Original article

The relationship between nutrients intake and preeclampsia in pregnant women

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BACKGROUND: This Study aimed to investigate the associations between macro- and micronutrients received in the first, second, and third trimesters and risk for preeclampsia considering demographic and reproductive characteristics and physical activity. **METHODS**: In this prospective cohort study, data was collected by filling a questionnaire through interviews with 700 pregnant women who had no parameters to affect pregnancy outcome (36 parameters). In addition, 48-hour dietary recalls were completed for eligible women at 11th-15th, 26th, and 34th-37th weeks of gestation. Physical activity was also assessed using a standard questionnaire. Data on 48-hour dietary recalls was analyzed using Nutrition-IV software. Data was analyzed in SPSS$_{18}$ using t-test and logistic regression analysis. **RESULTS:** The mean value of received saturated fatty acids in the first trimester in subjects who experienced preeclampsia later in pregnancy was higher than the rest of the pregnant women (p = 0.045). Manganese intake in the third trimester was significantly less in preeclamptic subjects compared to the others (p = 0.026). Moreover, vitamin C, vitamin E, fiber, and carbohydrate intakes during the third trimester were significantly less among the women with preeclampsia compared to the rest of the studied population (p = 0.034, p = 0.049, p = 0.046, and p = 0.035, respectively). Higher manganese (OR: 0.88; 95% CI: 0.76-0.90), vitamin C (OR: 0.985; 95% CI: 0.98-0.99), vitamin E (OR: 0.99; 95% CI: 0.984-0.996), fiber (OR: 0.97; 95% CI: 0.96-0.98), saturated fatty acids (OR: 1.028; 95% CI: 1.02-1.036), and carbohydrate (OR: 0.98; 95% CI: 0.97-0.99) intake increased the chance of preeclampsia in pregnant women. **CONCLUSIONS:** The amounts of received saturated fat in the first trimester and manganese, vitamin C, vitamin E, fiber, and carbohydrate during the third trimester are significantly associated with preeclampsia.

KEYWORDS: Nutrients, Intake, Fiber, Vitamin E, Vitamin C, Manganese, Preeclampsia

BACKGROUND

Preeclampsia is characterized by the development of hypertension and proteinuria after 20th week of gestation. It is found in 3-10% of pregnancies and remains a major cause of maternal and fetal morbidity and mortality worldwide.[1] This syndrome is a two-stage disorder. Stage 1 is preclinical and characterized by faulty trophoblastic vascular remodeling of uterine arteries that cause placental hypoxia. Stage 2 is caused by release of placental factors into the maternal circulation causing systemic inflammatory response and endothelial activation.[2]

Epidemiology of preeclampsia, being more common in poor women, long ago suggested that nutrients might be involved in the disorder. In addition, current concepts of the development of preeclampsia including endothelial dysfunction, inflammatory activation, oxidative stress, and predisposing maternal factors provide targets for well-designed nutritional investigations.[3]

Since in most previous studies the association of nutrients intake and preeclampsia has only been investigated among preeclamptic pregnant women,[4] this study assessed the relation between receiving nutrients and the risk of preeclampsia in different stages of pregnancy. Additionally, the association between nutrients intake and preeclampsia has rarely been studied prospectively in a study.[4] We thus conducted a prospective cohort study to investigate the association between the risk for preeclampsia and macro- and micronutrients received in the first, second, and third trimesters. On the other hand, some researchers believe that the obtained results about the association between different nutrients in the blood and preeclampsia should be interpreted with caution since maternal nutrient intake has not been studied.[5] Therefore, before any laboratory examination on serum levels of nutrients among pregnant women, it is necessary to evaluate the received nutrients as basic information and also the relation between this information and pregnancy outcome.

In this study, the association between preeclampsia risk and the intake of about 40 types of

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macro- and micronutrients during the first, second, and third trimesters was assessed based on demographic and reproductive characteristics and physical activity in pregnant women. It therefore seems to be a unique study.

METHODS

This prospective cohort study (approved by the institutional review board of Isfahan University) was conducted in four stages on a group of 700 Iranian pregnant women who referred to 18 health centers and 12 private offices from April 2009 to august 2010. Considering the fact that 65% of women in Isfahan refer to health centers, 20% to private offices, and 15% to both, convenient sampling was performed.

