fetal development can lead to many physiological and biochemical abnormalities [7].

Magnesium is involved in more than 300 important biochemical reactions [8]. According recent evidences, magnesium deficiency could associate with preeclampsia, gestational diabetes, intrauterine growth retardation, low birth weight, and the death of newborns [9-11]. Excessive intake of magnesium may leave catastrophic consequences on the fetus from obstetrical viewpoint [12]. High serum levels of magnesium cause changes in memory (mind), gastrointestinal disorders, respiratory distress, severe hypertension [12,13].

A cross-sectional study in Khoy by Tabrizi et al (2014) on 162 healthy women with confirmed pregnancy showed that the proportion of the magnesium deficiency were 13 percent [14]. Another cross sectional study by Dabbahmanesh et al (2011) in Shiraz showed that 24 percent of the population suffered from copper deficiency [15].

Urmia city is one of the largest border towns located at the northwest of Iran with a population of more than one million people. The city is self-sufficient in terms of food production. Furthermore, Primary Health Care (PHC) was launched in Urmia in 1973 as the first PHC-implemented city in Iran.

The nutritional status of the trace elements is affected by many factors such as the element content of the agriculture soil, food preparation methods, environmental pollution, ethnicity and physiological and nutritional factors [16,17]. Digestion, absorption and metabolism of the elements may be altered due to physiologic changes and elevated nutritional needs during pregnancy [3,17,18].

Many evidences suggest that pregnant women are highly susceptible to depletion and deficiency of copper due to their physiological needs [19]. The adequacy of both gastrointestinal and kidney functions determine the concentration of magnesium in the plasma [13]. Achieving toxic levels of magnesium through excessive dietary intake is very rare and usually occurs due to renal failure[20,21].

The study on the micronutrients nutritional status would be critical to identifying the best interventional strategy for battling with undesired situations. The present study aims to determine the serum copper and magnesium pattern in pregnant women covered by Urmia urban health centers and its relation with some nutritional and clinical factors in the third trimester of pregnancy in 2018.

Materials and method

Study subjects

In this analytical cross-sectional study, we included 6 urban health care centers and their subset health houses to study. According to a study (14) that magnesium deficiency was reported in 13% of pregnant women ($p = 0.13$ $d = 0.05$, $\alpha = 0.05$), the sample size was calculated using the Cochran formula (When the statistical society is unclear) of 174 subjects. To increase the accuracy of the results of the study, a total of 400 cases were randomly selected from 790 pregnant women who were referred for routine care in the third trimester in proportion to the number of pregnant women covered by each center.

The participants were justified for research goals and confidentiality of the data collection information and then if they wanted to collaborate with the authors, they were candidate to include in the study. Conscious informed consent was obtained from those who were willing to participate in the study. They were asked to come to the labs of the health centers on the next morning in fasting state. Afterward, from each participant at the next session, all of needed blood samples and demographic, clinical and nutritional information were taken.

Data collection and Anthropometric measurements

Socio-economic information of the participants including age, number of family members, study duration, home ownership status, area of the home, history of smoking, alcohol consumption, occupational status, marital status, place of residence, addiction and the history of being imprisoned were registered using health records.

Anthropometric and clinical information of participants includes height, current weight and blood pressure, body mass index, pre-pregnancy diabetes, hypertension, gestational age, abortion history, coagulation disorders, edema, history of autoimmune disease, metabolic bone disease, liver and kidney failure, adrenal and thyroid dysfunction and parathyroid dysfunction, dyslipidemia, gastrointestinal diseases including malabsorption, cardiovascular disease, cancer, infectious disease, chronic inflammatory disease, weight loss medications, anti-diabetic drugs, antidepressants, anti-inflammatory drugs water and hormone therapy during the last 6 months and twin pregnancy have been obtained.

The weight and height of the participants were measured by standard methods. Height was measured in a vertical position without any shoes and using a tape with a 0.1centimeters accuracy while behind the foot, the buttocks, the scapula and the head lean on the wall.

