Plasma total antioxidant capacity and its related factors in Iranian pregnant women

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ABSTRACT

الأهداف: اختبار سعة مجموع مضادات الأكسدة في البلازما، والعوامل المؤثرة عليه لدى الحوامل الإيرانيات الوافدات على عيادات الحمل والولادة.

الطريقة: أُجريت هذه الدراسة المقطعية في عيادة ناغافي للحمل والولادة، مجمع عيادات مستشفى شهيد بيهشاتي للعيادات المتخصصة، و10 مراكز للحمل والولادة تابعة لجامعة كاشان للعلوم الصحية، كاشان، إيران. شملت الدراسة 137 مشاركة حامل تتراوح أعمارهن ما بين 18-30 عاماً. لقد قمنا بمعاينة سعة مجموع مضادات الأكسدة في البلازما للحوامل البكور المشاركات في الدراسة خلال الفترة من أكتوبر 2010م إلى مارس 2011م، بالإضافة إلى تحديد العوامل المؤثرة عليه وهي: عمر الأم، والوزن، ومؤشر كتلة الجسم في الأسبوع 13 و21 و24 من الحمل، وعمر الحمل في الأسبوع 21 إلى 24 من الحمل. ولقد قمنا باستخدام الانحدار الخطي المتعدد من أجل تقييم العلاقة بين سعة مجموع مضادات الأكسدة في البلازما والعوامل المؤثرة عليه.

النتائج: لقد بلغ متوسط سعة مجموع مضادات الأكسدة في البلازما لدى الحوامل في الأسبوع 21 إلى 24 من الحمل 0.11±0.75 مليمول/لتر، وبلغ متوسط كتلة الجسم في البداية 4±25.06، و4.13±25.72 في الأسبوع 13، و4.19±26.95 كلغ/م^2 في الأسبوع 21 إلى 24 من الحمل. وأشار الانحدار الخطي المتعدد إلى وجود علاقة عكسية بين عمر الحمل وسعة مجموع مضادات الأكسدة (ß: -0.234, p=0.007) كما أظهر وجود علاقة واضحة من الناحية الإحصائية بين عمر الأم وسعة مجموع مضادات الأكسدة (ß: 0.150, p=0.080)، غير أنه لم يكن هناك أي علاقة بين العوامل المتغيرة الأخرى وسعة مجموع مضادات الأكسدة.

خاتمة: أظهرت الدراسة وجود علاقة عكسية بين عمر الحمل وسعة مجموع مضادات الأكسدة، كما كان هناك علاقة واضحة من الناحية الإحصائية بين عمر الأم وسعة مجموع مضادات الأكسدة وذلك في الفئة العمرية 18-30 عاماً بين الإيرانيات الحوامل في الشهر السادس من الحمل.

Objectives: To determine the plasma total antioxidant capacity (TAC) and its related factors in pregnant Iranian women attending maternity clinics.

Methods: In a cross-sectional study carried out in Naghavi Maternity Clinic, Shaheed Beheshti Specialty and Subspecialty Polyclinic and 10 antenatal centers, affiliated to Kashan University of Medical Sciences, Kashan, Iran, we determined the plasma TAC and its related factors including maternal age, weight, and body mass index (BMI) at the beginning, thirteenth, and twenty-first to twenty-fourth weeks of pregnancy, and gestational age at the twenty-first to twenty-fourth weeks of pregnancy in 137 primigravid pregnant women, 18-30 years old from October 2010 to March 2011. We used multiple linear regression to assess the relationship between TAC and its related factors.

Results: Plasma TAC in the twenty-first to twenty-fourth weeks of pregnancy was 0.75±0.11 mmol/l. The BMI at the beginning was 25.06±4, 25.72±4.13 at the thirteenth, and 26.95±4.19 kg/m^2 at the twenty-first to twenty-fourth weeks of pregnancy. Multiple regression analysis showed that gestational age was inversely associated with the plasma TAC (ß: -0.234, p=0.007). Regression analysis also suggested a trend toward significant association between maternal age and plasma TAC (ß: 0.150, p=0.080), but there was no association between other variables and plasma TAC.

Conclusion: Gestational age was inversely correlated with plasma TAC and maternal age had a trend toward significant association with TAC in 18-30 year-old Iranian pregnant women in their sixth month of pregnancy.

