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Evaluation of Serum Vitamin A, Vitamin E, Cholesterol, and Triglyceride Levels in Pregnant Women Diagnosed with Missed Abortion

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ABSTRACT

Introduction: Missed abortion is defined as the intrauterine death of an embryo or fetus. It occurs when there is no fetal heartbeat, but it does not result in bleeding or miscarriage. It accounts for approximately 15% of all pregnancies. Studies have linked the risk of early pregnancy loss to poor vitamin intake. Essential micronutrients in the human body, vitamin A and E, play crucial roles in maternal health and embryonic development. Cholesterol is presumed to play a role in human fertility because it is the main substrate of steroid synthesis. Studies have reported that normal lipid metabolism plays a role in pregnancy complications, such as endothelial damage and spontaneous miscarriage. Maternal hypercholesterolemia is linked to umbilical cord endothelial dysfunction. Additionally, dysregulation of fat metabolism characterized by significantly increased total cholesterol (TC) and triglyceride (TG) levels induces low-grade inflammation.

Methods: The study, conducted at the İstanbul Training and Research Hospital from 01.02.2023 to 01.08.2023, included blood samples obtained from 50 pregnant women aged 20-45, diagnosed with a missed miscarriage. The vitamin A, E, TC, and TG values of the blood samples were compared.

Results: Comparison of vitamin A, vitamin E, TC, and TG measurement values between the healthy and missed diagnosis groups in early pregnancy did not reveal significant differences. This study was designed to analyze serum vitamin A and E levels, cholesterol, and TG levels, potentially leading to early embryo and fetal losses, to assess the nutritional status and vitamin supplementation in early pregnancy. Due to the insufficient number of studies in the literature, further research with a larger sample size is needed.

Conclusion: In our study, no association was found between maternal serum levels of vitamin A and E, TC, TG, and missed abortions in early pregnancy.

Keywords: Missed abortion, vitamin A, E, total cholesterol, triglyceride

Introduction

Missed abortion is defined as the intrauterine death of an embryo or fetus. It occurs when there is no fetal heartbeat, but it does not result in bleeding or miscarriage. It accounts for approximately 15% of all pregnancies (1). Studies have linked the risk of early pregnancy loss to poor vitamin intake. Because the mother's nutritional status can influence the baby's development, vitamin supplementation is important for pregnant women and those planning pregnancy (2). Essential micronutrients in the human body such as vitamin A and E play crucial roles in maternal health and embryonic development (3,4).

Vitamin A is required for the growth and proliferation of epithelial cells (5). Vitamin A deficiency can lead to night blindness, pregnancy complications, an increase in fetal malformations, and affect embryonic development (6). In particular, it directly affects reproduction, the ability to conceive, and the healthy progression of pregnancy in ruminants (7).

Vitamin E is essential for maintaining metabolic functions in the human body and acts as an antioxidant by scavenging free radicals (3). Owing to its antioxidant effects, it protects tissues by preventing the oxidation of intracellular and intercellular membranes, thereby allowing them to function properly (8). Vitamin E deficiency in pregnant women can lead to placental aging, vascular endothelial damage, hypertensive disorders of pregnancy, early placental separation, miscarriage, and preterm birth, among other complications (9).

Cholesterol is presumed to play a role in human fertility because it is the main substrate for steroid synthesis (10). Studies have reported that normal lipid metabolism plays a role in pregnancy complications,

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such as endothelial damage and spontaneous miscarriages (11). Maternal hypercholesterolemia has been linked to umbilical cord endothelial dysfunction (12). Additionally, dysregulation of fat metabolism characterized by significantly increased total cholesterol (TC) and triglyceride (TG) levels induces low-grade inflammation (13,14). Temporary hypercholesterolemia is a physiological process that provides adequate cholesterol for fetal growth and meets the mother's energy needs during pregnancy (15). TC levels <280 mg/dL indicate maternal physiological hypercholesterolemia, while levels ≥280 mg/dL or TC levels above the 75th percentile in different trimesters of pregnancy indicate maternal supraphysiological hypercholesterolemia (MSPH) (16). The potential effects of MSPH on the placental microvascular system are not well understood. Endothelial dysfunction of both macro- and microvascular vessels in the placenta during pregnancy may be associated with MSPH (16,17).

This study was designed to analyze serum vitamin A and E levels, cholesterol, and TG levels, potentially leading to early embryo and fetal losses, to assess the nutritional status and vitamin supplementation in early pregnancy.

Methods

Our study was conducted using blood samples obtained from pregnant women who presented to University of Health Sciences Türkiye, İstanbul Training and Research Hospital and received approval from the Institutional Review Board (approval number: 54, date: 10.03.2023). A total of 50 pregnant women were included in the study, comprising 25 women with a diagnosis of missed abortion in the first trimester and 25 healthy controls. An informed consent form was obtained from the patients.