We used the Seca Digital Scale (Seca813; Germany) with a 0.1 kg accuracy to measure the subjects' weight with the lowest possible costume and without shoes.

Nutritional information of the subjects was acquired through a 24-hour, three-day recall questionnaire including zinc, copper, magnesium calcium, iron and fiber intake, or through the health records of pregnant women, including breastfeeding during pregnancy, body mass index, weight gain during pregnancy, alcohol intake, dietary supplementation, anemia condition and following of a specific diet.

Dietary assessment

Dietary assessment was fulfilled by three day 24-hour recall method [22]. Accordingly, the intake of some related minerals including magnesium, copper, iron, calcium, zinc and total dietary fibers were estimated as 3 consecutive days (one day off and two normal days). The intake at the first day was conducted as personal interview whereas the dietary assessment was done at the two other days as telephone call interview [23]. A modified version of Nutritionist IV software for Iranian community was used to analyze nutritional data.

Laboratory tests

Blood samples from all participants were collected by a trained person. At least 5 ml of whole blood were obtained from the venous vein after 10 hours of fasting. The samples were centrifuged at room temperature to separate the serum at 3500 rpm for 30 minutes, and then the samples were rapidly transferred to the nutrition department laboratory within a cold box. The serums were stored at -86 ° C until the end of the sample collection. All serum samples were determined by a standard kit (Dialab, Australia) using the BT-1500 auto analyzer (Biotechnical, Rome, Italy). Recovery percentage, which ranged from 70% to 120% is one of the criteria indicating accuracy of metal analysis in serum, was calculated for quality control data. Normal serum ranges for magnesium and copper were considered 1.1 – 2.2 mg/dl and 130-240 µg/dl respectively [24]. Dietary adequacy for copper and magnesium was determined based on Recommended Dietary Allowances (RDA) [25].

Statistical analysis

Prevalence data were reported as percentages and confidence intervals. The normality of distributions of variables was analyzed by Kolmogorov–Smirnov equality of distribution test. Data with normal distribution was summarized by mean, standard deviations and minimum-maximum values for data with non-normal 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 mean of quantitative variables for the total of all samples was compared between two separate groups by independent t-test. A p-value of less than 0.05 was considered statistically significant in the single variable analysis.

Logistic regression with 95% confidence intervals was used to calculate odds ratios (OR) for effective factors between various patterns of serum magnesium and/or copper concentrations. 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 was based on the criteria of the Institute of Medicine and recommended dietary allowances (RDA) for the minerals. The data were analyzed by statistical package for the social sciences (SPSS) version 21.

Findings

One of the participants (0.25%) (0.0024-0.0074, CI: 95%) had serum magnesium less than 1.1 mg/dl, and 96 people (24%) (0.198- 0.282, CI: 95%) showed serum magnesium higher than 2.2 mg/dl. Serum copper status among 400 studied population identified as follows: 10 people (2.5%) (0 0.01-0.04, CI: 95%) had serum copper less than 130 µg/dl and 52 subjects (13%) (0.097-0.163 CI: 95%) showed serum copper higher than 240 µg/dl.

Considering that copper and magnesium deficiency in the studied population is low, we exclude pregnant women with magnesium and serum copper deficiency. (We evaluated the relationships between normal and high serum copper or normal and high serum magnesium levels with clinical, nutritional, demographic and socio-economic factors). Of the 399 studied pregnant women in the third trimester, 24% had high serum magnesium and 76% had normal serum magnesium and of the 390 pregnant women in the third trimester 13% had higher and 87% had normal copper levels.

The statistical analysis of serum normal levels and copper and magnesium deficiency are presented in Tables 2, 3 and respectively.