Pregnant women who had no 36 conditions such as factors causing preeclampsia, preterm delivery, low birth weight, preterm premature rupture of membranes, and other factors such as smoking and drug addiction, digestive and metabolic diseases, hemoglobinopathies, eating disorders, allergies, mental diseases, and malignancy which affected pregnancy outcome were recruited.

Data was collected by a questionnaire which was completed through interviews with pregnant women and prenatal and obstetric care-related records. In addition, 48-hour dietary recalls were completed for eligible pregnant women at the 11^{th}-15^{th}, 26^{th}, and 34^{th}-37^{th} weeks of gestation.[6-8] Physical activity was considered as any physical movement due to skeletal muscles resulting in energy consumption. Data on physical activity was collected using a standard pregnancy physical activity questionnaire which consists of 4 parts including physical activity at home, exercise, leisure activities, and workplace activity.[9] Therefore, the performed physical activities within 48 hours were also assessed at the 11^{th}-15^{th}, 26^{th}, and 34^{th}-37^{th} weeks of gestation. Physical activity was measured in metabolic equivalent of task-hours (MET-hours) of each activity multiplied by the duration of the activity in the day. MET-hours is a unit for estimating the metabolic cost or oxygen consumption of a particular physical activity, according to a standard questionnaire. Total amount of activity was calculated by summing the activities in the 3 trimesters and was used for analysis.

The subjects were then followed until the end of pregnancy. The risk of preeclampsia was collected through patient records. Preeclampsia was considered as a blood pressure of 140/90 mm Hg or higher after 20 weeks of pregnancy along with proteinuria (greater than or equal to 300 mg per day).[2] Iron, folic acid, multivitamins, calcium, and omega-3 supplements were administered for the subjects by their caregivers (gynecologists and midwives) were also considered in the final analysis.

To increase reliability, all interviewers were trained in the same conditions. On the other hand, patient records were completed by experts which guaranteed their reliability. In addition, since the records are prepared in fixed and standardized forms, their reliability confidence has already been proven.

Data obtained from the 48-hour dietary recalls was analyzed using Nutrition-IV software. Data analysis was performed in $SPSS_{18}$ (IBM Company, the United States) using t-test and binary logistic regression analysis. P-values < 0.05 were considered significant in all tests.

RESULTS

According to our findings, 25 patients out of the 700 studied pregnant women (3.57%) were diagnosed with preeclampsia. However, the data of about 620 subjects was finally analyzed due to missing data. Their demographic and reproductive characteristics are shown in table 1. Minimum, maximum, and mean values of micro- and macronutrients were calculated in the first, second, and third trimesters (Table 2).

The mean of received saturated fat in the first trimester in subjects who experienced preeclampsia later in pregnancy was higher than the other pregnant women ($p = 0.045$). In addition, the mean values of vitamin C and vitamin E intake in the third trimester among preeclamptic women were significantly less than healthy pregnant women ($p = 0.034$ and $p = 0.049$, respectively). Manganese intake in the third trimester was significantly less among subjects with preeclampsia compared to the others ($p = 0.026$).

Other findings also indicated significant relations between fiber and carbohydrate intake during the third trimester and preeclampsia risk, i.e. the mean values of fiber and carbohydrate intake (in term of grams) were significantly lower in patients with preeclampsia ($p = 0.046$ and $p = 0.035$, respectively) (Table 3). Except for the mentioned variables, there were no significant differences between other micro- and macronutrients and the risk of preeclampsia (Table 2).

Table 1. Demographic and reproductive characteristic of the participants

Maternal characteristics	Preeclamptic Mothers				Non Preeclamptic Mothers				Total				p
	Min	Max	Mean ± SD	n	Min	Max	Mean ± SD	n	Min	Max	Mean ± SD	n	
Age	20	34	26.48 ± 4.21	25	16	39	25.60 ± 4.44	559	16	39	25.64 ± 4.43	584	0.331
Weight**	5	23	13.89 ± 5.00	23	-1.5	27	11.86 ± 4.11	529	-1.5	37	11.95 ± 4.16	552	0.022
Maternal BMI*	18.6	37.8	25.30 ± 5.29	24	15.2	40.5	23.42 ± 3.84	534	15.2	40.5	23.5 ± 3.93	558	0.022
Maternal weight*	47	99	66.88 ± 14.19	25	37	90	60.23 ± 10.14	552	37	99	66.52 ± 10.42	577	0.002
Gravida	1	5	1.56 ± 0.83	25	1	5	1.58 ± 0.76	561	1	5	1.58 ± 0.76	586	0.911
Number of children	1	3	1.06 ± 0.82	25	1	10	2.58 ± 0.93	560	1	10	2.58 ± 0.92	585	0.932

