The impact of parity on perinatal outcomes in pregnancies complicated by advanced maternal age

İleri maternal yaşla komplike gebeliklerde paritenin perinatal sonuçlara etkisi

Eralp Başer, Kerem Doğa Seçkin, Selçuk Erkılınç, Mehmet Fatih Karslı, İlkin Mahmut Yeral, Oktay Kaymak, Turhan Çağlar, Nuri Danışman

Department of Obstetrics and Gynecology, Zekai Tahir Burak Women's Health Education and Research Hospital, Ankara, Turkey

Abstract

Objective: The purpose of this study was to investigate the impact of parity on perinatal outcomes in pregnancies complicated by advanced maternal age.

Material and Methods: A total of 11 587 pregnancies were reviewed retrospectively from patient medical records. Singleton pregnancies greater than 24 weeks of gestation were included. The study group consisted of women ≥40 years old at the time of delivery, and the control group consisted of women aged between 20 and 30 years old. Data regarding age, parity, gestational age, mode of delivery, and obstetric and neonatal complications were collected. Firstly, pregnancies ≥40 years and the younger control group were compared altogether with respect to the obstetric and neonatal complications. Secondly, both groups were divided into subgroups according to parity, and a second comparison was made with controls.

Results: Mean maternal age in the study and control groups was 43±2.2 and 24±2.8 years, respectively. In women ≥40 years old, all of the investigated obstetric and neonatal complications except postpartum haemorrhage and foetal malformations were higher when compared to younger controls ($p<0.05$). In the nulliparous ≥40 year old group, the most significant complications were preterm delivery (45.3%), low 5-minute Apgar score (15.2%), and neonatal intensive care unit admission (15.2%). On the other hand, in the multiparous group, preeclampsia (16.6%), abruptio placentae (5.1%), foetal demise (7.2%), and macrosomia (9.6%) were found to be significantly higher when compared to controls.

Conclusion: The study suggests that pregnancies of maternal age ≥40 years carry increased risks for both neonatal and obstetric complications, and these risks seem to be effected by parity.

(J Turkish-German Gynecol Assoc 2013; 14: 205-9)

Key words: Advanced maternal age, parity, perinatal outcome, neonatal outcome

Received: 18 August, 2013 **Accepted:** 19 September, 2013

Özet

Amaç: Bu çalışmanın amacı, paritenin ileri maternal yaş ile komplike olmuş gebeliklerde perinatal sonuçlara olan etkisinin incelenmesidir.

Gereç ve Yöntemler: Toplam 11 587 gebeliğe ait takip dosyası retrospektif olarak incelendi. Çalışmaya 24 hafta üzeri tekiz gebelikler dahil edildi. Çalışma grubu doğum sırasında 40 yaş ve üzeri olan gebe kadınlardan, kontrol grubu ise 20-30 yaş arası gebe kadınlardan oluşturuldu. Hastaların yaş, parite, gestasyonel yaş, doğum şekli, obstetrik ve neonatal komplikasyonlara ait verileri toplandı. İlk olarak 40 yaş üzeri gebelerle genç kontrol grubunun tamamı obstetrik ve neonatal komplikasyonlar açısından karşılaştırıldı. Sonrasında, her iki grup da pariteye göre ayrılarak (nullipar ve multipar), ikinci bir karşılaştırma yapıldı.

Bulgular: Çalışma ve kontrol grubunda ortalama maternal yaşlar sırasıyla 43±2.2 ve 24±2.8 yıl idi. Kırk yaş üzeri kadınlarda, postpartum kanama ve fetal malformasyonlar dışında incelenen tüm obstetrik ve neonatal komplikasyonlar kontrollere göre daha sıktı ($p<0.05$). Nullipar 40 yaş üstü gebelerde kontrollere göre anlamlı olarak daha sık gözlenen en sık komplikasyonlar preterm doğum (%45.3), düşük 5.dakika APGAR skoru (%15.2), ve neonatal yoğun bakım ünitesine yatış (%15.2) idi. Diğer taraftan multipar grupta preeklampsi (%16.6), ablasyo plasenta (%5.1), fetal kayıp (%7.2) ve makrozomi (%9.6) kontrol grubuna göre daha sıktı ($p<0.05$).

