

Maternal Serum Nitric Oxide Levels in Adolescent Pregnancies

Hasan Onur TOPÇU¹, Ali İrfan GÜZEL¹, Kuntay KOKANALI¹, Sabri CAVKAYTAR¹, Dilek UYGUR¹,
Salim ERKAYA¹

Ankara, Turkey

OBJECTIVE: We aimed to evaluate maternal serum nitric oxide (MSNO) levels in adolescent pregnancies.

STUDY DESIGN: A total of forty five pregnancies were included to the study, of these eight were adolescent pregnancies (age range, 18-19 years old). Factors analyzed between adolescent pregnancies and reproductive age pregnancies (age range 20-35 years old) were; age, gravidity, parity, gestational weeks, umbilical and middle cerebral artery Doppler velocimetry values, birth weights, APGAR 5. minute scores and MSNO levels. Statistical analyses were carried out by using the statistical packages for SPSS 15.0 for Windows (SPSS Inc., Chicago, IL, USA) with Chi-square (χ^2) test and Student's t test. The receiver operator characteristic (ROC) curve analysis was used to establish the cutoff values for MSNO levels.

RESULTS: Demographic and clinical characteristics showed no statistically significant difference among the groups ($p>0.05$). MSNO levels were statistically significantly lower in adolescent age pregnancies.

CONCLUSION: According to current study, MSNO levels were statistically significantly different from reproductive age pregnancies. MSNO levels may be a discriminative marker in adolescent age pregnancies but further studies with larger participants are needed to get more definite results.

Keywords: Adolescent, Pregnancy, Maternal serum nitric oxide

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Introduction

Adolescent pregnancy and childbearing have become a social problem all over the world. In Turkey, approximately 6% of all newborns are delivered by adolescents.¹ Co-existing maternal and perinatal problems such as preterm birth, low birth weight, fetal growth restriction, stillbirth and newborn mortality are quite common during the adolescent pregnancies.^{2,3}

Nitric oxide (NO) is described as an endothelium-derived relaxant factor. It is an important transmitter for endothelium depended regulation of vascular tone and produced by endothelial cells.⁴ It regulates the blood pressure and inhibits the platelet aggregation and acts as an anticoagulant and anti atherogenic agent.⁵ During the pregnancy, NO regulates the placental blood flow.⁶

The differences of the serum NO levels between adolescent and reproductive age pregnancies may be the one of the reasons of poor perinatal outcomes of adolescent pregnancies. Therefore, we aimed to compare the NO levels in adolescent pregnancies with reproductive age pregnancies.

Material and Method

The present study was designed at Dr. Zekai Tahir Burak Women's Health Care Education and Research Hospital, Ankara, Turkey. A total of forty-five pregnancies were involved to the study. 8 out of forty-five pregnancies were adolescent pregnancies (age range; 18-19 years old) and 37 out of forty-five pregnancies were reproductive age pregnancies (age range; 20-35 years old). The exclusion criteria were: maternal smoking during pregnancy, multi-fetus pregnancies, and structural or chromosomal anomalies. The study was approved by the Ethical Committee and Institutional Review Board of Dr. Zekai Tahir Burak Women's Health Care Education and Research Hospital, and written informed consent was obtained from each participant.

Data analyzed between adolescent and reproductive age pregnancies were MSNO levels, age, gravidity, parity, gestational weeks, umbilical and middle cerebral artery Doppler velocimetry values, birth weights, APGAR 5. minute scores.

¹ Dr. Zekai Tahir Burak Women Health Educational and Research Hospital, Ankara

Address of Correspondence: Hasan Onur Topçu
Dr. Zekai Tahir Burak Women Health
Educational and Research Hospital
Ankara Turkey
dronurtopcu@gmail.com

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Gestational ages (weeks) were assessed by ultrasound examination (GE Logiq 200 PRO Ultrasound Device, USA) or according to last menstrual period, or both.

