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Original Article

Association between adverse perinatal outcomes and amino acid levels measured with nutrient questionnaire in adolescent pregnancies

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Abstract

Background: To evaluate the maternal serum amino acid levels in first trimester adolescent pregnancies by using a new developed dietary questionnaire.
Methods: A group of 169 pregnant women in the first trimester of their pregnancy were asked to complete the dietary questionnaire. Among all the women, 39 were adolescent pregnancies. The results of the questionnaire were evaluated by a nutrient database program (BeBiS software program) designed to evaluate Turkish traditional foods and commercial processed foods.
Results: There was no statistically significant difference between the groups in terms of body mass index and educational and socio-economic status. The mean age and gravidity was statistically significantly lower in adolescent pregnancies. The mean isoleucine, leucine, lysine, methionine, phenylalanine, tyrosine, threonine, valine, arginine, and proline levels were statistically significantly lower in adolescent pregnancies. Receiver operating characteristic (ROC) curve analysis showed the cut-off values of these amino acids. Of these amino acids; lower values of histidine, serine, and alanine were associated with lower birth weight, and lower values of histidine and alanine were associated with preterm delivery.
Conclusion: To the best of our knowledge, this is the first study evaluating the amino acid levels in adolescent pregnancies. According to this study, some amino acid levels were lower in adolescent pregnancies and associated with adverse perinatal outcomes. Further studies with maternal and perinatal outcomes are needed to demonstrate the effects of these amino acids in such pregnancies.

Keywords: adolescent; amino acid; dietary questionnaire; pregnancy

1. Introduction

Adolescent pregnancies are pregnancies that occur in women aged between 10 years and 19 year.[1] In 2011, a total of 333,771 live births were reported in the US.[2] In Turkey, the incidence of adolescent pregnancies was reported to be 4−7%, with such pregnancies generally in socioeconomically disadvantaged mothers with impaired iron−mineral metabolism related to nutritional deficiencies.[3−5] These pregnancies are under risk of adverse maternal and perinatal outcomes when compared with reproductive-age pregnancies. Leppälahti et al[6] reported that adolescent pregnancies were more socioeconomically disadvantaged versus reproductive-age pregnancies. In a previous study, adolescent pregnancies were reported to have lower gestational weeks at delivery, lower birth weights, and lower APGAR scores when compared with reproductive-age pregnancies.[7] Eclampsia, proteinuria, urinary tract infections, pyelonephritis, and anemia were also higher in adolescent

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pregnancies.[6] Baker et al[8] designed a study to evaluate the micronutrient status in adolescent pregnancies and found an association between impaired maternal micronutrient status and adverse perinatal outcomes in adolescent pregnancies.

In this report, we designed a prospective dietary questionnaire study in adolescent pregnancies to evaluate the maternal amino acid levels.

2. Methods

We designed this prospective study in Ergani State Hospital, between January 2010 and August 2010. This is a hospital in rural Turkey. Most of the patients have a lower socioeconomical and educational status. Health services are provided free of charge by the government. The study was performed according to the standards of the Helsinki Declaration. Informed consent was obtained from all participants.

Adolescent age was defined as age between 10 years and 19 years, according to the World Health Organization criteria.[1] A total of 160 pregnant women were included in the study; of these women, 121 were normal-age pregnancies (Group 1: age range, 20−37 years) and 39 were adolescent pregnancies (Group 2: age range, 16−19 years).

On the routine antenatal follow up, in the first trimester, the patients were asked to complete the new 92-item nutrient questionnaire developed by Satia et al[9] An appointed nurse, the same person in each case, helped the participants to complete the questionnaire. The results obtained from the questionnaire were uploaded to the nutrient database program (BeBiS software program; Bebispro for Windows, Stuttgart, Germany; Turkish Version (Bebis 4), Istanbul Program uses data from Bundeslebensmittelschlüssel (BLS) 11.3 and USDA 15, 2004) designed to evaluate the Turkish traditional foods and commercial processed foods and the validated mean amino acid levels were measured. Gestational age of the pregnant women was assessed according to the last menstrual period or ultrasonographic measurement (SDU-2200 Pro; Shimadzu, Kyoto, Japan), or both.

Data recorded were: age of the patients, gravidity, body mass index (BMI; calculated as kg/m^2), gestational weeks, socioeconomic and educational status, maternal amino acid levels and gestational week at birth, and birth weight of the new born.