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Risk of occurrence of preterm labor and low birth weight neonates,[1-4] postnatal growth,[5] and maternal and infant morbidity and mortality,[6-8] can be affected by maternal nutritional status. Many observational studies, as well as clinical trials, show that antioxidants are important in a wide range of physiological processes, such as pregnancy and fetal growth.[2,9-12] Pregnancy is a condition associated with increased susceptibility to oxidative stress, mostly because of increased oxygen requirement and mitochondria-rich placenta.[13] Oxidative stress and generalized endothelial dysfunction appear to increase the risk of preeclampsia,[14] low birth weight infants,[15] and many diseases, such as diabetes mellitus, cancer, and renal failure.[16] Pre-eclampsia is estimated to occur in 2-7% of all pregnancies, is a leading cause of maternal and perinatal mortality and morbidity throughout the world,[17-22] and is responsible for approximately 60000 deaths worldwide annually.[23] It has been suggested that several maternal and familial factors such as maternal age and body mass index (BMI),[24] chronic hypertension or renal diseases,[25] decreased serum levels of antioxidants and/or impaired regeneration of reduced forms of antioxidants[13] may be related to pre-eclampsia and increased oxidative stress. Yet, there are limited studies on plasma total antioxidant capacity (TAC) and its related factors in pregnant women. Therefore, we aimed to determine plasma TAC and its related factors including maternal age, weight, BMI, and gestational age in Iranian pregnant women in their sixth month of pregnancy.

Methods. We carried out the present study in Naghavi Maternity Clinic, Shaheed Beheshti Specialty and Subspecialty Polyclinic and 10 antenatal centers, affiliated to Kashan University of Medical Sciences, Kashan, Iran between October 2010 to March 2011. We interviewed 137 pregnant women and collected fasting blood samples. Inclusion criteria were primi gravidity, singleton pregnancy, and age between 18-30 years. Exclusion criteria were multiparity, hypertension, liver or renal disease, gestational diabetes mellitus (GDM), complete bed rest (CBR), and genitalia or systemic infection. All pregnant women were taking 400 µg folic acid daily from the beginning of pregnancy, and 50 mg ferrous sulfate from the second trimester. We designed the study according to the guidelines of the Declaration of Helsinki and received approval from the Ethics Committee of Tehran University of Medical Sciences. We also obtained written informed consent from all subjects. The women provided detailed health, reproductive, supplement usage, and lifestyle information through standardized face-to-face interviews. Trained interviewers administered the questionnaires at enrollment. We obtained maternal anthropometric measurements including weight at the beginning, thirteenth, and twenty-first to twenty-fourth weeks of pregnancy from the maternal clinics and antenatal centers. We measured the gestational age from the first day of the last menstrual period to the concurrent clinical assessment.[26] We collected 5 ml of early morning fasting blood samples at the twenty-first to twenty-fourth weeks of pregnancy. We separated and stored the plasma at -80°C until analysis at the reference laboratory in Kashan, Iran. We determined the plasma TAC using the ferric reducing antioxidant power (FRAP) assay developed by Benzie and Strain[27] using a Cecil 2021 spectrophotometer (Cecil, Cambridge, England) with a temperature controlled cuvette holder (Cecil, Cambridge, England). We performed the test at 37°C and used the 0-4 minute reaction time window. The final results are expressed as mmol Trolox equivalent/l.[27]

Statistical analysis. We used Pearson and multiple linear regression analysis to assess relationships between TAC and its related factors. We used the Statistical Package for Social Sciences (SPSS Inc., Chicago, Illinois, USA) version 17 for data analysis, and considered a *p*-value <0.05 as significant.

Results. One hundred and thirty-seven pregnant women who were primigravid and 18-30 years old participated in the study. Mean maternal age and weight at the beginning, thirteenth, and twenty-first to twenty-fourth weeks of pregnancy, gestational age at the twenty-first to twenty-fourth weeks of pregnancy and plasma TAC are shown in **Table 1**. The Kolmogorov-Smirnov test showed that all variables had a normal distribution except maternal age and gestational age. Spearman correlation analysis showed that maternal age and gestational age were correlated with the plasma TAC (**Table 2**). There was no association between other variables and plasma TAC according to Pearson correlation analysis. For regression analysis, maternal age, weight gain in the first and second trimester, weight (weight was used in regression model compared to BMI and weight at the beginning, thirteenth week of pregnancy due to stronger correlation) and gestational age at the twenty-first to twenty-fourth weeks of pregnancy were entered into the model as independent variables. As **Table 3** shows, gestational age was identified as a significant variable affecting the plasma TAC. Furthermore, multiple regression analysis suggested a

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Table 1 - General and clinical characteristics of 137 mothers in Kashan, Iran.

