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Evaluation of Serum Homocysteine, Zinc and Vitamin Levels in Pregnant Women

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Abstract

Aim: Certain vitamins and trace elements in metabolism of pregnant woman should be sufficient for both maternal health and fetal development. Molecules that negatively affect pregnancy should be well known and precautions should be taken in time against them. Homocysteine is an amino acid composed of methionine that converts into cystathionin or recycled into methionine. The cycle of homocysteine involves vitamins B6 and B12, folic acid and zinc. Homocysteine levels have been shown to increase in vitamin B12 and folic acid deficiency. It has been found that increased homocysteine levels play a role in many conditions such as cardiovascular, renal, and cerebral disorders and apoptosis. Hyperhomocysteinemia has been found to cause adverse effects in pregnancy such as preeclampsia, recurrent pregnancy loss, neural tube defects, intrauterine growth restriction, and fetal demise . Zinc, which is found in the structure of metalloenzymes, is a trace element playing an important role in homeostasis and protecting from oxidative stress as well. It is important in pregnant women, fertilization, fetal growth, and development of immunity. In this study, we aimed to determine the difference between homocysteine, folic acid, zinc, and vitamin B12 levels of pregnant women within the first trimester using and not using any kind of vitamin and/or trace element supplements.

Material and method: This study was conducted by screening data of patients applying to Obstetrics Department of Necip Fazıl City Hospital for routine pregnancy follow-up during first trimester between January-December 2020. Study was completed with a total of 60 healthy pregnant women, 30 not using any vitamin supplements (Group I) and 30 using vitamin supplements (Group II). Plasma homocysteine, serum folic acid, vitamin B12 and zinc levels were evaluated in the study.

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Results: The serum homocysteine, vitamin B12, folic acid and zinc levels of Group I were found as 13.8 ± 5.2 µmol / L, 308.1 ± 62.6 ng / L, 4.49 ± 2.35 µg / L, and 68.8 ± 30.4 µg / dl, respectively. The serum homocysteine, vitamin B12, folic acid and zinc levels of Group II were found as 8.2 ± 3.5 µmol / L, 351.4 ± 111.4 ng / L, 8.47 ± 2.62 µg / L, and 103.8 ± 43.0 µg / dl, respectively. Homocysteine level of Group I was found statistically significantly higher compared to Group II ($p<0.05$). A statistically significant decrease was found in serum levels in folic acid, vitamin B12 and zinc of Group I ($p <0.05$).

Conclusion: As a result, pregnant women are in high-risk group for deficiency of several vitamins and minerals due to rapid fetal growth and development.

In this study, we found that serum homocysteine levels, an indicator of oxidative stress, were increased in pregnant women while serum levels of zinc, vitamin B12 and folic acid were decreased. We think that it is essential in terms of maternal and fetal health to determine serum levels of zinc, vitamin B12, folic acid and homocysteine in pregnant women, and to add those molecules to dietary schedule if lacked.

Keywords: Folic acid, homocysteine, pregnancy, vitamin B12, zinc

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Introduction

Many physiological changes occur during pregnancy. These changes affect mother and fetus. Certain vitamins and trace elements in metabolism of pregnant woman should be sufficient for both maternal health and fetal development. Molecules that negatively affect maternal health and fetal development should be well known and precautions should be taken in time against them. Homocysteine is an amino acid composed of methionine that converts into cystathionin via transsulfuration or recycled into methionine via remethylation.

Remethylation process occurs firstly via transfer of methyl group of betaine to homocysteine through betaine homocysteine methyl transferase enzyme or secondly, by presence of methionine synthase enzyme together with vitamin B12 and folic acid as coenzyme,

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while conversion of homocysteine to cystathionine via transsulfuration occurs in the presence of cystathionine-β-synthetase enzyme and vitamin B6 as coenzyme (1, 2).

Homocysteine levels have been shown to increase in deficiency of vitamin B12 and folic acid (3). It has been found that increased serum homocysteine level plays a role in many conditions such as cardiovascular, renal, and cerebral disorders and apoptosis (4, 5). Hyperhomocysteinemia has been found to cause adverse effects in pregnancy such as preeclampsia, recurrent pregnancy loss, neural tube defects, intrauterine growth restriction, and fetal demise (6, 7). Vitamin B12 is a vitamin that plays a role in DNA synthesis and is important for development and function of neural tissue (8).