Based on Recommended Dietary Allowances (RDA), 337 subjects (84.5%), had enough intake of magnesium, and 356 participants (91.3%) received enough copper. None of the studied women received supplemental copper but 354 subjects (%88.7) were seen receiving supplemental magnesium.

With a 95% confidence intake of dietary and supplemental magnesium as well as dietary fiber in pregnant women with high serum levels of magnesium (High Mg group) were significantly higher than the normal serum magnesium group (Normal Mg group) while this group of studied women i.e. women with high serum levels of magnesium had less calcium intake (**Table 2, 3 and 4**).

It was found, High Cu group has higher intake of copper containing foods, higher BMI, higher frequency of iron deficiency anemia and lower intake of dietary calcium intake in comparison with Normal Cu group (**Table 2, 3 and 4**).

Since several variables have affected magnesium toxicity and serum copper toxicity. We used a logistic regression model with the choice of LR method with PE = 0.05 and with PR = 0.1 to estimate the impact coefficient of variables as predictive factors for serum copper and magnesium. (**Table 5 and 6**).

Binary logistic regression model showed that high concentration of serum magnesium was directly associated with dietary intake magnesium (OR: 2.252; 95% CI: 1.85-2.74), supplement magnesium (OR: 7.823; 95% CI: 3.676-16.649) and total dietary fiber (OR: 1.005; 95% CI: 1.000-1.01), and inversely associated with total calcium intake (OR: 0.739; 95% CI: 0.569-0.959). High concentration of serum copper was directly associated with dietary intake copper (OR: 2.252; 95% CI: 1.85-2.74), and negatively associated with BMI of pre-pregnancy and iron deficiency anemia (OR: 0.357; 95% CI: 0.168- 0.759).

Table 1: Description of the studied subjects

Variable	**Subjects with High and normal serum Copper (n=390) * range**	**Subjects with High and normal serum Magnesium (n=399) * range**
Age	27.2 (6.6) 14-44	27.5 (6.6) 14-44
Pregnancy week	32.4 (2.7) 28-39	32.4 (2.7) 28-39
Body mass index	26.04 (4.8) 15.4-45	25.9 (4.8) 15.4-45
Weight gain during pregnancy(kg)	7.9 (4.08) 4-25	7.9 (4.07) 4-25
Cu(mg/dl) or mg serum(μg/dl)	205.1 (32.2) 130.7-312.8	2.1 (0.17) 1.7-2.5

n: subject number.
**: mean ± standard deviation (X ± SD) and range: minimum–maximum values*

Table 2: Frequency distribution of demographic and nutritional data of study groups