* Before pregnancy
** Gained during pregnancy
BMI: Body mass index

Table 2. Maternal intake of macro- and micronutrients in the first (1st Tr.), second (2nd Tr.) and third (3rd Tr.) trimesters of pregnancy

	Preeclamptic Mothers		Non Preeclamptic Mothers		Total	
	Mean ± SD	n	Mean ± SD	n	Mean ± SD	n
Beta (1st Tr.)	3083.17 ± 5060.94	23	2761.38 ± 3758.99	561	2774.05 ± 3813.53	584
Beta (2nd Tr.)	1978.49 ± 2426.21	24	2153.92 ± 3849.71	554	2146.63 ± 3799.96	578
Beta (3rd Tr.)	1755.84 ± 2743.74	18	1555.38 ± 1932.03	492	1562.46 ± 1963.04	510
En (1st Tr.)	2130.67 ± 904.85	23	2030.49 ± 774.14	561	2034.43 ± 779.05	584
En (2nd Tr.)	2270.30 ± 911.55	24	2326.44 ± 821.97	554	2324.1130 ± 825.09	578
En (3rd Tr.)	2052.77 ± 691.49	17	2330.51 ± 1381.96	492	2321.24 ± 1365.08	509
Pr (1st Tr.)	96.82 ± 37.86	23	96.36 ± 37.17	561	93.49 ± 37.17	584
Pr (2nd Tr.)	101.51 ± 40.10	24	103.98 ± 36.57	554	103.87 ± 36.73	578
Pr (3rd Tr.)	94.92 ± 29.27	18	107.01 ± 83.67	492	106.58 ± 82.38	510
Carbo (1st Tr.)	301.97 ± 129.97	23	301.27 ± 126.05	561	301.29 ± 126.10	584
Carbo (2nd Tr.)	315.33 ± 114.73	24	344.00 ± 115.25	554	342.81 ± 115.27	578
Carbo* (3rd Tr.)	299.10 ± 93.23	18	343.07 ± 101.46	492	341.52 ± 101.42	510
Sugar (1st Tr.)	80.01 ± 57.80	23	91.45 ± 49.77	561	91.00 ± 50.11	584
Sugar (2nd Tr.)	101.17 ± 43.13	24	100.65 ± 51.58	554	100.68 ± 51.20	578
Sugar (3rd Tr.)	85.31 ± 42.60	18	103.36 ± 50.06	492	102.72 ± 49.89	510
Fiber (1st Tr.)	22.26 ± 11.58	23	20.50 ± 10.55	561	20.57 ± 10.59	584
Fiber (2nd Tr.)	24.54 ± 13.25	24	23.84 ± 12.21	554	23.87 ± 12.25	578
Fiber* (3rd Tr.)	19.56 ± 8.37	18	24.36 ± 11.95	492	24.19 ± 11.87	510
C (1st Tr.)	140.36 ± 91.72	23	150.93 ± 103.92	561	150.51 ± 103.42	584
C (2nd Tr.)	161.10 ± 109.25	24	154.72 ± 110.66	554	155.03 ± 110.52	578
C (3rd Tr.)	155.08 ± 101.80	18	186.56 ± 139.27	492	185.44 ± 138.17	510
*SFA (1st Tr.)	26.43 ± 15.68	25	21.61 ± 11.60	596	21.81 ± 11.80	621
SFA (2nd Tr.)	25.45 ± 12.25	26	25.09 ± 13.67	593	25.10 ± 13.60	619
SFA (3rd Tr.)	20.73 ± 8.44	17	25.89 ± 44.35	503	25.73 ± 43.65	520
MUFA (1st Tr.)	26.61 ± 14.69	25	24.56 ± 16.07	596	24.64 ± 16.02	621