Vitamin B12 is found in foods of animal origin, not found in plants and vegetables, and is absorbed from terminal ileum via intrinsic factor (9). Autoimmune disorders, especially pernicious anemia, genetic disorders, strict vegetarian diet, gastrointestinal surgery, parasites, Crohn's disease and use of medicine such as metformin or proton pump inhibitors are some causes of vitamin B12 deficiency (10, 11). Vitamin B12 is especially essential for placental development and embryogenesis in pregnant women (12). Vitamin B12 deficiency was found to cause impairment in lipid metabolism, and obesity in pregnant women, and lead to low birth weight along with insulin resistance in newborn (13). Folic acid is a water-soluble vitamin, involved in the synthesis of nucleic acids and, is effective in growth and development processes of body (14). Megaloblastic anemia, cardiovascular and allergic disorders occur in folic acid deficiency (15).

The need for folic acid is increased during pregnancy due to fetal tissue and organ development; deficiency of folic acid leads to several findings and disorders such as neural tube defects in fetus, placental development defects and postpartum depression in mother (16, 17). Zinc, which is found in the structure of metalloenzymes such as DNA polymerase, RNA polymerase, superoxide dismutase, carbonic anhydrase, alkaline phosphatase, carboxypeptidase, and alcohol dehydrogenase, is a trace element important for homeostasis, and protecting from oxidative stress (18, 19). It is important in pregnant women for fertilization, fetal growth, and immune development (20, 21).

In this study, we aimed to determine the difference between serum homocysteine, folic acid, zinc, and vitamin B12 levels of healthy, nonsmoker, and risk factor-free pregnant women within the first trimester, using and not using any kind of vitamin and/or trace element supplements since the beginning of pregnancy.

Material and Method

This study was conducted by screening medical records of patients applying to Obstetrics Department of Necip Fazıl City Hospital for routine pregnancy follow-up during first trimester between January-December 2020. A total of 60 healthy, nonsmoker, not receiving any

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treatment pregnant women were included in the study, 30 not using any vitamin supplements (Group I) and 30 using vitamin supplements (Group II). The vitamin preparations used were multivitamins, did not contain minerals. Mean gestational weeks of Group I and Group II were 10 ± 2 weeks and 12 ± 4 weeks, respectively. Plasma homocysteine, serum folic acid, vitamin B12 and zinc levels were evaluated in the study.

Serum homocysteine, vitamin B12 and folic acid were analyzed by electrochemiluminescence immunoassay method using Cobas e 602 autoanalyzer device (Roche Diagnostics, F.Hoffmann-La Roche Ltd., Kaiseraugst, Switzerland), and serum zinc level was analyzed by turbidimetric method using Beckman Coulter AU 680 (kraemer-USA) autoanalyzer.

Statistical Analysis

Data were analyzed using the SPSS 20.0 program for Windows (SPSS, Inc., Chicago, IL, USA). Normal distribution of continuous and discrete data was analyzed by Kolmogorov and Smirnov test, and homogeneity of variances was analyzed by Levene's test. Descriptive variables were expressed as mean ± standard deviation (SD).

Student t test was used for normally distributed data and Mann-Whitney U test was used for non-normally distributed data in comparison between groups. Spearman's rho method was used for correlation.

Results

Study was carried out with pregnant women within the first trimester. Mean age of Group I and Group II was 26.4 ± 3.09 years and 28.1 ± 4.2 years, respectively. No significant difference was found between the mean age of groups ($p>0.05$).

The serum homocysteine, vitamin B12, folic acid and zinc levels of Group I and Group II were found as 13.8 ± 5.2 vs 8.2 ± 3.5 µmol / L; 308.1 ± 62.6 vs 351.4 ± 111.4 ng / L; 4.49 ± 2.35 vs 8.47 ± 2.62 µg / L; and 68.8 ± 30.4 vs 103.8 ± 43.0 µg / dl, respectively. A statistically significant increase was found in homocysteine levels of the group not receiving vitamin supplements (Group I) ($p <0.05$).

A statistically significant decrease was found in serum folic acid, vitamin B12, and zinc levels of the group not receiving vitamin supplements (Group I) ($p <0.05$).

Table 1: Demographic and biochemical data of study groups

	Group I (n= 30)	Group II (n= 30)	*P* value
Homocysteine (µmol/L)	13.8 ± 5.2	8.2 ± 3.5	<0.005
Folic acid (µg/L)	4.49 ± 2.35	8.47 ± 2.62	<0.005
Vitamin B12 (ng/L)	308.1 ± 62.6	351.4 ± 111.4	<0.005
Zinc (µg/dl)	68.8 ± 30.4	103.8 ± 43.0	<0.005
Age (years)	26.4 ± 3.09	28.1 ± 4.2	>0.005

Discussion

Despite all technological advances in the world, maternal/fetal mortality and morbidity remain as an important problem. Vitamin and mineral deficiency, and other risk factors should be considered and treated for a healthy pregnancy process. Hyperhomocysteinemia has been shown to cause many adverse effects in pregnancy such as neural tube defects, placental detachment, recurrent pregnancy loss, intrauterine growth restriction, preeclampsia, and fetal demise (22, 23).