Sonuç: Bu çalışmada, maternal yaşın 40'ın üzerinde olduğu gebeliklerde neonatal ve obstetrik komplikasyonlarda artış olduğu, ve bu risklerin pariteden etkilendiği sonucuna varılmıştır.

(J Turkish-German Gynecol Assoc 2013; 14: 205-9)

Anahtar kelimeler: İleri maternal yaş, parite, perinatal sonuçlar, neonatal sonuçlar

Geliş Tarihi: 18 Ağustos 2013 **Kabul Tarihi:** 19 Eylül 2013

Introduction

Delayed childbearing has become increasingly common in the past decades, and this has raised concern for the possible risks for both the mother and the foetus. In numerous previous studies, a maternal age ≥40 years has been reported as a proper cut-off to better identify high-risk women with advanced maternal age (1). The majority of these pregnancies are achieved with assisted reproductive technologies (ART), which also increases the risk of complications.

The prevalence of advanced maternal age within all pregnancies has been previously reported to be around 1.5%; however, these numbers may change according to the population studied (2, 3). Advanced maternal age is well known to be

Address for Correspondence: *Eralp Başer, Department of Obstetrics and Gynecology, Zekai Tahir Burak Women's Health Education and Research Hospital, Ankara, Turkey. Phone: +90 530 460 27 74 e.mail: eralpbaser@gmail.com*

doi:10.5152/jtgga.2013.62347

associated with adverse maternal and foetal outcomes such as gestational diabetes mellitus, preterm delivery, antepartum haemorrhage (4). This study was designed to compare the complications and pregnancy outcomes of women aged 40 years and above with women aged 20-30 years, with special emphasis on the variations of these complications with regards to parity.

Material and Methods

A retrospective patient chart analysis was conducted for pregnancies that were followed-up at a tertiary referral hospital in Ankara, Turkey between January 1, 2011 and January 1, 2013. Institutional ethical and scientific approval was obtained. A total of 11,587 pregnancies were reviewed retrospectively. Singleton pregnancies after 24 weeks of gestation were included, and all gestational ages were confirmed by first or second trimester ultrasound measurements. Pregnant women with multifoetal pregnancies, chronic diseases, and previous uterine surgeries were excluded.

The study group consisted of women ≥40 years (n=190). Using a 1:3 ratio for cases:controls, the control group consisted of 600 women aged between 20 and 30 years, who were randomly selected. Women with multifoetal pregnancies, chronic diseases, and previous uterine surgeries were also not included in the control group. Data including age, parity, gestational age, mode of delivery and obstetrical and neonatal complications were collected and compared with respect to maternal age and parity. Nulliparity was defined as not having any previous history of deliveries >20 gestational weeks. Multiparity was defined as a previous history of ≥1 delivery >20 gestational weeks. Obstetric complications such as placenta previa, placental abruption, hypertension, preeclampsia, gestational diabetes mellitus, preterm delivery, low 1 and 5 minute Apgar scores, neonatal intensive care unit admission, intrauterine growth restriction (IUGR) and foetal demise were recorded for each patient.

Preeclampsia was defined as increased blood pressure ≥140/90 on two or more occasions, and ≥300 mg proteinuria in 24-hour urine, after 20 weeks of gestation. The diagnosis for gestational diabetes mellitus was based on the American College of Obstetrics and Gynecology guidelines for diagnosing gestational diabetes mellitus (5). Childbirth before 37 completed weeks (<259 days) was defined as preterm delivery. Postpartum haemorrhage (PPH) was defined as estimated blood loss (EBL) ≥500 mL after vaginal delivery, and ≥1000 mL after caesarean delivery. Low Apgar scores were defined as a 1 minute Apgar score <7 and a 5 minute Apgar score <9. The study and control groups were further divided into two subgroups according to parity (nulliparous and multiparous), and the two groups were compared with nulliparous and multiparous controls.

