

RESEARCH ARTICLE

Perinatal Outcomes in Advanced Age Pregnancies

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ABSTRACT

Objective: The aim of this study is to evaluate the impact of advanced maternal age on pregnancy outcomes

Methods: A retrospective analysis of 951 birth registry records of Zeynep Kamil Hospital, were analyzed between January 2003 and December 2007. Study group was made up of women ≥ 40 years old and control group was made up of women younger than 40 years.

Results: Mean maternal age was 41.48 years in the study group and 26.41 years in the control group. Mean gestational age at the time of delivery is 37.73 weeks in study group and 38.10 weeks in the control group. There was no statistical difference in terms of preterm delivery, multiple pregnancy, fetal anomaly, IUGR, superimpose preeclampsia oligohidramnios, presentation anomaly and placenta previa rates between the study and control groups. Incidence of preeclampsia ($p=0.041$), Chronic hypertension ($p=0.001$), GDM ($p=0.003$), is found to be higher in study group. Cesarean birth rate is higher ($p<0.05$) and hospitalization time is longer in study group ($p=0.001$). 1st minute and 5th minute APGAR scores of the study group (6.99 ± 2 , 8.27 ± 2) was lower than the 1st minute and 5th Minutes APGAR scores of the control group (7.38 ± 1.6 , 8.58 ± 1.7). Neonatal intensive care unit administration rate is seen also higher in study group ($p<0.01$).

Conclusion: Advanced maternal age was related to increased pregnancy complications and poor perinatal outcome. Preeclampsia, GDM, chronic hypertension is seen more common in advanced age pregnancies. Neonatal intensive care administration is higher and APGAR scores are lower; cesarean delivery was performed more common, and hospitalization time was longer in advanced age pregnancies. *J Clin Exp Invest 2016; 7 (2): 157-162*

Key words: perinatal outcome, advanced age pregnancy, pregnancy outcome

İleri Anne Yaşı Gebeliklerinde Perinatal Sonuçlar

ÖZET

Amaç: Bu çalışmanın amacı ileri anne yaşının gebelik sonuçları üzerindeki etkisini değerlendirmektir.

Yöntemler: Zeynep Kamil hastanesinde 2003-2007 yıllarında doğum yapmış 951 gebenin verileri retrospektif olarak değerlendirildi. Çalışma grubu 40 yaş ve üzeri gebelerden, kontrol grubu 40 yaş altı gebelerden oluşturuldu.

Bulgular: Ortalama anne yaşı çalışma grubunda 41,48 kontrol grubunda 26,41'dir. Doğumda ortalama gebelik haftası çalışma grubunda 37,73 kontrol grubunda 28,10'dur. Çalışma ve kontrol grupları arasında Preterm doğum, çoğul gebelik, fetal anomalisi, intrauterin gelişme geriliği, süperimpoze preeklampsi, oligohidramniyos, prezentasyon anomalisi ve plasenta previa oranları arasında istatistiksel anlamlı fark saptanmadı. Çalışma grubunda preeklampsi, kronik hipertansiyon, gestasyonel diyabet, insidansı kontrol grubundan istatistiksel olarak anlamlı olarak yüksek saptandı ($p=0,041$, $p=0,001$, $p=0,003$). Sezaryen doğum oranı, hastanede kalış süresi çalışma grubunda anlamlı olarak yüksek bulundu ($p<0,05$, $p=0,001$). Çalışma grubunda yenidoğan 1. ve 5. Dakika APGAR skorları kontrol grubundan düşük saptandı ($p<0,01$). Çalışma grubunda yenidoğan yoğun bakım ünitesine yatış oranı istatistiksel olarak anlamlı derece yüksek saptandı ($p<0,01$).

Sonuç: İleri anne yaşı yüksek gebelik komplikasyonları ve kötü perinatal sonuçlarla ilişkilidir. Preeklampsi, Gestasyonel Diyabet, kronik hipertansiyon ileri anne yaşı gebeliklerinde daha sık görülmektedir. İleri anne yaşı gebeliklerinde Yenidoğan yoğun bakım yatış oranı daha yüksek, APGAR skorları daha düşük, sezaryen doğum oranı daha yüksek hastanede kalış daha uzundur.

Anahtar kelimeler: Perinatal sonuçlar, ileri anne yaş gebelikleri, gebelik sonuçları

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INTRODUCTION

Pregnancies in the fourth decade and later have increased over the past years. This is attributed to delaying childbearing for career plans and financial goals. Increased use of assisted reproductive techniques also contribute to this increase [1-4]. It is traditionally accepted that, women 35 years and older have an increased risk for complications during pregnancy, and increased risk of adverse pregnancy outcomes [3-8]. The aim of this study is to evaluate the impact of advanced maternal age on pregnancy outcomes and compare the pregnancy complications in mothers over 40 years old and younger.