Homocysteine consists of methionine and is metabolized in two ways(3). The first pathway (transsulfuration pathway) is conversion to cysteine in the presence of cystathionine-β-synthetase enzyme and vitamin B6. The second way is remethylation pathway occurring in two ways. In remethylation pathway, conversion of homocysteine into methionine occurs either by methionine synthase enzyme together with vitamin B12 and folate or transfer of methyl group of betaine to homocysteine through betaine homocysteine methyl transferase enzyme (24).

Some of the homocysteine is transformed into homocysteine disulfide or homocysteine thiolactane during conversion process resulting in free radical formation such as superoxide and hydrogen peroxide which damage the endothelium together with homocysteine (25). In this way, the endothelium loses its anticoagulant properties and its tendency to coagulation increases. In addition, as endothelial structure is damaged, release of nitric oxide, one of the most potent vasodilator molecules secreted from the endothelium, is disrupted leading to reduced blood flow, decreased tissue perfusion and placental insufficiency. On the other hand, homocysteine induces hypercoagulopathy by accelerating the effects of factor V, X, and XII, inhibiting protein C activation, and increasing the release of plasminogen activators, thus causes maternal and fetal adverse effects by contributing to increased coagulation during pregnancy (26).

It was found in a study that increased serum homocysteine level was an independent risk factor for atherosclerosis and thromboembolic events (27). Vitamin B12 and folic acid are vitamins required in conversion of homocysteine into methionine. Serum homocysteine level was shown to increase in vitamin B12 and folic acid deficiency (28). Studies have shown that there was vitamin B12 and folic acid deficiency in recurrent pregnancy loss, and serum vitamin B12 and folic acid levels were negatively correlated with serum homocysteine level (29, 30). In our study, we found that serum homocysteine level was higher, and folic acid and vitamin B12 levels were lower in the group not receiving vitamin supplement compared supplement receiving group.

We suppose that the high homocysteine level in serum would damage the endothelium, leading to interrupted fetoplacental growth. In addition, we suppose that increased serum homocysteine level may disrupt structure of proteins, lipids, and many molecules by oxidation in metabolisms of both the mother and the fetus. Zinc is one of the trace elements involved in important reactions in the organism. Zinc, which is found in the structure of metalloenzymes such as DNA polymerase, RNA polymerase, superoxide dismutase, carbonic anhydrase, alkaline phosphatase, carboxypeptidase, alcohol dehydrogenase, and betaine homocysteine methyl transferase is a trace element shown to have a role in protecting from oxidative stress (18). Zinc is important in DNA and RNA replication, hence in tissue growth, and cell and organ development. On the other hand, it is effective in development of immune system, and in prevention of excessive inflammatory response and excessive apoptosis in cells (31, 32). Studies have found that serum zinc level altered during pregnancy and decreased by 67% (33, 34).

In our study, in accordance with the literature, serum zinc level was found lower in the non-supplemented group. We suppose that when zinc is not added to the diet of pregnant women, it would result in increased inflammatory cytokines, damaged syncytiotrophoblasts by apoptosis, and fetoplacental insufficiency. Considering that DNA and RNA polymerase enzymes function in presence of zinc, we think that growth and development of fetus will be negatively affected in zinc deficiency. In addition, the betaine homocysteine methyl transferase enzyme, which enables elimination of homocysteine, functions in presence of zinc. Therefore, we suppose that betaine homocysteine methyl transferase enzyme would not be activated in zinc deficiency, and as a result, serum homocysteine level would increase leading to reveal the harmful effects of homocysteine.

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As a result, pregnant women are in high-risk group for deficiency of several vitamins and minerals due to rapid fetal growth and development. In this study, we found that serum levels of homocysteine-an indicator of oxidative stress-, zinc, vitamin B12 and folic acid were decreased in pregnant women. We think that monitoring serum zinc, vitamin B12, folic acid, and homocysteine levels in pregnant women from the beginning of gestation and adding these molecules to diet of pregnant women who have deficiency are necessary for both maternal and fetal health.

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