Statistical analyses were performed with IBM SPSS 20.0 (SPSS Inc., Armonk, NY, USA) software. Continuous variables were expressed as mean±standard deviation (SD), discrete variables as median (range) and categorical variables as number and percentage. The Kolmogorov-Smirnov test was used to assess normal data distribution. The univariate analyses were investigated with Chi-square test (with Yates' correction), Fisher's Exact test and *t*-test, where appropriate. Odds ratio (OR) with 95% confidence interval (CI) was calculated for each complication. In addition, crude and adjusted log-linear binomial regression analyses were carried out for each complication separately by maternal age group, to estimate the relative risk ratios (RR). Women aged 20-30 were assigned as the basal controls in this model. P values were considered significant at the 0.05 level (two tailed).

Results

Mean age in the study and control groups were 43±2.2 and 24±2.8 years, respectively. Fifty-two per cent (n: 408) of the patients were nulliparous, and 48% (n: 383) of the patients were multiparous. The comparisons between the study and control group with regards to perinatal and neonatal outcomes are presented in Table 1. In the study group, the most significant complications that were found at rates higher than in the controls were as follows: preterm delivery (28.9%), preeclampsia (15.8%), gestational diabetes mellitus (6.8%), IUGR (9.5%), placenta previa (3.7%), abruptio placentae (5.8%), and foetal demise (7.8%) ($p<0.05$). The caesarean delivery rate was also higher in the study group (58.9%) when compared to controls (30.7%) ($p<0.05$). There were no significant differences between the groups with respect to PPH and foetal malformations ($p>0.05$). Mean gestational age was lower in the study group as compared to the control group (36.7±2.8 vs. 37.8±2.4 weeks, respectively; $p<0.05$). Crude and adjusted estimates of the association between maternal age group and parameters of adverse pregnancy outcomes are presented in Table 2.

The two groups were further divided into two subgroups according to parity, as nulliparous and multiparous; the study groups (≥40 years) were again compared with controls of similar parity. The comparison of the divided groups in terms of obstetric and perinatal outcomes is given in Table 3. In ≥40 year old nulliparous women, there was a trend towards increased obstetric and perinatal complications, including preterm delivery (45.3%), gestational diabetes mellitus (9.1%) and placenta previa (12%) ($p<0.05$). In ≥40 year old multiparous group, preeclampsia (16.6%), abruptio placentae (5.1%), foetal demise (7.2%), caesarean delivery (58%) and macrosomia (9.6%) were higher than in controls. However, there were no statistically significant differences between the ≥40 year old multiparous women and controls in terms of preterm delivery, IUGR, placenta previa, postpartum haemorrhage, and foetal malformations ($p>0.05$). Amniocentesis was performed in 27 patients in the study group, and 8 controls to rule out foetal chromosomal anomalies; all were reported as having a normal karyotype.

Discussion

Advanced maternal age is well known to increase the risk for perinatal complications and adverse pregnancy outcomes when compared to younger women. Current evidence suggests that these risks of advanced age begin to increase after the age of 35 years, and significantly accelerate after the age of 40 (6).