Serum magnesium					Serum copper			
	Group 1 high serum magnesium	**Group 2 normal serum magnesium**	**Total (n=399)**	**P Value**	**Group 1 high serum copper**	**Group 2 normal serum copper**	**Total (n=390)**	**P Value**
	Frequency (%)	**Frequency (%)**	**frequency (%)**		**Frequency (%)**	**Frequency (%)**	**Frequency (%)**	
Age <18 18-19.9 20-24.9 25-29.9 30-35 >35	6(6.2) 6(6.2) 25(26.1) 23(24) 27(28.1) 9(9.4)	26(8.6) 21(6.9) 65(21.4) 90(29.7) 66(21.8) 35(11.6)	(8)32 (6.8)27 (22.6)90 (28.4)113 (23.4)93 (11)44	0.602	2(3.8) 6(11.5) 11(21.2) 15(28.8) 11(21.2) 7(13.5)	30(8.9) 20(5.9) 76(22.5) 95(28.1) 80(23.7) 37(10.9)	32(8.2) 26(6.7) 87(22.3) 110(28.2) 91(23.3) 44(11.3)	0.557
Season Summer Fall	52(54.2) 44(45.8)	140(46.2) 163(53.8)	192(48.1) 207(51.9)	0.174	28(53.8) 24(46.2)	159(47) 179(53)	187(47.9) 203(52.1)	0.361
Education Guidance sch. High school Bachelor Msc and higher	27(28.1) 45(46.9) 20(20.8) 4(4.2)	100(33) 126(41.6) 59(19.5) 18(5.9)	127(31.8) 171(42.9) 79(19.8) 22(5.5)	0.681	19(36.5) 18(34.6) 11(21.2) 4(7.7)	106(31.4) 150(44.4) 66(19.5) 16(4.7)	125(32.1) 168(43.1) 77(19.7) 20(5.1)	0.531
Income More than expenses Equal Less than expenses	25(26) 56(58.3) 15(15.6)	85(28.1) 176(58.1) 42(13.9)	110(27.6) 232(58.1) 57(14.3)	0.875	17(32.7) 28(53.8) 7(13.5)	88(26) 200(59.2) 50(14.8)	105(26.9) 228(58.5) 57(14.6)	0.602
Occupational status Employed Housewife	5(5.2) 91(94.8)	24(7.9) 279(92.1)	29(7.3) 370(92.7)	0.372	7(13.5) 45(86.5)	22(6.5) 316(93.5)	29(7.4) 361(92.6)	0.075
Home status the owner Tenant	67(69.8) 29(30.2)	192(63.4) 111(36.6)	259(64.9) 140(35.1)	0.250	36(69.2) 16(30.8)	219(64.8) 119(35.2)	255(65.4) 135(34.6)	0.531
Smoking Yes No	2(2.1) 94(97.9)	2(0.7) 301(99.3)	4(1) 394(99)	0.223	1(1.9) 51(98.1)	3(0.9) 335(99.1)	4(1) 386(99)	0.490

Intake food Mg and Cu (RDA) Low Normal	 7(7.3) 89(92.7)	 55(18.2) 248(81.8)	 62(15.5) 337(84.5)	 0.010	 0(0) 52(100)	 34(10.1) 304(89.9)	 34(8.7) 356(91.3)	 0.014
Mg supplementation No Yes	 4(4.2) 92(95.8)	 41(13.5) 262(86.5)	 45(11.3) 354(88.7)	 0.011	 -	 -	 -	 -
Intake fiber (RDA) Low Normal	 82(85.4) 14(14.6)	 262(86.5) 41(13.5)	 344(86.2) 55(13.8)	 0.794	 42(80.8) 10(19.2)	 296(87.6) 42(12.4)	 338(86.7) 52(13.3)	 0.179
Total	96(24)	303(76)	399(100)		52(13.3)	338(86.7)	390(100)	

RDA: recommended dietary allowance.
P_value; for comparison of frequencies, chi-square test was used
Differences between Groups 1 and 2 are statistically significant; p < 0.05.