2.1. Statistical analysis

Means and standard deviations (SD) were calculated for continuous variables. Participant characteristics and demographics were analyzed descriptively. The normal distribution of the variables was analyzed by the Kolmogorov−Smirnov test. Student *t* test and Chi-square (χ^2) test were used to evaluate associations between the categorical and continuous variables respectively. The binary logistic regression method was used to find the risk variables for adolescent pregnancies by including all variables in the model and calculating the odds ratios. Receiver operating characteristic (ROC) curve analysis was used to assess the discriminative role of amino acids. All variables were included in the backward stepwise procedure. Two-sided *p*-values were considered statistically significant at $p < 0.05$. Statistical analyses were carried out using the statistical package SPSS version 15.0 for Windows (SPSS Inc., Chicago, IL, USA).

3. Results

Table 1 presents the clinical characteristics of the groups. The mean ages of the patients in Groups 1 and 2 were 26.01 ± 4.90 years and 19.61 ± 4.25 years, respectively ($p < 0.05$). The mean gravidity (min−max) was 3.16 (2−6) in Group 1 and 1.02 (0−1) in Group 2 ($p = 0.007$). There was no statistically significant difference between groups in terms of BMI and gestational weeks.

Table 2 shows the mean amino acid levels between the groups. There was a statistically significant difference between the groups in terms of isoleucine, leucine, lysine, methionine, phenylalanine, tyrosine, threonine, valine, arginine, and proline levels ($p < 0.05$). The mean cysteine, tryptophan, histidine, aspartate, glutamate, glycine, and serine levels were similar between the groups ($p > 0.05$).

Receiver operating curve (ROC) curve analysis (Fig. 1) demonstrated the area under curve (AUC) for isoleucine, leucine, lysine, methionine, phenylalanine, tyrosine, threonine, valine, arginine, and proline levels, and Table 3 depicts the AUC, cut-off value and sensitivity and specificity of these variables.

Table 4 demonstrates the levels of lower amino acid levels that were established according to the reference values of a previous study,[10] and the association of these amino acids with adverse perinatal outcomes including preterm delivery and lower fetal birth weight levels. In adolescent pregnancies, lower tryptophan, histidine, serine, and alanine levels were associated with adverse perinatal outcomes.

4. Discussion

In this prospective study, we asked 169 pregnant women to complete a newly developed antioxidant dietary questionnaire

Table 1
The comparison of the clinical characteristics of the groups.

	Normal-age pregnancies ($n = 121$)	Adolescent-age pregnancies ($n = 39$)	p
Age (years)	26.01 ± 4.90	19.61 ± 4.25	< 0.001
BMI (kg/m^2)	24.28 ± 2.94	24.52 ± 2.28	0.144
Gravidity	3.16 (2−6)	1.02 (0−1)	0.007
Gestational wks	7.50 ± 1.10	7.76 ± 0.74	0.166
Birth weight (g)	3464.23 ± 555.12	2985.42 ± 551.12	< 0.001
Birth wk	38.40 ± 2.42	36.87 ± 1.82	< 0.001

BMI = body mass index.

Table 2
Comparison of amino acid levels between the groups.[a]

	Normal-age pregnancies ($n = 121$)	Adolescent pregnancies ($n = 39$)	p
Isoleucine	1250.44 ± 597.05	926.14 ± 766.01	**0.003**
Leucine	1404.71 ± 691.45	1022.90 ± 726.51	**0.001**
Lysine	816.30 ± 598.38	577.42 ± 387.80	**0.016**
Methionine	3859 ± 190.11	2910.12 ± 197.65	**0.004**
Phenylalanine	9070.95 ± 420.86	6618.42 ± 479.22	**0.001**
Tyrosine	7395.67 ± 295.92	5968.02 ± 417.43	**0.001**
Theronine	5749.52 ± 402.86	4265.90 ± 326.40	**0.030**
Valine	1126.93 ± 496.62	913.67 ± 672.41	**0.001**
Arginine	8188.62 ± 501.80	6023.02 ± 422.20	**0.003**
Proline	1526.73 ± 770.99	1166.48 ± 900.15	**0.002**
Cysteine	6117.51 ± 441.75	4509.54 ± 517.21	0.066
Tryptophan	6205.02 ± 527.02	5365.02 ± 690.25	0.419
Histidine	2867.22 ± 299.84	1943.76 ± 216.71	0.076
Aspartate	31618.32 ± 2308.71	26255.43 ± 2722.02	0.224
Glutamate	34269.31 ± 2879.18	24165.66 ± 2596.41	0.051
Serine	6745.02 ± 674.84	4872.06 ± 564.74	0.117
Glycine	12179.31 ± 724.21	9870.62 ± 896.05	0.101

Bold values indicate statistically significant difference ($p < 0.05$).
[a] The levels of amino acids were defined as mg/dL.