MUFA (2nd Tr.)	30.38 ± 17.63	26	27.05 ± 16.26	592	27.19 ± 16.31	618
MUFA (3rd Tr.)	20.68 ± 9.53	17	27.75 ± 42.10	503	27.52 ± 41.45	520
PUFA (1st Tr.)	31.23 ± 14.58	25	30.45 ± 12.77	595	30.48 ± 12.83	620
PUFA (2nd Tr.)	35.21 ± 19.30	26	33.65 ± 11.59	592	33.71 ± 11.99	618
PUFA (3rd Tr.)	30.11 ± 12.90	17	34.00 ± 17.59	502	33.86 ± 17.47	519
DHA (1st Tr.)	0.77 ± 0.56	25	0.68 ± 0.80	596	0.68 ± 0.79	621
DHA (2nd Tr.)	0.73 ± 0.52	26	0.78 ± 1.37	593	0.77 ± 1.35	619
DHA (3rd Tr.)	0.63 ± 0.46	17	0.87 ± 2.09	502	0.86 ± 2.06	519
Retinol (1st Tr.)	128.06 ± 259.25	23	206.66 ± 792.41	561	203.57 ± 778.40	584
Retinol (2nd Tr.)	96.20 ± 65.64	24	222.92 ± 865.61	554	217.66 ± 847.89	578
Retinol (3rd Tr.)	206.27 ± 576.23	18	218.05 ± 1011.55	492	217.63 ± 999.07	510
Vita A (mg) (1st Tr.)	916.00 ± 1136.93	23	862.02 ± 1052.04	561	864.15 ± 1054.52	584
Vita A (mg) (2nd Tr.)	698.63 ± 462.67	24	824.80 ± 1211.24	554	819.57 ± 1189.64	578
Vita A (mg) (3rd Tr.)	682.46 ± 700.72	18	711.69 ± 1166.67	492	710.66 ± 1153	510
Vita A (u) (1st Tr.)	7847.83 ± 1048.07	23	6943.67 ± 7145.49	561	6979.28 ± 7295	584
Vita A (u) (2nd Tr.)	5419.10 ± 4528.16	24	6121.62 ± 7443.97	554	6092.45 ± 7344.72	578
Vita A (u) (3rd Tr.)	5086.10 ± 4606.96	18	5016.43 ± 5243.85	492	5018.89 ± 5218.67	510
Vita C (1st Tr.)	159.45 ± 110.57	25	152.67 ± 109.62	596	152.94 ± 109.57	621
Vita C (2nd Tr.)	169.69 ± 123.60	26	154.10 ± 109.78	592	154.76 ± 110.33	618
Vita C* (3rd Tr.)	125.16 ± 85.84	17	186.90 ± 138.44	502	184.87 ± 137.42	519
Vita D (1st Tr.)	3.45 ± 5.44	25	5.84 ± 73.00	594	5.75 ± 71.52	619
Vita D (2nd Tr.)	3.71 ± 3.29	26	3.11 ± 3.39	591	3.13 ± 3.38	617
Vita D (3rd Tr.)	3.08 ± 4.52	17	5.25 ± 46.70	501	5.18 ± 45.94	518
CHOL (1st Tr.)	238.99 ± 114.23	25	234.28 ± 206.44	596	234.47 ± 203.48	621
CHOL (2nd Tr.)	248.97 ± 116.54	26	259.96 ± 138.54	593	259.50 ± 137.62	619
CHOL (3rd Tr.)	251.92 ± 139.15	17	268.37 ± 346.36	502	267.83 ± 341.52	519
EPA (1st Tr.)	0.77 ± 0.56	25	0.64 ± 0.55	596	0.64 ± 0.55	621
EPA (2nd Tr.)	0.74 ± 0.52	26	0.73 ± 0.56	593	0.73 ± 0.56	619
EPA (3rd Tr.)	0.63 ± 0.46	17	0.82 ± 1.89	502	0.81 ± 1.86	519