Table 3: Frequency distribution of clinical variables of study groups

Serum magnesium					Serum copper			
	Group 1 high serum magnesium	**Group 2 normal serum magnesium**	**In total (n=399)**	**P Value**	**Group 1 high serum copper**	**Group 2 normal serum copper**	**In total (n=399)**	**P Value**
	frequency (%)	**Frequency (%)**	**Frequency (%)**		**frequency (%)**	**frequency (%)**	**frequency (%)**	
Body mass index* <18.5 18.5-24.9 25-29.9 30-34.9 ≥35	 9(9.4) 36(37.5) 33(34.4) 15(15.6) 3(3.1)	 8(2.6) 125(41.3) 107(35.3) 51(16.8) 12(4)	 17(4.3) 161(40.4) 140(35.1) 66(16.5) 15(3.8)	 0.083	 1(1.9) 14(26.9) 16(30.8) 17(32.7) 4(7.7)	 16(4.7) 140(41.4) 122(36.1) 49(14.5) 11(3.3)	 17(4.4) 154(39.5) 138(35.4) 66(16.9) 15(3.8)	 0.005
Weight gain during pregnancy* Low Normal High	 13(13.5) 78(81.3) 5(5.2)	 64(21.1) 219(72.3) 20(6.6)	 77(19.3) 297(74.4) 25(6.3)	 0.203	 11(21.2) 35(67.3) 6(11.5)	 63(18.6) 257(76) 18(5.4)	 74(19) 292(74.9) 24(6.2)	 0.179
Pregnancy age * 28-32 33-35 36-42	 60(62.5) 21(21.9) 15(15.6)	 184(60.7) 80(26.4) 39(12.9)	 244(61.2) 101(25.3) 54(13.5)	 0.596	 28(53.8) 15(28.9) 9(17.3)	 212(62.7) 82(24.3) 44(13)	 240(61.5) 97(24.9) 53(13.6)	 0.457
Lactation with pregnancy ** Yes No	 2(2.1) 94(97.9)	 6(2) 297(98)	 8(2) 391(98)	 0.950	 0(0) 52(100)	 8(2.4) 330(97.6)	 8(2.1) 382(97.9)	 0.604
Anemia * Yes No	 (13.5)13 (84.5)83	 49(16.2) 254(83.8)	 62(15.5) 337(84.5)	 0.535	 13(25) 39(75)	 48(14.2) 290(85.8)	 61(15.6) 329(84.4)	 0.046
Heartburn* Yes No	 (7.3)7 (92.7)89	 39(12.9) 264(87.1)	 46(11.5) 353(8.5)	 0.136	 6(11.5) 46(88.5)	 39(11.5) 299(88.5)	 45(11.5) 345(88.5)	 1.000
Twin pregnancy* Yes No	 2(2.1) 94(97.9)	 5(1.7) 298(98.3)	 7(1.8) 392(98.2)	 0.778	 0(0) 52(100)	 7(2.1) 331(97.9)	 7(1.8) 383(98.2)	 0.601
Total	96(24)	303(76)	399		52	338	390	
Stillborn history* Yes No	 (1.5)1 (98.5)64	 (4.3)9 (95.7)199	 10(0.04) 263(0.96)	 0.292	 1(2.8) 35(97.2)	 9(3.8) 225(96.2)	 10(0.004) 260(0.96)	 0.753
Abortion history* Yes No	 (32.3)21 (67.7)44	 (27.9)58 (72.1)150	 79(28.9) 194(71.1)	 0.492	 26(72.2) 10(27.8)	 68(29.1) 166(70.9)	 78(28.9) 192(71.1)	 0.874
Total	(23.8) 65	(76.1)208	273(100)		36(13.3)	234(86.7)	270(100)	
Birth interval (week)* ≤154 ≥155 Total	 9(14.5) 53(85.5) 62(25.2)	 30(16.3) 154(83.7) 184(74.8)	 39(15.9) 207(84.1) 246(100)	 0.739	 2(5.9) 32(94.1) 34(14)	 37(17.7) 172(82.3) 209(86)	 39(16) 204(84) 243	 0.082

**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 4: Concentration of serum magnesium and serum copper levels related to the clinical and nutritional variables, stratified by magnesium and copper Status in the examined pregnant women (mean ± SD)

Serum magnesium					Serum copper			
	Group 1 High serum magnesium*	**Group 2 Normal serum magnesium***	**In total * range n=399**	**Independent t-test p value**	**Group 1 High serum copper***	**Group 2 Normal**	**In total * range n=390**	**Independent t-test p value**