Table 1. Comparison of perinatal and neonatal complications between women aged ≥40 years and controls (20-30 years)

	Women aged >40 years (n=190) n (%)	Women aged 20-30 years (n=600) n (%)	OR (%95 CI)	p
Preterm delivery	55 (28.9)	118 (19.6)	1.67 (1.37-1.94)	0.009
Gestational diabetes mellitus	13 (6.8)	18 (3)	5.67 (2.37-4.95)	0.005
Preeclampsia	30 (15.8)	22 (3.6)	4.93 (2.77-8.79)	<0.001
Intrauterine growth restriction	19 (9.5)	30 (5)	2.11 (1.16-3.85)	0.033
Placenta previa	7 (3.7)	3 (0.5)	7.62 (1.95-29.78)	<0.001
Foetal anomaly	8 (4.2)	16 (2.6)	1.71 (0.71-4.11)	0.22
Intrauterine foetal demise	15 (7.8)	13 (2.1)	2.70 (1.45-6.14)	0.005
Ablatio placenta	11 (5.8)	7 (1.2)	5.21 (1.99-13.65)	<0.001
Caesarean delivery	112 (58.9)	185 (30.8)	1.64 (1.46-1.90)	0.011
Postpartum haemorrhage	6 (3.1)	15 (2.5)	1.23 (0.87-3.24)	0.32
Low birth weight	53 (27.9)	124 (20.6)	3.61 (1.91-6.81)	0.020
Macrosomia	21 (11.1)	20 (3.3)	2.14 (0.75-6.10)	<0.001
Neonatal intensive care admission	18 (9,4)	46 (7.6)	2.21 (1.24-3.93)	0.003
Neonatal mortality	12 (6.3)	16 (2.6)	2.46 (1.14-5.29)	0.013
1-minute Apgar score <7	32 (16.8)	47 (7.8)	2.38 (1.47-4.86)	<0.001
5-minute Apgar score <9	34 (17.9)	51 (8.5)	2.35 (1.47-3.75)	<0.001

Table 2. Crude and adjusted relative risks (RR) of association between advanced maternal age (>40 years) and obstetrical-neonatal complications when compared to the control group

	Women aged > 40 years (n=190)	
	Crude RR (95% CI)	Adjusted RR[1] (95% CI)
Preterm delivery	0.92 (0.82-1.12)	1.08 (0.95-1.12)
Gestational diabetes mellitus	1.84 (1.74-1.91)	1.78 (1.72-1.83)
Preeclampsia	1.88 (1.77-1.98)	1.81 (1.69-1.95)
Intrauterine growth restriction	1.61 (1.53-1.68)	1.34 (1.24-1.47)
Placenta previa	2.12 (2.04-2.21)	1.84 (1.72-1.99)
Foetal anomaly	1.03 (0.92-1.12)	1.06 (0.96-1.11)
Intrauterine foetal demise	1.55 (1.43-1.62)	1.47 (1.39-1.54)
Ablatio placenta	1.79 (1.71-1.87)	1.74 (1.66-1.83)
Caesarean delivery	1.91 (1.83-1.96)	1.86 (1.80-1.91)
Postpartum haemorrhage	1.02 (0.93-1.07)	1.00 (0.91-1.04)
Low birth weight	1.44 (1.37-1.54)	1.51 (1.42-1.58)
Macrosomia	1.71 (1.60-1.77)	1.52 (1.45-1.61)
Neonatal intensive care admission	1.69 (1.59-1.73)	1.61 (1.54-1.69)
Neonatal mortality	1.63 (1.54-1.71)	1.54 (1.42-1.59)
1-minute Apgar score <7	1.38 (1.31-1.47)	1.49 (1.42-1.54)
5-minute Apgar score <9	1.35 (1.28-1.39)	1.46 (1.40-1.51)

[1] Adjusted for parity

In this study, we found that preeclampsia, gestational diabetes mellitus, placenta previa, foetal demise, abruptio placentae, preterm delivery, and IUGR were higher in the women aged ≥40 years, when compared to controls. Previous studies have reported similar findings to this study (7, 8). For example, a paper on neonatal outcomes in advanced maternal age reported that maternal age ≥40 years was associated with a higher incidence of preterm birth, low birth weight and stillbirth (9). Another study had previously stated that advanced maternal age was a risk factor for abruptio placentae (10). Gestational diabetes mellitus, preeclampsia and preterm delivery were also reported to have a higher incidence among the pregnancies with maternal age over 40 years (4, 11). In the log-linear binomial regression analyses performed in this study, we found that women aged ≥40 years had significantly increased RRs for all obstetric and neonatal complications except foetal anomalies and obstetric haemorrhage.

