Survey the relationship between diet and occurrence of preeclampsia in the pregnant women of Tehran city

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A-R-T-I-C-L-E I-N-F-O

A-B-S-T-R-A-C-T

Background & Aims of the Study: Preeclampsia is the most common clinical symptom of pregnancy period. According to the importance of preeclampsia and the lack of definite and effective factors on it, this study was performed by the aim of survey the relationship between diet and occurrence of preeclampsia in the pregnant women of Tehran city in 2012.

Materials & Methods: This longitudinal study (prospective) was performed on 1033 pregnant women in prenatal clinics in Tehran city. At the beginning of the study, it were completed the food eating frequency and demographic questionnaires from all samples once before twentieth week through face to face interviews. Nutritional data that were achieved from the questionnaire of every understudied unit that recorded all of foods consumed by mother were changed to the gram by the researcher and analyzed by the software of N4 to calculate nutrient intake of mothers. Pregnant women were followed since the entrance to the study to the time of delivery. The significance level used in the tests was less than 0.05.

Results: Twenty pregnant women (1.9%) form 1033 studied women were diagnosed preeclampsia. The results of independent T-test showed that the average intake level of antioxidant nutrients (such as zinc, vitamin A, C, E) in women with preeclampsia were significantly low.

Conclusions: The results showed that the reduction in daily intake of antioxidant nutrients is associated with the occurrence of preeclampsia.

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Background

Preeclampsia is the most common clinical symptom during pregnancy that is associated with bleeding and infection and is one of the three causes of pregnant women deaths in the world (1). Preeclampsia is complicated the approximately 2-3% of all pregnancies and it is responsible for approximately 60000 mother deaths each year in the world (2). Systolic

blood pressure of higher or equals to the 140 mmHg in at least two measuring with duration of 4-6 hours after twentieth week of pregnancy with proteinuria in the amount of 300 mg and higher or 1+ and higher in dipstick test is suggestive of preeclampsia (3). Factors that can be considered as risk factors arenulliparity, age over 35 years, obesity, and race, multiparity (4). Perinatal and maternal outcomes in preeclampsia is depends on the gestational age, severity of illness, quality of care, previous medical problems (5, 6). Maternal outcomes are including placental abruption, pulmonary edema, acute renal failure, liver failure, hemorrhage, shock, eclampsia and death. HELP syndrome is a serious complication of this disease that is characterized by hemolysis, elevated liver enzymes and decreased blood platelet and it is associated with poor prognosis in pregnancy (7).

Other neonatal outcomes are including preterm birth, intrauterine growth restriction, cerebral hypoxia, low birth weight and perinatal mortality (8). Despite the fact that the preeclampsia is an important cause of maternal and neonatal morbidity and mortality but the pathophysiology and etiology is not fully known. Researchers have proposed many theories for this issue(9). Recently it is raised the hypothesis that preeclampsia syndrome is a two-step disorder. The first is pre-clinical stage that is characterized by incorrect remodeling of uterine arteries in effect of trophoblastic invasion that is leading to placental hypoxia. (Placental oxidative stress). The second stage is occurring by the release of placental factors into the maternal circulation and cause systemic inflammatory response and the activation of the endothelium. (10). Oxidative stress is caused by an imbalance between increased productions of reactive oxygen intermediates (ROS) and antioxidant defense mechanism defects (11). These findings led to increased attention to the potentially beneficial effects of antioxidants in the prevention of preeclampsia. Examples of antioxidants are vitamins A, C, E and zinc,

which these antioxidants prevent from overproduction of toxic free radicals and their damages. In the studies which antioxidants are used as a factor in the prevention of preeclampsia, preeclampsia has been reduced up to 50% (12). Scientists also found that vitamin C along with vitamin A and E levels reduced in preeclampsia(13). However, in a study that was conducted in 2006, 6% of mothers taking vitamin C and 5% of those who did not used vitamin C develop preeclampsia that it was not statistically significant (14, 15). In the study that was performed byKapil, Assalmy, Swanson it was found that zinc deficiency is associated with preeclampsia. (16, 18) However, in all studies to provide reliable results more samples arerecommended (12).

Aims of the study: In according to the severe complications of preeclampsia for the mother and fetus and also inconsistent results on the role of antioxidants in preeclampsia, this study is conducted to determine the relationship between nutrient antioxidants (vitamins A, C, E and zinc) with occurrence of preeclampsia.