The blood samples were obtained from the antecubital vein. The samples were centrifuged for 10 minutes at 3,000 revolutions per minute, and then were stored at -70 °C. Plasma MSNO levels were measured by using Griess reaction.⁷

Statistics

Data are presented as mean \pm SD or incidence as appropriate. Categorical data were compared with the χ^2 test. Continuous variables were analyzed with the Student t test. The receiver operator characteristic (ROC) curve analysis was used to establish the cutoff values for NO levels. All variables were included in the backward stepwise procedure. Two-sided p values were considered statistically significant at $p < .05$. Statistical analyses were carried out by using the statistical packages for SPSS 17.0 for Windows (SPSS Inc., Chicago, IL, USA).

Results

A total of 45 cases were included to the current study, 8 (17.7 %) of these were in adolescent age period (age range; 15-19 years old). The mean age of the cases was 17.75 ± 0.70 years old in adolescent group and 24.86 ± 4.70 years old in control group. There was a statistically significant difference between the groups among age ($p < 0.05$). The mean gravidity of the cases was 1.95 (min-max: 1-5) and the mean parity of the cases was 0.91 (min-max: 0-3) in control group and those were 1.00 (min-max: 0-1) and 0.00 (range 0-0) in adolescent group, respectively. There was no statistically significant difference between the groups in terms of; gestational weeks, birth weights, APGAR scores, maternal umbilical artery pulsatility index, resistance index and middle cerebral artery Doppler velocimetry values (Table 1).

Figure 1 depicted the MSNO levels was 8.80 ± 4.06 $\mu\text{mol/L}$ in control group and 5.07 ± 3.13 $\mu\text{mol/L}$ in adolescent group.

These results between the groups showed statistically significant between the groups ($p = 0.019$). Receiver operator characteristics (ROC) curve analysis showed that; MSNO levels may be discriminative marker in adolescent pregnancies with an AUC (95 CI %) of 0.770 (0.613-0.928) (Figure 2).

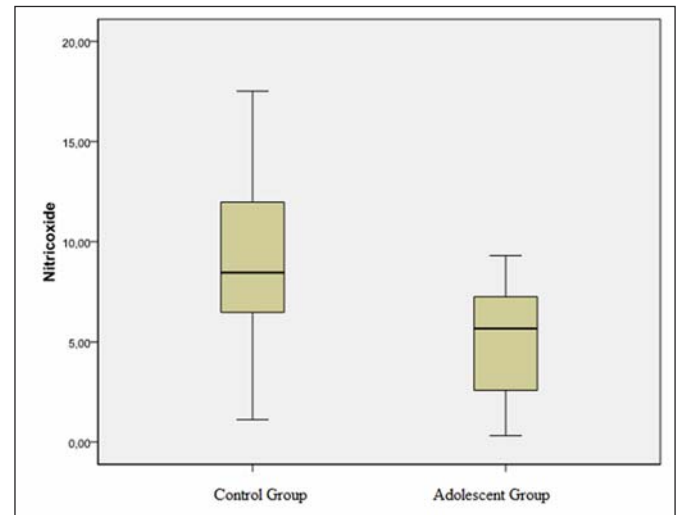


Figure 1: Nitric oxide levels in adolescent and control group

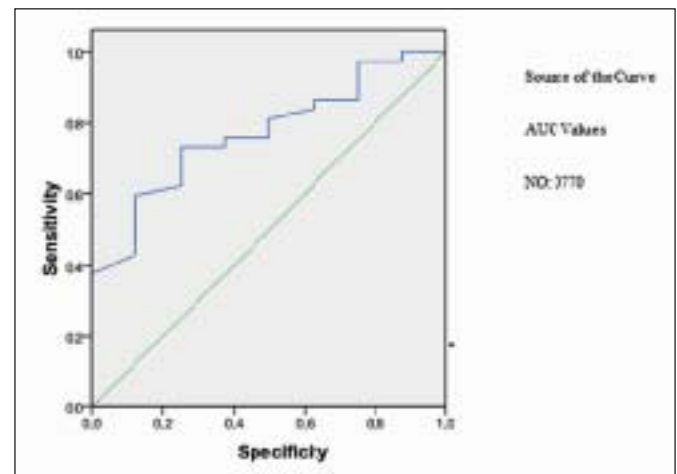


Figure 2: ROC curve for nitricoxide in adolescent pregnancies

Table 1: The demographic and clinical characteristics of the cases

	Adolescent group (n=8)	Control group (n=37)	p
Age (years)	17.75 \pm 0.70	24.86 \pm 4.70	<0.01
Gravidity*	1 (0-1)	1.95(1-5)	0.01
Parity*	0	0.91(0-3)	0.02
Gestational weeks	34.21 \pm 2.33	35.70 \pm 2.48	0.128
Birth weight (g)	3361.25 \pm 272.78	3310.27 \pm 373.23	0.731
APGAR scores (5. minute)*	7.12(7-8)	7.08(7-8)	0.700
Nitric oxide ($\mu\text{mol/L}$)	5.07 \pm 3.13	8.80 \pm 4.06	0.019