Table 2. Maternal intake of macro- and micronutrients in the first (1st Tr.), second (2nd Tr.) and third (3rd Tr.) trimesters of pregnancy (continued)

	Preeclamptic Mothers		Non Preeclamptic Mothers		Total	
	Mean ± SD	n	Mean ± SD	n	Mean ± SD	n
Car (1st Tr.)	595.49 ± 1026.94	23	490.65 ± 659.74	561	494.77 ± 674.17	584
Car (2nd Tr.)	359.65 ± 465.92	24	386.77 ± 670.88	554	385.64 ± 663.35	578
Car (3rd Tr.)	309.10 ± 468.57	18	286.24 ± 375.08	492	287.05 ± 378.23	510
Vita E (1st Tr.)	1.48 ± 1.89	25	1.61 ± 3.07	596	1.61 ± 3.04	621
Vita E (2nd Tr.)	1.18 ± 1.91	26	1.63 ± 2.95	593	1.61 ± 2.91	619
Vita E (3rd Tr.)	0.62 ± 0.56	17	2.20 ± 4.30	502	2.15 ± 4.23	519
Zn (1st Tr.)	8.08 ± 4.16	23	7.49 ± 4.68	561	7.51 ± 4.66	584
Zn (2nd Tr.)	8.66 ± 4.75	24	8.38 ± 6.66	554	8.39 ± 6.59	578
Zn (3rd Tr.)	9.84 ± 9.93	18	9.12 ± 15.60	492	9.14 ± 15.43	510
Se (1st Tr.)	50.41 ± 33.40	23	43.44 ± 34.17	561	43.7 1 ± 34.14	584
Se (2nd Tr.)	55.05 ± 39.55	24	47.47 ± 34.31	554	47.79 ± 34.55	578
Se (3rd Tr.)	40.95 ± 22.88	18	49.43 ± 38.17	492	49.13 ± 37.75	510
Mn (1st Tr.)	6.70 ± 4.53	23	6.30 ± 4.87	561	6.32 ± 4.85	584
Mn (2nd Tr.)	6.61 ± 3.41	24	7.00 ± 4.90	554	6.98 ± 4.85	578
Mn* (3rd Tr.)	4.51 ± 3.48	18	6.97 ± 4.63	492	6.89 ± 4.62	510
Mg (1st Tr.)	229.80 ± 117.24	23	214.57 ± 109.92	561	215.17 ± 110.15	584
Mg (2nd Tr.)	249.68 ± 138.14	24	232.98 ± 122.08	554	233.67 ± 122.70	578
Mg (3rd Tr.)	211.77 ± 104.00	18	245.98 ± 150.42	492	244.78 ± 149.09	510
Cu (1st Tr.)	4.17 ± 9.45	23	2.99 ± 5.64	561	3.03 ± 5.83	584
Cu (2nd Tr.)	3.93 ± 4.04	24	3.40 ± 6.42	554	3.43 ± 6.34	578
Cu (3rd Tr.)	1.63 ± 1.74	18	2.70 ± 4.82	492	2.66 ± 4.75	510
Ca (1st Tr.)	921.45 ± 482.90	23	840.68 ± 404.56	561	843.86 ± 407.75	584
Ca (2nd Tr.)	942.09 ± 378.88	24	955.02 ± 433.56	554	954.49 ± 431.14	578
Ca (3rd Tr.)	904.31 ± 400.10	18	918.90 ± 424.68	492	918.39 ± 423.47	510
K (1st Tr.)	2971.82 ± 1319.41	23	2955.64 ± 1272.03	561	2956.28 ± 1272.76	584
K (2nd Tr.)	3379.57 ± 1572.38	24	3265.14 ± 1328.02	554	3269.90 ± 1337.66	578
K (3rd Tr.)	2880.27 ± 1037.70	18	3196.48 ± 1651.90	492	3185.32 ± 1634.52	510
NaCl (1st Tr.)	2843.95 ± 1466.37	23	2821.25 ± 1553.14	561	2822.14 ± 1548.63	584
NaCl (2nd Tr.)	2943.85 ± 1158.32	24	3104.73 ± 1705.79	554	3098.05 ± 1686.167	578
NaCl (3rd Tr.)	2679.43 ± 1458.32	18	3108.67 ± 1621.67	492	3093.52 ± 1616.83	510
Fe (1st Tr.)	19.80 ± 8.16	23	18.76 ± 8.60	561	18.80 ± 8.57	584
Fe (2nd Tr.)	19.62 ± 7.08	24	20.68 ± 9.05	554	20.64 ± 8.98	578
Fe (3rd Tr.)	20.30 ± 8.77	18	20.55 ± 10.51	492	20.54 ± 10.46	510
P (1st Tr.)	1077.55 ± 544.90	23	941.98 ± 416.48	561	947.32 ± 422.51	584
P (2nd Tr.)	1119.70 ± 543.88	24	2821.25 ± 1553.14	561	2822.14 ± 1548.63	584
P (3rd Tr.)	975.88 ± 392.53	18	3104.73 ± 1705.79	554	3098.05 ± 1686.167	578
B1 (1st Tr.)	1.625 ± 0.60	23	1.62 ± 0.70	561	1.62 ± 0.70	584
B1 (2nd Tr.)	1.67 ± 0.58	24	1.77 ± 0.67	554	1.77 ± 0.66	578
B1 (3rd Tr.)	1.60 ± 0.71	18	1.77 ± 0.75	492	1.77 ± 0.76	510
B2 (1st Tr.)	1.57 ± 0.67	23	1.55 ± 0.74	561	1.55 ± 0.74	584
B2 (2nd Tr.)	1.75 ± 0.68	24	1.70 ± 0.92	554	1.71 ± 0.9	578
B2 (3rd Tr.)	1.49 ± 0.56	18	1.69 ± 1.29	492	1. 69 ± 1.29	510
B3 (1st Tr.)	20.66 ± 8.98	23	20.17 ± 9.03	561	20.19 ± 9.02	584
B3 (2nd Tr.)	22.06 ± 9.19	24	22.88 ± 9.18	554	22.84 ± 9.18	578
B3 (3rd Tr.)	20.57 ± 9.18	18	24.08 ± 26.55	492	23.96 ± 26.14	510
B12 (1st Tr.)	3.32 ± 2.73	23	3.98 ± 8.36	561	3.95 ± 8.22	584
B12 (2nd Tr.)	3.41 ± 2.03	24	4.75 ± 9.92	554	4.70 ± 9.72	578
B12 (3rd Tr.)	3.85 ± 6.06	18	5.14 ± 15.73	492	5.10 ± 15.50	510
FOL (1st Tr.)	297.36 ± 125.39	23	290.79 ± 183.72	561	291.04 ± 181.71	584
FOL (2nd Tr.)	340.79 ± 194.99	24	306.00 ± 131.97	554	307.44 ± 135.12	578
FOL (3rd Tr.)	269.52 ± 155.38	18	328.51 ± 179.39	492	326.43 ± 178.80	510