The exclusion criteria for the study involved patients with systemic illnesses, uterine anatomical abnormalities, multiple pregnancies, multivitamin supplement use, and in vitro fertilization. None of the selected pregnant women used multivitamins because this was one of the exclusion criteria.

Serum levels of vitamins A and E, TC, and TG were assessed in each pregnant woman. The following data were also recorded for the patients: age, gravidity, parity, number of previous miscarriages, height, weight, body mass index (BMI), and gestational age measured during ultrasonographic examination.

Laboratory work was conducted at the İstanbul Training and Research Hospital Biochemistry Laboratory. Blood samples were collected in monette tubes after a fasting period of 10-12 hours, were centrifuged at 4000 revolutions per minute for 10 min, and the levels of TC and TG were determined using the Roche Cobas c 501 analyzer (California, USA). Vitamin A and E levels were analyzed at the İstanbul Training and Research Hospital Biochemistry Laboratory. A separate blood sample was collected in a monette tube, and 1 mL of ethyl alcohol was added to 0.3 mL of serum. The mixture was vortexed for thorough mixing. Subsequently, the mixture was centrifuged at 2000 revolutions per minute for 3 min, and 0.2 mL of n-hexane was added to the upper layer. This step allowed the extraction of vitamins A and E into the n-hexane phase. The extraction process was repeated twice, and the combined n-hexane phases were evaporated under nitrogen gas until dry. The residue in the tube was dissolved in 0.2 mL of methanol and prepared for analysis by high-performance liquid chromatography (HPLC-10) (Nashua, New Hampshire, USA). Vitamins A and E were determined using an octadecyl-silica-2 HPLC column (Nashua, New Hampshire, USA) with a mobile phase consisting of methanol: acetonitrile: chloroform (47:42:11, v/v). The flow rate of the mobile phase was set at 1 mL/min. Vitamin E and vitamin A were determined at 296 and 326 nm, respectively. In cases of inappropriate or suspicious results, samples were retested.

Statistical Analysis

Descriptive statistics such as mean, standard deviation, median, minimum, maximum, frequency, and percentage were used to describe the data. The distribution of variables was assessed using the Kolmogorov-Smirnov test. For the analysis of quantitative independent variables, the Mann-Whitney U test was employed. For the analysis of qualitative independent variables, the chi-square test was used, and in cases in which the conditions for the chi-square test were not met, the Fisher's exact test was applied. Statistical analyses were conducted using SPSS version 28.0.

Results

The study included a total of 50 cases. The ages of the patients ranged from 20 to 45 years, with a mean age of 30.1±6.0 years. The mean BMI of pregnant women who participated in the study was 23.5±1.9. Among the participants, 25 had no fetal heartbeats detected during the ultrasound examinations, whereas 25 did have fetal heartbeats. The gestational age of the pregnant women included in the study ranged from 6.4 to 12.0 weeks, with an average of 8.8±1.8 weeks. All participants (100%) had spontaneous pregnancies. None of the patients had comorbid diseases or were taking medications. Among the participating pregnant women, 43 (86.0%) had no history of previous miscarriages, whereas 7 (14.2%) had a history of medical abortions. The mean laboratory values obtained from our study were as follows: Vitamin A: 465±165 ng/mL, vitamin E: 12.5±3.6 ng/mL, cholesterol: 160±25.2 mg/dL, TG: 99.2±35.4 mg/dL.

In the ultrasound examination, patients without fetal heart activity (FHA) were classified as having missed abortion and were compared with the control group with FHA.

Between the groups with and without FHA, there were no significant differences in age, BMI, gravidity, parity number, parity rate, number of previous miscarriages, miscarriage rate, or mode of delivery in the previous pregnancy ($p>0.05$).

The gestational age determined by ultrasound was similar in both groups, with a mean of 8.1±1.3 weeks in the control group with FHA and 8.3±1.2 weeks in the group without FHA, and the difference was not statistically significant ($p>0.05$).

The levels of vitamin A were 445±210 ng/mL in the group without FHA and 485±102 ng/mL in the control group, and there was no statistically significant difference in vitamin A levels between the two groups ($p>0.05$).

Vitamin E levels were measured as 12.4±4.2 ng/mL in the group without FHA and 12.5±3.0 ng/mL in the control group, with no statistically significant difference in these values between the two groups (p>0.05).

The TC levels, the group with missed abortion had levels of 159±27.6 mg/dL, whereas the control group had levels of 160±23.1 mg/dL. The TG levels were 98.0±35.3 mg/dL in the group with missed abortion and 100±36.3 mg/dL in the control group. There were no significant differences in TC and TG levels between the two groups (p>0.05) (Table 1).