Materials & Methods

Present study is longitudinal (prospective) study that was conducted on the 1100 pregnant women that referred to the prenatal clinics of Tehran university hospitals (Mirzakochak Khan, Shohada, Vali-Asr, Amirolmomenin, Arash, Akbarabadi and najmieh) after obtaining informed consent in 2012. After entering the study and obtaining the full name and telephone number, all mothers were treated with routine care during pregnancy and they were actively followed up until delivery in the above-mentioned centersexception of abortion (67 cases) that were excluded from the study. Under-studied population was pregnant women with gestational age of 14-20 weeks that had inclusion criteria to enter this study. Inclusion criteria were no history of chronic diseases, age between 18 to 35 years, singleton pregnancy, not smoking, alcohol and drugs usage and

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Iranian citizenship.Sampling for this study was a multi-stage Sampling that was carried out as follows:

The first step: selection of targeted hospitals that were depended to the Tehran university

The second step: Identify the prenatal clinic centers in hospitals and coding of them, systemically. The third step: The number of university needed prenatal care centers was determined based on average daily clients admitted to the prenatal clinic and each of the prenatal clinics randomly determined. Such that the prenatal clinics were selected, randomly and systemically. The fourth step: In each of prenatal clinic, 92 pregnant women were recruited in according to the inclusion criteria of this study.

Finally, 1033 pregnant women were studied withfourteenth week to the twentieth gestational weeks until delivery. Questioners were trained in two sessions on how to complete a food frequency questionnaireand the correct ways of questions and answers from the patientby a trained dietitian. It were completed the food eating frequency and demographic questionnaire from all of samples once before the twentieth week by face to face interview. Nutritional data that were achieved from the questionnaire of every understudied unit that recorded all of foods consumed by mother were changed to the gram by the researcher. And the achieved information from questionnaireswas analyzed by Nutritionist IV software to calculate nutrient intake of mother.

Demographic questionnaire included age, occupation, education and reproductive history of previous pregnancies, height, weight, blood pressure of pregnant women, passive smokers had lived with mother. If there is a blood pressure of 140/90 mmHg or higher and proteinuria after twentieth week of pregnancy, the diagnosis of preeclampsia was given to the mother by the obstetrician in the clinics of hospital.

In this study, all samples were aware of the objectives of the study and in addition to the awareness from their rights, they completed written consent to participate in the study. In addition, the research team analyzed the data, confidentially.

Data analysis: The data were analyzed by the software of SPSS Version 16 and use of central statistical indices, independent T-test and chi-square tests. Significance level of these tests in this study was considered lower than 0.05.

Results

The results showed that preeclampsia had occurred in 1.9% (n=20) of understudied mothers. The mean and standard deviation of understudied women were 26.78±4.36 and 72.4% of mothers were in the range of 20-30 years of old. The mean and standard deviation of body mass index (BMI) was 25.46±4.61 kilograms/square meter in the first visit that more than half of the mothers had normal BMI. 18.8% of pregnant mother had BMI of more than 29 that is considered as a major risk factor for preeclampsia. 13.3% (137 peoples) of them was employed and 86.7% (869 peoples) of them were housewives. 53.3% of them were nulliparous mothers. 1.2% of mothers were illiterate and only 26.9% of them had university education and majority of them (50.9%) of them were high school graduates. Since participating mothers did not smoke, smoking rates of their household assessed that was about 12.4%.

56.9%, 92.7% and 34.4% of participating mothers were used from iron, folic acid and multivitamins supplements, respectively. And also, most of them were used from foreign multivitamins supplements more than Iranian supplements. (13% versus 12.4%) and also, 69.6% of participating mothers were delivered by cesarean section that is two times higher than natural child birth.

As indicated in Table 1 there is no difference between the two groups of with and without preeclampsia in terms of mean age, parity, BMI, education, and employment status.