METHODS

A hospital-based retrospective analysis of birth registry records of Zeynep Kamil Hospital, a tertiary clinic, are analyzed between January 2003 and December 2007 in Istanbul. A total of 951 women who gave birth in the hospital were included in the study. Study group is made up of women who were ≥ 40 years old at the time of delivery. Control group is made up of women younger than 40 years at the time of delivery by random sampling. Study group consists of 711 (74.8%) and the control group consists of 240 (25.2%) women. Gestational age is determined by the date of last menstrual period, first or second trimester ultrasound screening examination. IUGR (Intrauterin growth restriction) is defined as estimated fetal weight under 10th percentile for gestational age calculated by ultrasound. Obstetric outcomes are assessed.

Statistical analysis

Statistical analysis was performed using NCSS (Number Cruncher Statistical System, 2007&PASS 2008 Statistical Software). The mean and standard deviations were calculated for continuous variables. Chi-square, independent sample t-tests and Fisher test were used to evaluate associations between the categorical and continuous variables. Continuous variables were compared with two-sided sample t test and for nonparametric analysis the Mann-Whitney U test was used. Two-sided P values were considered to be statistically significant at $p < 0.05$.

RESULTS

Patient characteristics of both age-groups were summarized in Table 1 and 2. Mean maternal age is 41.5 years in study group, and 26.4 years in the control

group. Mean gestational age at the time of delivery is 37.7 years in study group and 38.1 years in control group. There is no statistical difference for mean gestational age at the time of delivery between two groups. When we evaluate previous pregnancy characteristics and the obstetric history; there is no statistical difference in previous caesarian, previous pregnancy induced hypertension rates between the control and study group, but macrosomia in previous pregnancy seen more common in the study group (Table 1,2).

Table 1. Maternal characteristics of the study and the control groups (Mean \pm Standard deviation)

	Study group (n=711)	Control group (n=240)	P
Maternal age	41.48 \pm 2.16	26.41 \pm 5.32	
Gestational age	37.73 \pm 3.82	38.10 \pm 3.29	0.238
Gravida	5.23 \pm 2.73	2.41 \pm 1.52	0.001
Parity	3.47 \pm 2.03	1.68 \pm 1.06	0.001
Abortus	1.70 \pm 1.30	1.29 \pm 0.74	0.031
D&C	2.06 \pm 1.50	1.38 \pm 0.76	0.041

Student t test

Table 2. Characteristics of previous pregnancies

Obstetric history	Study group (n=711)	Control group (n=240)	p
	n (%)	n (%)	
Caesarian birth	78 (11)	31 (12.9)	0.413
Macrosomia	35 (4.9)	1 (0.4)	0.002
PIH	6 (0.8)	0 (0)	0.153
Multiple pregnancy	9 (1.3)	2 (0.8)	0.588

PIH: pregnancy induced hypertension

Evaluating obstetric complications during pregnancy we find statistical difference in terms of GDM (Gestational diabetes mellitus), chronic hypertension and preeclampsia rates between study and control group. We didn't find statistical difference in terms of preterm delivery, multiple pregnancy, fetal anomaly, IUGR, superimpose preeclampsia oligohydramnios presentation anomaly and placenta previa rates between the study and control groups. We find higher rates of GDM, chronic hypertension and preeclampsia in study group. GDM is seen at 4 (6.6%) patients in study, 4 (1.7%) patients in control group. This difference is statistically significant ($p=0.003$). Chronic hypertension is seen at 98 (13.8%) patient in study, and 6 (2.5%) patient in control group. This difference is sta-

tistically significant ($p=0.001$). Preeclampsia is seen at 69 (9.7%) patients in the study group, 13 patients (5.4%) in control group. This difference is statistically significant ($p=0.041$). (Table 3) We didn't find statistical difference in terms of preterm delivery, multiple pregnancy, fetal anomaly, IUGR, superimpose preeclampsia oligohydramnios presentation anomaly and placenta previa rates between the study and control groups (Table 3).

Table 3. Obstetric complications

Perinatal Complications	Study group (n=711) n (%)	Control group (n=240) n (%)	p
Preterm delivery	58 (8.2)	22 (9.2)	0.626
Multiple pregnancy	13 (1.8)	3 (1.3)	0.547
Fetal anomaly	14 (2)	5 (2.1)	0.913
Chronic Hypertension	98 (13.8)	6 (2.5)	0.001
IUGR	9 (1.3)	1 (0.4)	0.265
Preeclampsia	69 (9.7)	13 (5.4)	0.041
Superimposed Pre-eclampsia	10 (1.4)	0 (0)	0.065
Oligohydramnios	49 (6.9)	18 (7.5)	0.750
Presentation anomaly	34 (4.8)	10 (4.2)	0.695
Placenta previa	15 (2.1)	1 (0.4)	0.078
Gestational diabetes mellitus	47 (6.6)	4 (1.7)	0.003
Assisted reproductive technology required	13 (1.8)	2 (0.8)	0.285

Chi-Square test; IUGR: Intrauterin growth restriction

There is statistically significant difference between groups in terms of mode of delivery. Caesarian birth rate is 46.8% ($n=333$) in study group and 25% ($n=333$) in control group Caesarian birth rate is higher in study group ($p<0.05$). Hospitalization time is also found to be longer in study group ($p=0.001$) (Table 4,5).