	n=107	n=281			n=50	serum copper* n=338		
Diet magnesium(mg)	414.4±39.5	362.7±41.7	46.7±375.2	<0.001	50.3±388.5	45.7±372.4	374.6±46.6	0.020
Supplement Mg (mg)	95.6±23.2	85.3±35.3	33.1±87.8	0.001	31.9±91.4	33.6±86.9	87.5±33.4	0.365
Total Mg intake (mg)	510.1±44.1	448±54.3	58.4±463	<0.001	55.3±480	58.4±459.4	462.1±58.4	0.018
Diet Zn (mg)	13.1±1.7	13.2±5.4	4.8±13.2	0.832	1.6±13.3	1.8±12.8	12.9±1.8	0.089
Supplement Zn(mg)	2.8±8.2	3.6±9.2	9±3.3	0.451	8.6±3	9.1±3.4	3.36±9.05	0.803
Total Zn intake (mg)	15.8±8.8	16.7±10.9	10.5±16.5	0.456	8.9±16.4	9.7±16.3	16.3±9.59	0.926
Diet Fe (mg)	21.1±2.6	20.9±3.02	2.9±21	0.52	3.01±20.6	2.9±21	20.9±2.9	0.926
Supplement Fe (mg)	61.9±16.9	60.9±23.4	22±61.2	0.64	22.4±65.9	22.1±60.4	61.1±22.1	0.095
Total Fe intake (mg)	83.1±17.5	81.9±23.7	22.4±82.2	0.580	23.07±86.5	22.4±81.4	82.1±22.5	0.128
Diet Ca (mg)	854±116.7	898.5±120.6	121±887.8	0.002	110.4±872	123±890.3	887.9±121.4	0.315
Supplement Ca(mg)	144.7±99.3	210.9±208.5	190±195	<0.001	128.8±158	196.8±199.2	193.7±189.5	0.051
Total Ca intake (mg)	998.8±163.8	1109.5±240.6	229.3±1082.9	<0.001	191±1030.1	233.8±1089.6	1081.6±229.2	0.046
Diet Cu(gr)	1.49±0.48	1.52±0.51	0.5±1.5	0.505	0.4±2.1	0.44±1.4	1.5±0.5	<0.001
Diet fiber	24.2±3.1	22.7±3	3.1±23.1	<0.001	23.3±3.4	23.07±3.09	23.1±3.14	0.623
Supplement folic acid	0.414±0.15	384±0.20	0.19±0.39	0.140	0.4±0.17	0.389±0.196	0.39±0.19	0.697
Supplement vit D	382.6±88.3	378.3±159.6	145.5±379.3	0.737	375.9±104.1	378±151.9	377.8±146.3	0.920
Serum Cu or Mg	206.1±36.7	202.2±33.7	203.2±34.4	0.346	2.2±0.16	2.1±0.18	2.1±0.17	0.023
Weight gain during pregnancy(kg)	3.8±8.36	4.16±7.80	4±7.9	0.243	7.7±4.8	7.9±3.9	7.9±4.08	0.760
Number of pregnancy	1.1±2.23	1.1±2.25	1.18±2.25	0.876	2.3±1.2	2.25±1.16	2.26±1.1	0.750
Parity	0.95±1.03	1.08±1.01	1.05±1.01	0.863	1.1±1.05	1.02±1.05	2.26±1.1	0.618

*: mean ± standard deviation (X±SD) and range: minimum–maximum values
Number of pregnancy or frequent reproductive cycling, including number of abortions, stillborn, and child birth.
Parity including number of stillborn and child birth.
To compare mean clinical and nutritional variables between different serum magnesium or copper groups, t tests for independent samples were used
Differences between Groups 1 and 2 are statistically significant; $p < 0.05$.

Table 5: Results of automatic binary logistic regression analysis with high serum magnesium as dependent variable, and the total calcium intake, intake diet fiber, supplement magnesium and intake diet magnesium, as explanatory variables

Significant explanatory variables	Odds ratio	Lower–upper 95 % CI	P
Total ca intake	0.997	0.996-0.999	0.001
Food magnesium	1.039	1.029-1.050	<0.001
Supplement magnesium	1.016	1.00-1.027	0.007
Intake diet fiber	1.109	1.008-1.219	0.033

Table 6: Results of automatic binary logistic regression analysis with high serum copper as dependent variable, and the total calcium intake, total Mg intake, body mass index and anemia, as explanatory variables