A previous study from Turkey investigated the maternal and foetal outcomes of pregnancies in women aged 35 and older (12). The authors compared 565 women of advanced maternal age (≥35 years), with 3,607 controls (<35 years). Preeclampsia, antepartum bleeding, and caesarean delivery frequency was higher in the advanced maternal age group (p=0.001). They also reported that Apgar scores of the infants were lower in women with advanced maternal age. We also found similar results in this study. They reported that newborn weights and NICU admission rates were similar between the two groups in their study. However, in this study, we found higher frequencies of low birth weight infants and higher NICU admissions in women of advanced age. This difference may be due to the fact that our cases of advanced maternal age consisted of women aged ≥40 years, while in the study of Üstün et al. (12),

Table 3. Comparison of perinatal and neonatal outcomes between women aged ≥40 years and controls, according to parity

	Nulliparous			Multiparous		
Variables	≥40 years (n= 33) n (%)	20-30 years (n= 375) n (%)	p	≥40 years (n=157) n (%)	20-30 years (n= 225) n (%)	p
Preterm delivery	15 (45.3)	67 (17.9)	0.001	40 (23.4)	53 (23.5)	0.31
Gestational diabetes mellitus	3 (9.1)	14 (3.7)	0.02	10 (6.4)	4 (1.7)	0.018
Preeclampsia	4 (9.4)	14 (3.7)	0.36	26 (16.6)	8 (3.5)	0.00
Intrauterine growth restriction	3 (8.7)	17 (4.5)	0.2	16 (10.2)	13 (5.7)	0.106
Placenta previa	4 (12)	1 (0.26)	0.00	3 (1.9)	2 (0.9)	0.38
Foetal anomaly	2 (6.1)	9 (2.4)	0.21	6 (3.8)	7 (3.1)	0.519
Intrauterine foetal demise	4 (12)	8 (2.1)	0.001	11 (7.2)	5(2.2)	0.009
Ablatio placenta	3 (9.2)	4 (1.1)	0.001	8 (5.1)	3 (1.3)	0.03
Caesarean delivery	21 (63)	147 (39.2)	0.01	91 (58)	38 (16.9)	0.006
Postpartum haemorrhage	1 (3.03)	11 (2.9)	0.24	5 (3.2)	4 (1.8)	0.43
Low birth weight	12 (36.4)	72 (19.2)	0.001	41 (25.7)	52 (23.1)	0.51
Macrosomia	6 (18.2)	11 (2.9)	0.00	15 (9.6)	9 (4)	0.027
Neonatal intensive care admission	5 (15.2)	26 (6.9)	0.002	13 (8.2)	20 (8.9)	0.521
Neonatal mortality	3 (9.1)	5 (1.3)	0.002	9 (5.7)	11 (4.9)	0.72
1-minute Apgar score <7	3 (9.9)	16 (4.3)	0.001	29 (18.5)	31 (13.7)	0.27
5-minute Apgar score <9	5 (15.2)	20 (5.3)	0.000	29 (18.5)	31 (13.7)	0.21

it consisted of women aged ≥35 years. In another study from Turkey, 237 advanced maternal age (≥35 years) pregnancies were retrospectively analysed and compared with younger age controls for maternal and foetal outcomes (13). The rates of preeclampsia, gestational diabetes, low Apgar scores and intrauterine foetal demise were higher in the advanced age group. On the contrary, caesarean delivery rates were higher in the control group. Rates of prematurity, low birth weight infants and foetal anomalies were similar between the groups. The findings of this study were very similar to our findings, except that the rates of caesarean delivery and low birth weight infants were also higher in the advanced maternal age group in our study.