Variable	Mean ± SD	Range
Maternal age (years)	25.3 ± 3.65	18-30
Weight at the beginning of pregnancy (kg)	63.18 ± 10.68	43-96
Weight at the 13th weeks of pregnancy (kg)	65.48 ± 10.88	43-105
Weight at the 21-24th weeks of pregnancy (kg)	68.6 ± 11.08	45-106
Weight gain in the first trimester (kg)*	2.51 ± 1.95	0-9
Weight gain in the second trimester (kg)†	3.25 ± 2.5	0-20
Weight gain in the first and second trimester (kg)‡	5.44 ± 3.09	0-17
BMI at the beginning of pregnancy (kg)	25.06 ± 4.0	17.01-36.58
BMI at the 13th weeks of pregnancy (kg)	25.72 ± 4.13	17.5-40.01
BMI at the 21-24th weeks of pregnancy (kg)	26.95 ± 4.19	18.42-40.39
Gestational age at the 21-24th weeks of pregnancy (weeks)	22.97 ± 1.11	21-24
Plasma total antioxidant capacity (mmol/l)	0.75 ± 0.11	0.43-1.3

*weight gain (n=115),†weight gain (n=123), ‡weight gain (n=125)

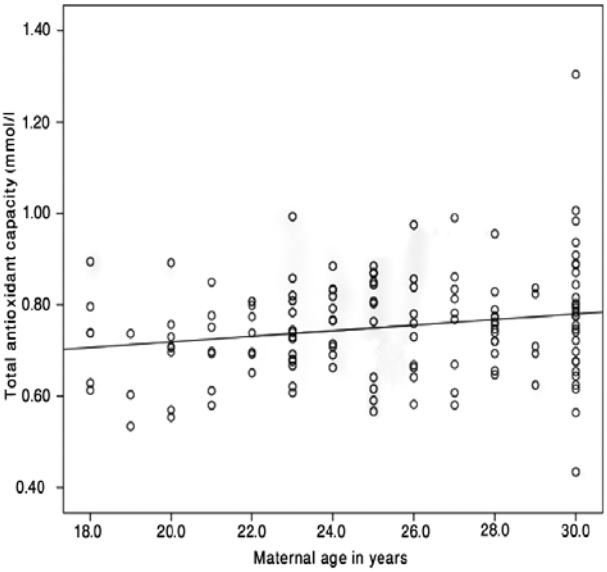

Figure 1 - Relationship of the plasma total antioxidant capacity to maternal age from 18 to 30 years in pregnant women (r=0.178, *p*=0.037)

Table 2 - Results of Pearson's correlation coefficient (r) between independent variables and plasma total antioxidant capacity (TAC) at the 21-24th weeks of pregnancy of the subjects from Kashan, Iran.

Variables	Plasma TAC (r)	*P*-value
Maternal age (years)	0.178	0.037*
Weight at the beginning of pregnancy (kg)	-0.041	0.63
Weight at the 13th weeks of pregnancy (kg)	-0.023	0.79
Weight at the 21-24th weeks of pregnancy (kg)	-0.044	0.6
Weight gain in the first trimester (kg)	0.05	0.56
Weight gain in the second trimester (kg)	-0.119	0.174
Weight gain in the first and second trimester (kg)	-0.016	0.86
BMI at the beginning of pregnancy (kg)	0.011	0.89
BMI at the 13th week of pregnancy (kg)	0.027	0.75
BMI at the 21-24th week of pregnancy (kg)	0.006	0.94
Gestational age at the 21-24th week of pregnancy (weeks)	-0.241	0.005*

*p<0.05 Spearman correlation analysis significant, BMI - body mass index

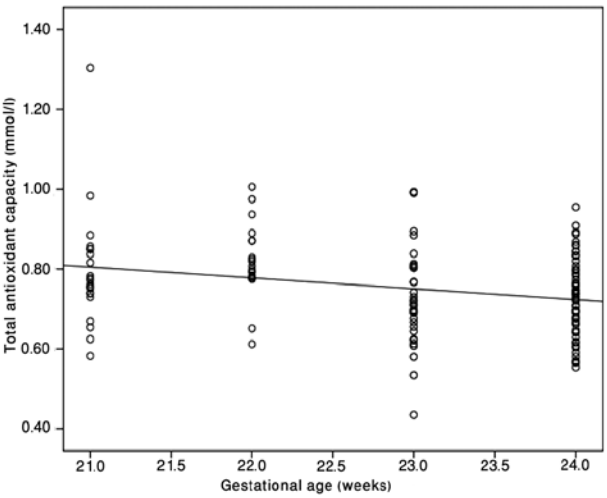

Figure 2 - Relationship of the plasma total antioxidant capacity to gestational age at the 21-24th weeks of pregnancy (r=-0.241, *p*=0.005).