Significant explanatory variables	Odds ratio	Lower–upper 95 % CI	P
Copper intake	7.37	3.38-16.07	<0.001
Total Mg intake	1.007	1.001-1.013	0.019
Body mass index			0.024
<18.5	0.078	0.006-0.584	0.046
18.5-24.9	0.227	0.057-0.663	0.034
25-29.9	0.272	0.069-785	0.060
30-34.9	0.644	136-1.584	0.527
≥35	Reference	-	
Total Ca intake	0.998	0.997-1.000	0.045
Anemia			
Yes	0.369	0.166-0.819	0.014
No	-		

Discussion

The current study, which includes a large number of pregnant women in the third trimester from different socioeconomic areas of the Urmia, indicates that the frequency of copper and magnesium deficiency is not noticeable while the frequencies of the serum magnesium and copper high concentrations are remarkable and requires further research and health interventions.

In a national cross-sectional study of 5021 American adults, King et al showed that 68% of American adults and 78.5% of women in this country had low magnesium levels below the recommended RDA values due to Western dietary patterns (containing high red meat, high-fat dairy products and refined grains that contain lower magnesium content) [26]. In a survey conducted in Urmia, it was found 337 pregnant women in the third trimester (84.5%) got enough magnesium from the diet (fruits and vegetables and high-magnesium beans) based on the RDA's recommendations for pregnant women.

Itoh et al showed a direct correlation between serum magnesium and supplemented magnesium [27]. The group supplemented by magnesium has higher levels of serum magnesium than that of control group. In other study the authors concluded there is a strong correlation between serum magnesium and dietary intake of it [28]. This finding was confirmed by our investigation too. According to our study, the serum magnesium level is closely related to the amount of magnesium consumed from the supplement and foods.

Based upon a review study reported by Milne et al, one of the factors influencing serum copper differences is copper intake, so that serum copper is positively correlated to it [29]. The results of this study are confirmed by our findings.

In our study, it was found 13% of the population studied had high serum copper concentrations with mean ± SD of 20.5 ± 3.2μg/L which was higher than that of a study in Khorasan province with 2233 studied population aged 15-65 years (14.7 ± 3.3μg/L) [30]. In a cross-sectional study, Dabbaghmanesh et al showed that 24 percent of the population had copper deficiency [15]. According to a study conducted by Choi et al it was seen high serum copper levels 70.2% of pregnant women in the third trimester [17]. Estrogen is one of the factors affecting the concentration of serum copper that rises during pregnancy and could cause an enhancement in ceruloplasmin synthesis [31]. Estrogen secretion is reinforced in pregnancy, on the other hand, it is one of the principle factors affecting serum copper levels by increasing serum copper production via enhancing the available copper due to the transfer of copper from the maternal tissues, especially the liver [31,32].

Furthermore, copper absorption is also elevated during pregnancy owing to the increased needs of pregnant women for copper-containing enzymes such as cytochrome c oxidase which is required for aerobic respiration and superoxide dismutase which could scavenge the superoxide radicals and converting them into hydrogen peroxide followed by a catalase action and H2O production [3,17,33].

As regards the increasing needs of the food meet through the agricultural crops in the world, copper pollution occurs in agricultural soils due to the arbitrary use of pesticides, fungicides, industrial wastewater and sewage irrigation. Therefore, food safety and food security could be affected by mentioned factors [34].

According to the results of a study conducted by Amal et al, serum copper levels in the anemia group were not statistically significant compared to those without anemia [35]. However, Ece et al showed that children with iron deficiency anemia (IDA) has a higher serum copper than that of Control group [36]. Ma et al in a case-control study on 1070 third trimester women showed that the serum copper levels in pregnant women with IDA were not different from that of normal pregnant women [37]. Whiles our results showed that pregnant women with IDA in third trimester had higher serum copper than non-anemic pregnant mothers. These findings were consisted with the results of the Upadhyaya et al conducted on pregnant women at birth time. The results represented the pregnant women with iron deficiency anemia reflected a significantly higher serum copper than that of those without IDA [32]. The high serum copper in pregnant women with anemia can be attributed to the fact that iron deficiency increases the concentration of copper in the liver and in both serum and placenta [37]. An increase in serum copper in anemic mothers could take into account as a compensatory mechanism to combat anemia. This mechanism is accompanied by the increased synthesis of ceruloplasmin, which has a ferroxidase activity [32].