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Table 1: Distribution of personal and social characteristics of under-studied peoples in two groups of with and without preeclampsia

Demographic characteristics		With preeclampsia	Without preeclampsia	P-Value
The mean of age		28.00 ±4.09	26.76 ± 4.36	0.210
Average number of pregnancy		1.95 ± 0.99	1.67 ± 0.94	0.244
The mean of BMI		25.42 ± 2.68	25.46 ± 4.54	0.948
Education level	Illiterate	0 (0%)	12 (1.2%)	0.507
	elementary	1 (5%)	91 (9%)	
	Middle school	4 (20%)	121 (11.9%)	
	High school	13 (65%)	513 (50.6%)	
	university	2 (10%)	276 (27.2%)	
Occupation	Housekeeper	18 (90%)	878 (86.7%)	0.492
	working	2 (10%)	135 (13.3%)	

Table 2: The frequency distribution of daily nutritional intake in under-studied pregnant mothers at 14-20 weeks of gestation (n=1033)

Nutrient	mean	Standard deviation	minimum	maximum	Lower than RDA	As the amount of RDA
Vitamin A (microgram)	1230.7	1196.4	86.6	7764.8	443 (42.9%)	590 (57.1%)
Vitamin C (milligram)	150.8	121.7	14.4	731.8	353 (34.2%)	680 (65.8%)
Vitamin E (milligram)	3.1	2.6	0.32	22.1	1017 (98.5%)	16 (1.5%)
Zinc (milligram)	8.99	4.2	1.88	26.8	786 (76.1%)	247 (23.9%)

In this study, 42.9%, 34.2%, 98.5% and 76.1% of under-studied pregnant women had daily intake of vitamin A, C, E and zinc lower than recommended value, respectively (Table 2).

The RDA for pregnant women of vitamin A, E and C are 770, 85 and 11 mg, respectively (19). The results of this study showed that in 100% of women with preeclampsia, the intake amount of zinc and vitamin E was lower than RDA that this result was significant only for zinc (Table 3).

Table 3: Frequency distribution of antioxidant nutrient intake between the groups of with and without preeclampsia

antioxidant nutrient		With preeclampsia		Without preeclampsia		P
		N	%	N	%	
Vitamin A intake	> RDA	8	40	435	42.9	0.792
	As the amount of RDA	12	60	578	57.1	
Vitamin E intake	> RDA	20	100	997	98.4	0.571
	As the amount of RDA	0	0	16	1.6	
Vitamin C intake	> RDA	3	15	350	34.6	0.068
	As the amount of RDA	17	85	663	65.4	
Zinc intake	> RDA	20	100	766	75.6	0.011
	< RDA	0	0	247	24.4	

Independent T-test showed that there is a significant difference in the mean intake of anti-oxidant nutrient between two groups of with and without preeclampsia. Such that, the mean intake of these nutrients was lower significantly in the group of with preeclampsia. (Table 4)

Table 4: The mean and standard deviation of nutrient intake in according to the occurrence of preeclampsia in the under-studied mothers

Nutrient	With preeclampsia Mean±SD	Without preeclampsia Mean±SD	T-test
Vitamin A (microgram)	837.4± 1209.1	1200.9±1231.1	P<0.001
Vitamin C (milligram)	44.2±127.06	122.7±151.3	P<0.001
Vitamin E (milligram)	0.7±2.2	2.7±3.1	P<0.001
Zinc (milligram)	1.5±6.8	4.28±9.03	P<0.001

Discussion

In this study, 20 pregnant women (1.9%) of 1033 women who enrolled in the study suffered from preeclampsia. According to the study in Tehran, the incidence of preeclampsia is about 6.5% (20) that is higher than the results of present study. This issue is occurred due to the presence of mothers with higher age and BMI. In this study, the mean intake of vitamin A was 1230.7 microgram/day that about 42.9% of women received lower than RDA recommendation. Thus, vitamin A deficiency is evident in this group and can involve complications.So that asignificant percentage of pregnant women in rural areas of Nepal suffering from night blindness due to vitamin A deficiency (21). Also the results of the study of DelvarianZadeh show the similar results about the intake of vitamin A (22) also 34.2% of under studied women received lower vitamin C than the amount of RDA recommendation during pregnancy that is similar the results of Mortazavi study in Sabzevar (23).

Unfortunately, in this study the intake of vitamin E was lower than other antioxidant, such that 98.5% of pregnant women intakes lower than RDA recommendation that was similar to the study of Mortazavi (23) and Rumbold (14). The daily RDA recommendation of zinc during pregnancy is 11 mg/day but in this study the daily intake of zinc was 8.99 mg/day that 76.1% of samples intakes lower than the recommended amount of zinc. The average intake of zinc in the developing countries is 5-11 mg/day. It shows that 82 to 100% of pregnant women of the world do not get enough zinc (24). In the Jain (25) and Selina (26) study also the reported amount of zinc intake is lower than recommendation (27).