by Satia et al.[9] This is a 92-item self-administered questionnaire modeled after a semiquantitative food frequency questionnaire. The results of the questionnaire were uploaded to the nutrient database program (BeBiS software program, Bebispro for Windows, Bundeslebensmittelschlüssel (BLS) 11.3 and USDA 15, 2004. Stuttgart, Germany) designed to

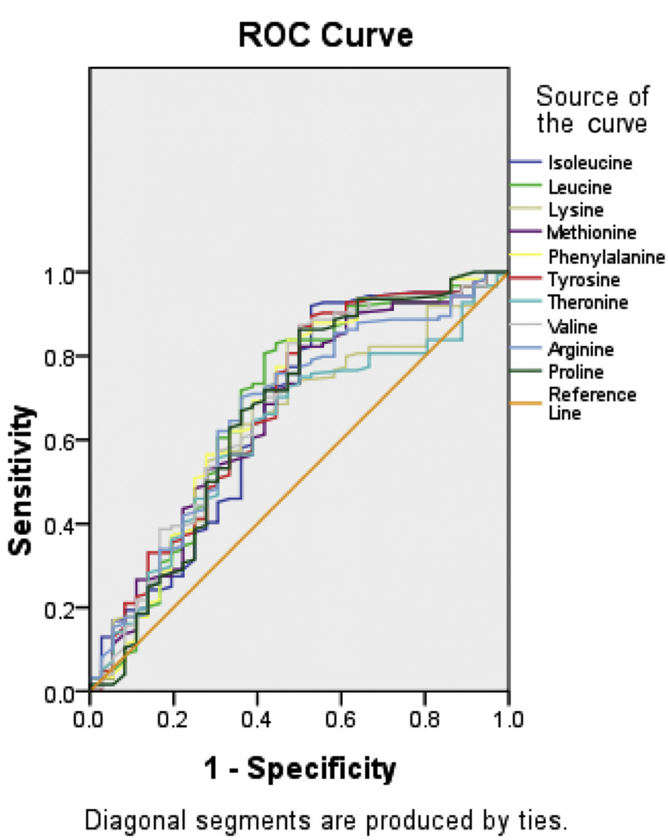

Fig. 1. ROC analyses of amino acids. ROC = receiver operating characteristic.

Table 3
The results of AUC, with cut off values of the lower amino acids in adolescent pregnancies.

	AUC	p	95% CI	Cut off value	Sensitivity (%)−specificity (%)
Isoleucine	0.664	0.003	0.552−0.776	573.20	91.9−52.8
Leucine	0.677	0.001	0.565−0.788	543.90	91.1−61.1
Lysine	0.631	0.016	0.528−0.735	335.75	82.3−66.7
Methionine	0.660	0.004	0.552−0.767	140.20	89.5−63.9
Phenylalanine	0.679	0.001	0.568−0.791	296.10	93.5−63.9
Tyrosine	0.677	0.001	0.569−0.786	253.90	94.4−69.4
Theronine	0.619	0.030	0.516−0.721	235.55	79.8−66.7
Valine	0.680	0.001	0.572−0.789	476.45	90.3−61.1
Arginine	0.664	0.003	0.559−0.768	284.70	87.9−63.9
Proline	0.666	0.002	0.552−0.779	412.75	93.5−63.9

AUC = area under curve; CI = confidence interval.

evaluate the Turkish foods and commercial foods and the validated mean amino acid levels were measured. The mean amino acid levels (isoleucine, leucine, lysine, methionine, phenylalanine, tyrosine, threonine, valine, arginine, and proline) were lower in adolescent pregnancies.

Adolescent pregnancies are risky pregnancies for both mother and newborn. A large percentage of these pregnancies occur in low- and middle-income countries. In these countries, 14% of all unsafe abortions occur in adolescent age women. In Latin America, the risk of maternal death is four times higher in adolescent mothers than mothers in reproductive-age pregnancies. In such young mothers, many medical complications can arise such as anemia, sexually transmitted diseases, postpartum hemorrhage, depression, and can also cause the mothers to leave school. In newborns from adolescent pregnancies, the rates of stillbirth, preterm birth, low birth weight, asphyxia, and future health problems are higher than in reproductive-age pregnancies.[11]

The etiology of adverse outcomes in adolescent pregnancies has been debated. Adolescent mothers are a disadvantaged risk group due to their lower socioeconomic status, lower educational status, malnutrition, and micronutrient deficiencies.[8,12] American College of Obstetrics and Gynecology (ACOG; Washington, DC, USA) also indicated that family income is related with earlier sexual activity and that in higher-income adolescents, condom use was more common and resulted in lower pregnancy rates.[13] In Turkey, adolescents are also under risk of impaired nutritional status and related symptoms.[14] This study was performed in rural Turkey, an area in which the nutritional status of adolescents was found to be worse when compared with other regions of the country.[15]

Association between maternal nutritional status and fetal growth has been well established in reproductive-age pregnancies.[16] Maternal malnutrition adversely affects the perinatal outcomes and leads to intrauterine growth restriction, low birth weight and infant morbidity and mortality.[17,18]

Adolescents tend to consume micronutrient-poor, energy-dense diets due to lower socio-economic status.[19] Baker et al[8] found that serum folate, vitamin B12, total homocysteine, and serum 25-hydroxyvitamin D concentrations were lower in

Table 4
The levels of lower amino acids and their association between adverse perinatal outcomes.