Beta: Beta-carotene; En: Energy; Pr: Proteins; Carbo: Carbohydrates; C: Carbon; SFA: Saturated fatty acids; MUFA: Mono-unsaturated fatty acids; PUFA: Poly-unsaturated fatty acids; DHA: Docosahexaenoic acid; Vita: Vitamin; CHOL: Cholesterol; EPA: Eicosapentaenoic acid; Car: Carotenoid; Zn: Zinc; Se: Selenium; Mn: Manganese; Mg: Magnesium; Cu: Copper; Ca: Calcium; K: Potassium; NaCl: Sodium chloride; Fe: Iron; P: Phosphorus; FOL: Folate

In this study, all variables associated with preeclampsia were also analyzed by logistic regression analysis (Table 3). The most significant risk factor for preeclampsia was manganese intake in the third trimester. The next one was saturated fatty acids intake during the first trimester. Then there were vitamin E, carbohydrate, fiber, and vitamin C intake in the third trimester.

Based on the calculated values of MET-hours of physical activity per day, no significant relations were found between physical activity during the first, second, third trimesters and risk of preeclampsia (Table 4).

According to personal and reproductive characteristics which are shown in table 1, only the mother's

Table 3. The association of nutrients intake in the first (1st Tr.), second (2nd Tr.) and third (3rd Tr.) trimesters of pregnancy with preeclampsia by logistic regression

	β	p	Odds Ratio (95% CI)
Mn (3rd Tr.)	-0.122	0.02	0.88(0.76,0.90)
SFA (1st Tr.)	0.28	0.045	1.028(1.02,1.036)
Vita E (3rd Tr.)	-0.370	0.045	0.99(0.984,0.996)
Vita C (3rd Tr.)	-0.001	0.04	0.985(0.98,0.99)
Carbo (3rd Tr.)	-0.001	0.035	0.98(0.97,0.99)
Fiber (3rd Tr.)	-0.006	0.046	0.97(0.96,0.98)

Mn: Manganese; SFA: Saturated fatty acids; Carbo: Carbohydrates; Vita: Vitamin

Table 4. The difference in physical activity (MET-hours per day) between mothers with and without preeclampsia in the first (1st Tr.), second (2nd Tr.) and third (3rd Tr.) trimesters of pregnancy