Al-Saleh et al. conducted a case control study on pregnant women with or without overweight and obesity at delivery time. The authors showed no significant difference in serum copper in normal and obese pregnant women [38]. Lewicka et al. [39] reported high pre-pregnancy BMI was not associated with serum copper levels in pregnant women while according to our study, pregnant women with high pre-pregnancy BMI had higher serum copper than mothers with lower BMI during third-trimester. In an epidemiological study of 1,150 pregnant women, Dreosti et al. found the pregnant mothers with obesity at 18 and 32 weeks of gestational age had higher serum copper than that of women with normal or low body weight [31]. The cause of the result is not clearly explained but it seems copper indirectly oxidizes fatty acid and produces energy in the mitochondria, and helps the body metabolism to degrade fatty acids and reduce fat [40].

Song et al. reported low serum magnesium levels among 180 healthy obese women compared to non-obese ones [41]. Similarly, Lewicka et al. conducted that pregnant women with high pre-pregnancy BMI had higher serum magnesium than mothers with lower BMI during labor [39]. On the other hand, Laires e t al could not show any differences in serum magnesium levels between obese and non-obese subjects. They did not report any correlations between serum levels of magnesium and anthropometric variables as well [42]. Similarly, our results did not detect a correlation between BMI and serum magnesium in studied women.

Based on our data, it was seen a negative correlation between serum magnesium and calcium intake. According to Williams et al suggestion, as respect the mechanism of absorption of magnesium and calcium across the intestinal epithelium nearly conforms a similar way, they may compete together for passing from the epithelial membrane. Such competitions may also be seen in reabsorption of them in renal tubules. As a result, high intake of calcium could be resulted in a reduction in serum magnesium levels [43].

According to the results of our study, serum magnesium has a positive correlation with the dietary fiber intake. This may be due to high-fiber foods have more magnesium and increased dietary intake could cause elevation in serum magnesium levels [26].

It must be admitted that the atomic absorption spectrophotometer was not available to us for the measurement of magnesium and serum copper. It is recommended to evaluate the amounts of copper and magnesium in the agricultural soil of Urmia to finding the root of the problem.

Conclusion

In this study, we could detect the serum overload of copper and magnesium in pregnant women of Urmia. We also evaluated the possible clinical and nutritional determinants affected on the status of the minerals. Based on a nutritional program of Ministry of Health and Medical Education, it was administered multivitamin and mineral capsules for all pregnant mothers from the 16th week of pregnancy without any serum testes for the minerals. Each of the capsules contains 100 mg of magnesium. It is necessary to improve the growth and development of the fetus and to achieve a health pregnancy; it should be paid more attention to nutritional status of minerals including magnesium and copper. As a result, the magnesium supplements should be recommended only when the magnesium deficiency was occurred. Finally, the authors suggest further studies to confirm the results presented here.

Declarations

Name of the institution where the work was done

Urmia University of Medical Sciences

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Conflict of Interest Statement

The authors declare no conflict of interest.

Authors' contributions

S.Gh and M.Gh performed the research; S.Gh and M.Gh were involved in clinical aspects of the study; S.Gh and M.Gh coordinated dietary assessment; S.Gh and M. Gholizadeh were involved in laboratory aspects of the study; H.R.Kh and M.Gh analyzed the data; S.Gh and M.Gh wrote the first draft of the manuscript. S.Gh had primary responsibility for final content. All authors read and approved the final manuscript.

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