*:Data was presented mean (min-max) and p values calculated by χ^2 test

Discussion

There is a great deal of debate about adverse perinatal outcomes of adolescent pregnancies, whether those are due to maternal low age and biological immaturity⁸ or caused by the poor social and economic social situation of adolescents.⁹ In our study, we excluded the likely social and economic social situation and we ensured that all the participants had an enough prenatal care.

Principally, all of the pregnancies should be wanted and planned by women and her partner. In practice, 48% of pregnancies worldwide in 2008 were unintended.¹⁰ In contrast, Nunez-Urquiza et al.,¹¹ reported a lower ratio as 22.73%, non-planned or non-wanted pregnancies on adolescents. Having regular and good follow-up among pregnancy is frequently seen as a normal behavior on planned pregnancy, however the adolescent pregnancies, especially the ones who had unplanned or unwanted may be more reluctant having health services. Kinsman and Slap,¹² reported an association with between the unplanned adolescent pregnancies and poor perinatal outcomes due to being reluctant to have well prenatal care.

The incidence of low birth weight on adolescent pregnancies is found more than twice that found in reproductive age pregnancies and 14% of births to adolescents less than 17 years old have premature delivery.¹³ In our study, we compared the adolescent and reproductive age pregnancies for the incidence of low birth weight and premature delivery and we did not find any difference for these parameters.

Intrauterine growth retardation may result in decreased trophoblast and placental endothelial NO synthesis. Many study showed the reduced activity of NO synthase activity in the pregnancies complicated by fetal growth restriction and preeclampsia.^{14,15} In the pregnant animal models, it was shown that the inhibitors of nitric oxide synthase lead to the intrauterine growth retardation.¹⁶⁻¹⁸

In a study by Hata et al.,¹⁹ it was reported that the serum NO metabolites were significantly lower in small for gestational age infants than those in appropriate for gestational age infants. Also Giles et al.²⁰ reported that there was a significantly reduction of NO synthase activity in women with abnormal umbilical artery flow velocity waveforms.

In conclusion, we found that the MSNO levels are lower in the adolescent pregnancies than reproductive age pregnancies and this may be one of the reasons that cause poor perinatal outcomes on adolescent pregnancies. According ROC curve analysis MSNO levels may be a discriminative marker in adolescent age pregnancies but further studies with larger participants are needed to get more definite results.

Adolesan Gebeliklerde Maternal Serum Nitrik Oksit Seviyeleri

AMAÇ: Amacımız adolesan gebeliklerdeki maternal serum nitrik oksit (MSNO) seviyelerinin değerlendirilmesi.

GEREÇ VE YÖNTEM: Çalışmamıza toplam 45 gebe dahil edildi. Bunlardan 8 tanesi 18-19 yaşları arasında adolesan gebeler idi. Adolesan gebelerle, yaşları 20-35 arası değişen 37 yetişkin yaş gebe; yaş, gravidite, parite, gebelik haftası, umbilikal ve orta serebral arter dopler velosimetri değerleri, doğum kilo-ları, 5. dakika APGAR skorları ve MSNO seviyeleri açısından karşılaştırıldı. Kategorik datalar için χ^2 test, sürekli değişkenler için Student t test kullanıldı. MSNO seviyelerinin eşik değerleri için ROC eğrisinden yararlanıldı. İstatistik işlemleri için SPSS 17 paket programı (SPSS Inc., Chicago, IL, USA) kullanıldı.

BULGULAR: Demografik ve klinik özellikler açısından iki grup arasında istatistiksel bir farklılık izlenmedi ($p>0.05$). Adolesan gebe grubunda MSNO seviyeleri, yetişkin yaş grubundaki gebelere oranla istatistiksel olarak anlamlı düşük bulundu.