Physical Activity	Preeclamptic Mothers				Non Preeclamptic Mothers				Total				p
	Min	Max	Mean ± SD	n	Min	Max	Mean ± SD	n	Min	Max	Mean ± SD	n	
1st Tr.	6.63	32.25	17.25 ± 7.55	23	0.46	100.48	18.26 ± 11.06	537	0.46	100.48	18.22 ± 10.94	560	0.666
2nd Tr.	5.75	20.75	16.87 ± 7.04	23	1.78	110.75	16.63 ± 10.73	532	1.78	110.75	16.64 ± 10.60	555	0.915
3rd Tr.	4.50	29.25	17.30 ± 8.54	16	0.25	100.50	15.51 ± 11.04	484	0.25	100.50	15.56 ± 10.97	500	0.519

body mass index (BMI) before pregnancy, pregnancy weight gain, and weight before pregnancy were significantly associated with preeclampsia (p = 0.02, p = 0.02, and p = 0.002, respectively). Moreover, there was no significant association between receiving omega-3, multivitamins, and calcium supplements and the risk of preeclampsia (p > 0.05).

DISCUSSION

According to our results, the mean of saturated fat intake during the first trimester in pregnant women who developed preeclampsia in later phases of pregnancy was more than the other subjects (p = 0.045).

More than two decades ago, Chung et al. observed that low-income African American women from Alabama with toxemia in the third trimester had increased intake of total fat as well as increased intakes of specific polyunsaturated, monounsaturated, and saturated fatty acids.[10] In some studies, the association between intake of saturated fatty acids and preeclampsia has been attributed to endothelial dysfunction caused by acute or chronic consumption of these macronutrients.[11,12] Consumption of saturated fatty acids increases low-density lipoprotein cholesterol (LDL-C) levels.[13] On the other hand, some investigations have shown serum levels of LDL-C in women with preeclampsia in the later stages of pregnancy to be 10.4% higher than other pregnant women.[14] In addition, some studies have explained the association between fatty acids intake and preeclampsia later in pregnancy by lipotoxicity due to intake of fatty acids which affects the maternal and placental endothelial function.[15]

Moreover, manganese intake during the third trimester was significantly less in preeclamptic mothers compared to the others (p = 0.026). Although we did not find any study about the association between manganese intake and risk of preeclampsia, some researchers have reported an association between serum manganese levels and risk of preeclampsia which could confirm our finding. For instance, some authors concluded that low concentration of manganese in serum would lead to an accumulation of superoxides which can consequently trigger preeclampsia and its complications.[16-18] In addition, low serum manganese concentration involves in the pathogenesis of preeclampsia through the impairment of endothelial function.[18] Similarly, Akinloye et al. suggested that reduced serum manganese concentrations in the blood of preeclamptic pregnant women may be more of a cause than a resultant effect.[5]

Another result obtained in this study was lower vitamin E levels in preeclamptic patients in the third trimester (p = 0.049). Vitamin E has also been reported to be reduced in preeclamptic women in some other studies.[19-21] Grischke reported that vitamin E to have a protective effect against preeclampsia and hypertension.[22] Low vitamin E intake was also associated with a significant increase in the risk of hypertensive disorders of pregnancy, even after adjustments made for confounding factors.[23] As an antioxidant, vitamin E may inhibit the lipid peroxidation chain reaction, minimize the excessive generation of free radicals by inhibition of nicotinamide adenine dinucleotide phosphate [NAD(P)H] oxidase in both placental tissue and maternal neutrophils, reduce placental apoptosis, and inhibit leukocyte and endothelial cell activation.[24]

However, there are also some reports on the absence of an association between low levels of vitamin E and preeclampsia. It may reflect the failure to consider the increased lipids to be present in preeclampsia. In addition, in these sick women, it is not possible to discriminate cause and effect.[3]