	Birth weight < 2500g (*n* = 14)	Birth weight ≥ 2500g (*n* = 25)	*p*	Preterm delivery (< 37 wks) (*n* = 15)	Preterm delivery (≥ 37 wks) (*n* = 24)	*p*
Isoleucine	3 (21.4)	12 (48)	0.097	3 (20)	12 (50)	0.061
Leucine	8 (57.1)	14 (56)	0.607	8 (53.3)	14 (58.3)	0.509
Lysine	9 (64.3)	19 (76)	0.405	10 (66.7)	18 (75)	0.418
Methionine	4 (28.6)	11 (44)	0.274	4 (26.7)	11 (45.8)	0.196
Phenylalanine	7 (50.0)	13 (53)	0.584	7 (46.7)	13 (54.2)	0.450
Tyrosine	8 (57.1)	13 (52)	0.511	8 (53.3)	13 (54.2)	0.679
Theronine	13 (92.9)	23 (96)	0.595	14 (93.3)	22 (95.8)	0.208
Valine	11 (78.6)	21 (84)	0.545	14 (93.3)	21 (87.5)	0.498
Arginine	8 (57.1)	16 (64)	0.466	9 (60)	15 (62.5)	0.570
Proline	8 (57.1)	14 (56)	0.607	8 (53.3)	14 (58.3)	0.509
Cysteine	1(7.1)	2 (8.0)	0.711	1 (6.7)	2 (8.3)	0.674
Tryptophan	12 (85.7)	15 (60.0)	**0.043**	12 (80)	15 (62.5)	0.215
Histidine	11 (78.5)	11 (44.0)	**0.023**	7 (46.7)	19 (79.2)	**0.041**
Glutamate	1(7.1)	0	0.359	1 (6.7)	0	0.385
Serine	12 (85.7)	14 (56)	**0.034**	9 (60)	20 (83.3)	0.107
Glycine	10 (71.4)	14 (56)	0.274	10 (66.7)	14 (58.3)	0.430
Alanine	14 (100)	18 (72)	**0.031**	15 (100)	17 (70.8)	**0.023**

Data is presented as *n* (%), *n* showing the lower levels of aminocides calculated according to Ref 11.
Bold values indicate statistically significant difference ($p < 0.05$).

adolescent pregnancies, and that this poor micronutrient intake and status caused adverse perinatal outcomes in such pregnancies. Frisancho et al[20] reported that even if adolescent pregnancies consumed nutrition similar with that of reproductive-age women, the adverse outcomes of pregnancies were higher in adolescent pregnancies. They concluded that this could be because in rapidly growing teenagers, the nutritional requirements of pregnancy may be greater than those in reproductive-age pregnancies.

Amino acids are one of the main nutrient sources for fetal growth, meeting 20−40% of fetal energy requirements.[21] Previous reports clarified the association between amino acid levels and perinatal outcomes. Evans et al[22] studied maternal fetal amino acid concentrations and fetal outcomes during preeclampsia and observed significantly higher maternal and cord-blood amino acid concentrations in preeclampsia. Cetin et al[23] also reported lower amino acid concentrations in fetuses with intrauterine growth restriction. In a previous study evaluating amniotic fluid amino acid levels in nonimmune hydrops fetalis, the authors reported lower mean phosphoserine and serine levels and higher taurine, α-aminoadipic acid, glycine, cysteine, NH(4), and arginine levels.[24] We also found significantly lower levels of isoleucine, leucine, lysine, methionine, phenylalanine, tyrosine, threonine, valine, arginine, and proline in adolescent pregnancies. Among these amino acids, tryptophan, histidine, serine, and alanine levels were associated with adverse perinatal outcomes, which is an interesting result of this study.

To the best of our knowledge, this is the first study evaluating maternal amino acid levels in adolescent pregnancies by using a dietary antioxidant questionnaire. In conclusion, we think that lower maternal amino acid levels may be the cause of adverse perinatal outcomes in adolescent pregnancies. Further studies with greater numbers of participants may give more accurate results on this topic.

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