SONUÇ: MSNO seviyeleri çalışmamızda adolesan yaş grubunda, yetişkin yaş grubuna göre anlamlı düşük bulunmuştur. MSNO seviyeleri adolesan gebe grubunda ayırıcı bir marker olarak kullanılabilir ancak bunun olması için daha geniş örneklem grubuyla yapılacak çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Adolesan, Gebelik, Maternal serum nitrik oksit

References

1. Turkey Demographic and Health Survey 2008:73-5.
2. Phipps, M.G., J.D. Blume, S.M. De Monner, Young maternal age associated with increased risk of postneonatal death. *Obstet Gynecol* 2002;100(3):481-6.
3. Paranjothy S. et al. Teenage pregnancy: who suffers? *Arch Dis Child* 2009;94(3):239-45.
4. Gielen S. et al. Exercise-induced modulation of endothelial nitric oxide production. *Curr Pharm Biotechnol* 2011;12(9):1375-84.
5. Demir B. et al. The role of homocysteine, asymmetric dimethylarginine and nitric oxide in pre-eclampsia. *J Obstet Gynaecol* 2012;32(6):525-8.
6. Huang L.T. et al. Roles of nitric oxide and asymmetric dimethylarginine in pregnancy and fetal programming. *Int J Mol Sci*, 2012;13(11):14606-22.
7. Granger D.L. et al. Measurement of nitrate and nitrite in biological samples using nitrate reductase and Griess reaction. *Methods Enzymol* 1996;268:142-51.
8. Fraser A.M. J.E. Brockert and R.H. Ward Association of young maternal age with adverse reproductive outcomes. *N Engl J Med* 1995;332(17):1113-7.

9. Olausson P.M. S. Cnattingius and R.L. Goldenberg, Determinants of poor pregnancy outcomes among teenagers in Sweden. *Obstet Gynecol* 1997;89(3):451-7.
10. Secura G. Long-acting reversible contraception: a practical solution to reduce unintended pregnancy. *Minerva Ginecol* 2013;65(3):271-7.
11. Nunez-Urquiza R.M. et al., [Unwanted adolescent pregnancy and post-partum utilization of contraceptive methods]. *Salud Publica Mex* 2003;45 Suppl 1:92-102.
12. Kinsman S.B. and G.B. Slap, Barriers to adolescent prenatal care. *J Adolesc Health* 1992;13(2):146-54.
13. Felice M.E. et al. Adolescent pregnancy-current trends and issues: 1998 American Academy of Pediatrics Committee on Adolescence, 1998-1999. *Pediatrics* 1999; 103(2):516-20.
14. Brennecke S.P. DiIulio, J.L. Gude N.M. and King, R. G. Nitric oxide synthase activity of preterm human placental tissue is reduced in preeclampsia. *Placenta* 1994;15, A6.
15. Morris N.H. et al. Nitric oxide synthase activities in placental tissue from normotensive, pre-eclamptic and growth retarded pregnancies. *Br J Obstet Gynaecol* 1995; 102(9):711-4.
16. Salas S.P. et al. Effects of long-term nitric oxide synthesis inhibition on plasma volume expansion and fetal growth in the pregnant rat. *Hypertension* 1995;26(6 Pt 2):1019-23.
17. Molnar M. et al. Prolonged blockade of nitric oxide synthesis in gravid rats produces sustained hypertension, proteinuria, thrombocytopenia, and intrauterine growth retardation. *Am J Obstet Gynecol* 1994;170(5 Pt 1):1458-66.
18. Diket A.L. et al. Nitric oxide inhibition causes intrauterine growth retardation and hind-limb disruptions in rats. *Am J Obstet Gynecol* 1994;171(5):1243-50.
19. Hata T. et al. Maternal and fetal nitric oxide synthesis is decreased in pregnancies with small for gestational age infants. *Hum Reprod* 1998;13(4):1070-3.
20. Giles W. et al. Placental nitric oxide synthase activity and abnormal umbilical artery flow velocity waveforms. *Obstet Gynecol* 1997;89(1):49-52.