Discussion

This study, conducted with a total of 50 cases, examined the clinical and laboratory characteristics of missed abortions. The average age and BMI of the patients reflected the general characteristics of the pregnant women in the study. Our findings indicated that the influence of age and BMI on the incidence of missed abortions was not statistically significant. According to the results of the ultrasound examination, there was no significant difference in gestational weeks between the groups with and without FHA. The gestational age of pregnant women without FHA was similar to that of the control group. The study also investigated the impact of vitamin A and E levels on the incidence of missed abortions. Our findings showed no significant difference in these vitamin levels between the two groups, indicating that vitamin A and E levels may not be determinants of the risk of missed abortion.

We conducted a literature search but did not find sufficient studies that correlated vitamin A, E, TC, and TG levels with early pregnancy losses.

In a study by Chen et al. (18), in contrast to our study, the authors found that vitamin A levels were low and vitamin E levels were high in early pregnancy.

Vitamin A deficiency has been reported to lead to early pregnancy loss and weak births in cattle (19).

Meng et al. (20) reported normal levels of vitamin E in early pregnancy, similar to our study.

A study by Shamim et al. (21) conducted on pregnant women in rural Bangladesh reported that low plasma α-tocopherol levels and the mother's vitamin E status in the first trimester could affect the risk of early pregnancy loss.

In 2013, Sönmez (22) reported early pregnancy loss in rats with vitamin E deficiency.

Amundsen et al. (23) reported no difference in TC and TG values in early pregnancy in pregnant women with live fetuses, similar to our study in which both groups had normal TC and TG values.

Vrijkotte et al. (24) found no relationship between TC and TG levels and fetal loss in early pregnancies, consistent with our study.

Wang et al. (25) found higher TC and TG levels in early pregnancy among pregnant women with adverse pregnancy outcomes. In contrast, our study did not find statistically significant differences in TC and TG levels between the FHA and missed abortion groups (25).

Study Limitations

Due to the insufficient number of studies in the literature, further research with a larger sample size is needed. The number of patients and controls in this study is one of the limitations of this study. In addition, the fact that its difference from other results in the literature has not been clearly determined indicates that more work should be performed in this direction.

Table 1. Comparison of serum vitamin A, vitamin E, cholesterol, and triglyceride levels among pregnant women diagnosed with missed abortion

		FHA (-)		FHA (+)		p
		Mean ± SD, (n, %)	Median	Mean ± SD, (n, %)	Median	
Age		29.2±6.2	28.0	31.0±5.8	30.0	0.176[m]
BMI		23.8±1.5	22.1	24.1±2.1	23.5	0.006[m]
Gravity		2.2±1.2	2.0	2.6±1.5	2.0	0.488[m]
Parity		1.04±0.89	1.00	1.4±1.5	1.00	0.663[m]
Parity	(-)	7 (28.0%)		10 (40.0%)		0.370[x²]
	(+)	18 (72.0%)		15 (60.0%)		
Abortus		0.28±0.68	0.00	0.12±0.44	0.00	0.240[m]
Abortus	(-)	20 (80.0%)		23 (92.0%)		0.221[x²]
	(+)	5 (20.0%)		2 (8.0%)		
Delivery type	NSD	17 (68.0%)		18 (72.0%)		0.758[x²]
	CS	8 (32.0%)		7 (28.0%)		
USG week		8.3±1.2	10.1	8.1±1.3	8.0	0.116[m]
Vitamin A		445±210	400	485±102	484	0.118[m]
Vitamin E		12.4±4.2	11.2	12.5±3.0	12.0	0.322[m]
Cholesterol		159±27.6	155	160±23.1	154	1,000[m]
Triglyceride		98.0±35.3	92.0	100±36.3	90.0	0.854[m]

[m]Mann-Whitney U test, [x]Chi-square test, BMI: Body mass index, FHA: Fetal heart activity, NSD: Normal spontaneous delivery, CS: Cesarean section, USG: Ultrasonography, SD: Standard deviation

Conclusion

This study comprehensively analyzed the clinical and laboratory characteristics of missed abortions. The findings suggest that age, BMI, gestational age, and laboratory parameters, such as vitamin A and E levels, TC, and TG, may not have a statistically significant impact on the incidence of missed abortion. We found few studies related to our article topic in the literature; therefore, the discussion section is limited. These results could serve as an important reference for future research and clinical applications.

Ethics

Ethics Committee Approval: Our study was conducted using blood samples obtained from pregnant women who presented to University of Health Sciences Türkiye, İstanbul Training and Research Hospital and received approval from the Institutional Review Board (approval number: 54, date: 10.03.2023).

Informed Consent: An informed consent form was obtained from the patients.

Footnotes

Authorship Contributions: Surgical and Medical Practices - A.K.K., Concept - A.K.K., A.Ç., Design - A.K.K., C.T., Data Collection or Processing - A.K.K., C.T., Analysis or Interpretation - A.K.K., A.Ç., C.T., Literature Search - A.K.K., A.Ç., C.T., Writing - A.K.K., A.Ç.

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