Table 3 - Results of multiple regression analysis between independent variables with the plasma TAC at the 21-24th weeks of pregnancy.

Variable	Unstandardized coefficients		Standardized coefficients	*P*-value
	β	Standard error	β	
Maternal age (years)	0.005	0.003	0.150	0.080
Weight at the 21-24th weeks of pregnancy (kg)	0.000	0.001	-0.072	0.411
Weight gain at the first and second trimester (kg)	0.001	0.003	0.029	0.735
Gestational age at the 21-24th weeks of pregnancy	-0.024	0.009	-0.234	0.007*

*p<0.05 multiple regression analysis significant, ß - regression coefficient

trend toward significant association between maternal age and plasma TAC (**Table 3**). **Figure 1** illustrates the correlation between plasma TAC and maternal age, and shows a positive relationship between the plasma TAC and maternal age in 18-30 year-old pregnant women. **Figure 2** illustrates the correlation between plasma TAC and gestational age at the twenty-first to twenty-fourth weeks of pregnancy, and shows a reverse relationship between the plasma TAC and gestational age in pregnant women who were at the twenty-first to twenty-fourth weeks of pregnancy.

Discussion. The current study shows that while older gestation age was associated with lower plasma TAC, maternal age had a trend toward positive association with plasma TAC levels in 18-30 year-old pregnant women who were in their sixth month of pregnancy. In our study, TAC was 0.75 mmol/L. Genc et al[28] reported that TAC was 0.98 at the tenth to fourteenth weeks, and 0.87 at the twentieth to twenty-fourth weeks of gestation in healthy pregnant women, and 0.84 at the tenth to fourteenth weeks, and 0.62 at the twentieth to twenty-fourth weeks of gestation, in pre-eclamptic women. In another study performed in the third trimester TAC, was 1.53 in normal pregnant women, and 1.39 in pregnant women with intrauterine fetal growth restriction.[29] Overall, during pregnancy, mostly because of increased oxygen requirement and mitochondria-rich placenta, there is an increased susceptibility to oxidative stress and reduction of TAC.[30,31] The low plasma TAC level in our study compared with other studies is probably due to the pregnant women's nutritional state,[30] and inadequate consumption of antioxidants.[28]

Our results revealed that plasma TAC was not related to weight or BMI at the beginning, thirteenth week, and twenty-first to twenty-fourth weeks of pregnancy. A study by Saker et al[30] reported reduced TAC in large for gestational age (LGA) newborns compared with controls. Increased SOD activity may be a compensatory mechanism responding to increased peroxide levels in obesity.[32] Furthermore, increased expenditure of vitamins A and E and/or enhanced entrapment of these vitamins in the adipose tissue have been reported in obesity,[33] thus, supplementation with antioxidants including vitamins and trace elements might help to shift this oxidant-antioxidant balance.[34] Unlike other similar studies, weight gain was not high in our pregnant women; therefore, plasma TAC was not associated with weight or BMI.

The present study showed that pregnancy at a younger age is associated with lower plasma TAC. This finding is likely due to poor nutritional status of younger pregnant women. Inadequate consumption of antioxidants and micronutrients can affect TAC. Also, micronutrients malnutrition in pregnant women can cause intrauterine growth restriction, which is associated with increased susceptibility of lipids to oxidation and production of free radicals during pregnancy,[35,36] indirectly decrease levels of antioxidants.[37,38] Oxidized lipids can activate neutrophils.[39,40] The activated neutrophils can reenter the maternal systemic circulation and cause vascular dysfunction associated with pre-eclampsia.[14,41] On the other hand, the increasing size of the placenta at the end of the sixth month of pregnancy and elevated production of oxidized lipids,[14] can result in a decrease in the plasma TAC value and an increase in stress oxidative. Therefore, the plasma TAC status during pregnancy, especially in the sixth month of pregnancy, may be a marker of oxidative stress and the prediction of the development of pre-eclampsia. One of the limitations of this study was that blood analysis was obtained only once.

In conclusion, our study showed that older gestation age was inversely associated with plasma TAC, but maternal age had a trend toward positive association with plasma TAC levels in 18-30 year-old pregnant women who were in their sixth month of pregnancy.

Further studies are recommended to assess the effects of supplementation with antioxidants on TAC in pregnant women.

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