A very recent study investigated the frequency of postpartum haemorrhage in women with advanced maternal age (14). In this retrospective study, a total of 12,868 women aged ≥35 years were compared with 52,200 women aged <35 years. It was reported that, although the risk of postpartum haemorrhage seemed to increase in advanced aged women, this was attributable to factors other than maternal age. Interestingly, it was found that advanced age was found to be associated with less PPH in the multivariate analysis. In our study, the frequency of PPH was similar between advanced age and control groups. In this study, in order to compare women for the aforementioned outcome measures according to parity, we divided the study population into two groups as nulliparous and multiparous. Gestational diabetes mellitus, preterm delivery and placenta previa were found to be significantly higher in nulliparous older women, whereas foetal demise and abruptio placentae were found to be higher in both nulliparous and multiparous women. There was a significantly increased risk of preeclampsia only in multiparous older women compared to young multiparous controls. These findings are similar to those from the literature, except for those regarding placenta previa and preeclampsia. In a previous study, multiparity was found to be associated with placenta previa (15). On the other hand, Chan et al. (4) also found that an increased incidence of placenta previa existed among mothers ≥40 years, in contrast to other studies. Another study also stated that preeclampsia was higher both in nulliparous and multiparous older aged women; however, we could demonstrate this increase only in multiparous advanced maternal age women (16).

In a systematic review, an increased risk of caesarean birth was reported among women at advanced maternal age, compared with both nulliparous and multiparous younger women (16). In this study, nulliparous women ≥40 years had an increased risk of caesarean delivery compared to younger nulliparous controls. Although the higher caesarean delivery rate may be attributable to higher obstetric complications, obstetricians might have been prudent when deciding upon the mode of delivery in order to prevent neonatal complications.

In this study, neonatal complications including low birth weight, low Apgar scores and NICU admissions were higher in older nulliparous women. Cleary-Goldman reported that maternal age above 40 years of age was significantly associated with perinatal death and low birth weight (9). The correlation between advanced maternal age and low birth weight might be related to age-related changes in uterine vasculature. Miller et al. (17) published a study on this matter, and claimed that advanced maternal age is an independent risk factor for uteroplacental insufficiency.

Macrosomia was found to be higher in both nulliparous and multiparous advanced aged women in this study. The higher

incidence of macrosomia might be attributable to the higher incidence of gestational diabetes mellitus among advanced age women. Advanced maternal age was previously reported to be a risk factor for having a child with malformations (18). Interestingly, there was no significant difference between advanced age women and controls with respect to foetal anomalies, both in nulliparous and multiparous women.

In summary, the results of the current study indicate the increased risk of maternal, foetal and neonatal complications in pregnancies complicated with advanced maternal age. Moreover, the risk was more prominent in nulliparous older women. Obstetricians must be especially cautious for adverse events in this subset of patients.

Ethics Committee Approval: *The study was approved by the Zekai Tahir Burak Women's Health Education and Research Hospital Institutional Scientific and Ethical Review Board.*

Informed Consent: *N/A.*

Peer-review: *Externally peer-reviewed.*

Author contributions: *Concept – E.B., K.D.S., N.D.; Design – E.B., M.F.K., N.D.; Supervision – N.D., T.Ç., E.B.; Resource – N.D., T.Ç., O.K.; Materials – N.D, T.Ç. O.K.; Data Collection&/or Processing – E.B., K.D.S., S.E., M.F.K.; Analysis&/or Interpretation – E.B., K.D.S., M.F.K.; Literature Search – E.B., S.E., K.D.S.; Writing – E.B., K.D.S., S.E.; Critical Reviews – N.D., T.Ç.*

Conflict of Interest: *The authors declared no conflict of interest.*

Financial Disclosure: *The authors declared that this study received no financial support.*

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