Our findings indicated that a significant difference in mean of vitamin C intake in patients with preeclampsia in the third trimester compared with other mothers ($p = 0.034$). In fact, vitamin C intake in mothers with preeclampsia was significantly less than healthy mothers. Zhang et al. suggested that the incidence of preeclampsia was doubled in women whose daily intake of ascorbic acid was less than 85 mg.[25] In another study, low dietary intake of vitamin C in the 25th gestational week was associated with a trend toward an increased incidence of severe preeclampsia, eclampsia, or hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome.[26] Vitamin C, the most effective defense against free radicals in the peripheral circulation, is the first antioxidant to be exhausted during oxidative stress. Increased intake of fruits and vegetables rich in vitamin C may decrease preeclampsia risk by inhibiting LDL oxidation, by attenuating the production of reactive oxygen species by vascular cells, and by limiting cellular responses to oxidized LDL. For instance, expression of adhesion molecules, which play a pivotal role in the regulation of vascular tone, is attenuated when vitamin C is increased and endothelial nitric oxide synthesis is inactivated. Increased vitamin C intake may also play a role in modulating endothelial function through regulation of the inflammatory response to oxidative stress.[25]

We also found that mean of fiber intake in the third trimester of women with preeclampsia was less than women without preeclampsia ($p = 0.045$). In a prospective study, Qiu et al. reported that women who consumed a high amount of dietary fiber during early pregnancy had a reduced risk of subsequent preeclampsia compared with those who had little fiber.[27] The findings of Frederick et al. supported previous reports that suggested diets high in fiber and potassium to be associated with a reduced risk of hypertension.[28] Dietary fiber decreases oxidative stress. It also protects DNA molecules against H_2O_2-induced oxidative damage. Meanwhile, it was reported that the products of short-chain fatty acids during fermentation of dietary fiber in the intestines, such as butyrate and acetate, could prevent DNA and cell damage induced by H_2O_2. Butyrate was also found to be able to induce the activity of glutathione S- transferase, resulting in an enhanced antioxidant capacity of the organism.[29]

The last result was the significant difference between the two groups in carbohydrate intakes during the third trimester. The average carbohydrate intake in the third trimester in patients with preeclampsia was significantly lower than normal subjects ($p = 0.035$). Foods that contain carbohydrate are important sources of many nutrients, including water-soluble vitamins and minerals as well as fiber.[30] Therefore, it is possible that the association of preeclampsia with lower carbohydrates consumption along with lower intake of fiber and water-soluble vitamins including vitamin C provide the cause of developing preeclampsia. Such a theory seems more reasonable considering the highly significant direct association between intake of fiber and water-soluble vitamins and carbohydrate consumption ($p < 0.001$). In addition, both the amount and the kind of carbohydrates in a food will influence its effect on blood glucose level.[30] As a result, receiving lower carbohydrate may lead to hypoglycemia. In fact, multivariate analysis revealed that women with hypoglycemia were more likely to develop preeclampsia or eclampsia.[31]

Moreover, according to the literature, getting a low-carbohydrate diet before and during pregnancy is associated with low nutrient intake[32] which can in turn lead to oxidative stress[33] whose association with preeclampsia has been shown. However, other researchers have suggested the association between low-carbohydrate intake during the third trimester and preeclampsia to be possibly caused by a disease rather than its cause.[4] Therefore, further, more accurate studies are required to clarify the exact relations.

An important finding of the present study is that out of the 40 received micro- and macronutrients in the first, second, and third trimesters (Table 2), manganese intake in the third trimester had the highest association with risk for preeclampsia. However, more detailed studies are recommended to assess serum manganese levels and enzymes containing it in addition to dietary manganese intake. In addition, using logistic regression analysis revealed that the effects of manganese intake in the third trimester, saturated fatty acids in the first trimester, and vitamin E intake in the third trimester were more than other variables. In other words, the effects of carbohydrate, fiber, and vitamin C intake were eliminated after adjusting.

CONCLUSIONS

Based on the results of this study, the mean value of received saturated fat in the first trimester in subjects who experienced preeclampsia later in pregnancy was higher than the other pregnant women (p = 0.045). Manganese intake in the third trimester significantly less in preeclamptic subjects compared to the others (p = 0.026). Moreover, intakes of vitamin C, vitamin E, fiber, and carbohydrate during the third trimester were signify-cantly less among pregnant women who developed preeclampsia (p = 0.034, p = 0.049, p = 0.046, and p = 0.035, respectively). Except for the mentioned variables, there were no significant associations between other micro- and macronutrients in all trimesters and the risk of preeclampsia. In addition, the observed significant relations were independent of demographic and reproductive characteristics, estimated physical activity, and supplements (multivitamins, omega-3, and calcium).

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