The results of this study showed that in the mothers who suffered from preeclampsia, the daily intake of vitamin A, C, E and zinc was lower than mothers without preeclampsia. This may reflect the role of antioxidants in having or not having preeclampsia.Recently, the role of oxidative stress or increased lipid peroxide in preeclampsia is considered. In women with preeclampsia, there is an imbalance between the activities of antioxidant enzymes and peroxide production (11). Materials such as zinc are required for the activity of enzymes such as superoxide dismutase, which is involved in removing free radicals. The deficiency of this mineral nutrient during pregnancy may have a role in the pathogenesis of preeclampsia by reducing the activity of superoxide dismutase and increasing the lipid peroxides (26).

In the cross sectional study of Jain; the mean serum zinc level was lower in mothers who suffered from preeclampsia (25) which is similar to the present study. And also in the Selina study, the serum zinc level was lower in women with mild and severe preeclampsia (26). Harma study also indicates this issue (28). But in the case-control study that was performed in 2008 on the pregnant women with the gestational age of 35-36 weeks, serum zinc

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levels in healthy mothers and mothers with preeclampsia had significantly difference (2).

Vitamin C is a powerful antioxidant that is soluble in water that is improved vascular function and diuresis by renewing the cycle of vitamin E(29). In this study, intake of vitamin C in patients who suffered from preeclampsia was significantly lower than non-sufferers. Zhang also with the survey of 109 pregnant women with preeclampsia and 259 control women showed that the women who intake vitamin C lower than the recommendation have lower serum level of vitamin C and are at risk of preeclampsia (30). The Joshi prospective study in 2005 showed that in women with preeclampsia, the MDA (oxidative stress index) increaseand the amount of vitamin E, C significantly decrease (31).

Moreover, vitamin A and E, which are fat-soluble vitamins as antioxidants, prevent the spread of lipid peroxides(32). In this study, the intake of these micronutrients in patients with preeclampsia was significantly lower.In the case-control study Nikpoor also there is a significant difference in the level of vitamin E intake between the mothers with and without preeclampsia(33). In Nikpoor et al study, the chance of preeclampsia in the women who intakes lower than 15 mg vitamin E was higher than women who intakes higher doses(33). In the study of Gulmezoglu, a smaller percentage of women who received antioxidant supplements such as vitamin A and E needs to the antihypertensive drugs and pregnancy period were more than the control group (34). Michelle and colleagues also found that in the women with high levels of carotene, the risk of preeclampsia reduced in about 50% (35). By review of controlled clinical trials that performed by Villar in 2003, it is clear that the lack of antioxidants such as vitamins A, C, E in pregnant women increases the risk of preeclampsia (36).

Although there are similar results in several studies about the relationship between antioxidant nutrients with preeclampsia but in

Rumbold study in 2006, there isn't any significant difference in the amount vitamin E and C with preeclampsia (37). It was not found any evidence based on the relationship between the effects of antioxidant and reducing of preeclampsia or gestational hypertension in the Oken study in East Massachusetts(38). The cause of inconsistent results may be due to small sample size of this study, as well as differences in the method of collection and the duration of the study. Although, this study has significant sample size but one of the limitation of this study is only 20 patients (1.9%) suffering from preeclampsia. But the effects of confounding variables with some Exclusion criteria were neutral. Fortunately, there was not any significant difference in mean age, parity, BMI, level of education between the two groups.

Conclusion

The results showed that reducing intake of antioxidant nutrients may play a role in preeclampsia. For this reason, some researchers by considering the recent life style recommending the use of vitamin supplements. Since the results of this study showed that a substantial percentage of pregnant women had inadequate intakes of antioxidants, the strength of this recommendation is increased. Thus increasing the knowledge about the importance of antioxidant micronutrients and their contribution to the success and health of the mother and fetus during pregnancy should be considered as the key to improving outcomes. Pregnant women should also be trained on the importance of proper nutrition during pregnancy.

Footnotes

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Conflict of Interest:

The authors declared no conflict of interest.

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