When we evaluate newborn characteristics we find that 1st minute and 5th minute APGAR scores of the study group are lower than the 1st minute and 5th minutes APGAR scores of the control group ($p=0.001$, $p=0.002$). We also find higher rate of Neonatal intensive care unit administration in study group ($p<0.01$). There is no statistically significant difference between the groups in terms of mean fetal weight and fetal gender (Table 4,6).

Table 4. Delivery mode and neonatal intensive care necessity of two groups

	Study Group Mean \pm SD	Control Group Mean \pm SD	p	
Age	41,48 \pm 2,16	26,41 \pm 5,32		
	n (%)	n (%)		
Delivery	C/S	333 (46.8)	60 (25)	<0.001
	Vaginal	378 (53.2)	180 (75)	
Neonatal Intensive Care Administration	Yes	124 (17.4)	19 (7.9)	<0.001
	No	587 (82.6)	221 (92.1)	

C/S: Caesarian section, SD: Standard deviation

Table 5. Duration of hospitalization in the study and the control groups

	Study group (n=711) Mean \pm SD	Control group (n=240) Mean \pm SD	*p
Duration of hospitalization	4.50 \pm 4.93	2.75 \pm 2.25	0.001

*Mann Whitney U test

Table 6. Newborn characteristics

	Study group (n=711) Mean \pm SD	Control group (n=240) Mean \pm SD	p
APGAR at 1 ^o minute	6.99 \pm 2.02	7.38 \pm 1.69	0.001
APGAR at 5 ^o minute	8.27 \pm 2.07	8.58 \pm 1.72	0.002
Birth weight	3037.37 \pm 821.47	3135.43 \pm 715.32	0.085
	n (%)	n (%)	
Gender			
Female	355 (51.4)	128 (54.9)	0.347
Male	336 (48.6)	105 (45.1)	

DISCUSSION

It is generally accepted that, women 35 years and older have an increased risk for complications during pregnancy. Increased incidence of preterm labor, preeclampsia, chronic hypertension, gestational diabetes mellitus, increased maternal and fetal mortality and increased cesarean birth rate have been observed in advanced age pregnancies by many author [4-8]. But recently increased risk of pregnancy complications and adverse perinatal outcome associated with advanced maternal age has been questioned. It is suggested that if advanced aged women don't have underlying con-

ditions like DM (diabetes mellitus) or hypertension incidence of pregnancy complications and perinatal complications in advanced age pregnancies will be comparable to the younger age pregnancies [9,10]

It is well known that chronic hypertension increases progressively after third decade [4,5] this increase is attributed to vascular responsiveness to endothelial vasodilators [4,5,11]. Chronic hypertension is seen more common in advanced age pregnancies [6,8,12-14]. Yasin et al. and Tuck et al reported that chronic hypertension complicates up 10% to 20% of advanced age pregnancies [15,16]. In agreement with these reports we find higher incidence of chronic hypertension in advanced age pregnancies. In our study chronic hypertension is seen at 98 (13.8%) patient in study group and 6 (2.5%) patients in control group and this difference is statistically significant. In contrast with these studies Yun Wang et al did not find an increase in advanced age pregnancies for chronic hypertension [9].

Many studies have demonstrated an increased risk of preeclampsia in advanced age pregnancies [1,4,6,8,12,17-19]. Prysak et al 1995 reported the incidence of preeclampsia at 25-29 age pregnancies %3 in multiparous and 7% in nulliparous. After the age of 35 they reported incidence of preeclampsia as 7% in multiparous and 14% in nulliparous. They found 2 times greater risk of preeclampsia in advanced age pregnancies [4,18]. Bobrowski and Bottoms, Bianco et al. and Barton et al also find three times increased risk of preeclampsia in advanced age pregnancies [1,6,19]. In agreement with these reports we find increased risk of developing preeclampsia in the advanced age pregnancies. Preeclampsia is seen at 69 (9.7%) patient in study group, 13 patient (5.4%) in control group. This difference is statistically significant ($p=0.041$). We observed nearly doubled risk of preeclampsia (9.7% versus 5.4%) in the advanced age pregnancies compared with their younger counterparts. In contrary of these findings Clearly-Goldman et al didn't confirm an increased risk of preeclampsia in advanced age pregnancies in Faster trial [14]. Jacobson et al conducted a population based study and did not find an increased risk of preeclampsia in advanced age pregnancies [7]. They reported the incidence of preeclampsia 2.92% in 20-29 aged pregnancies. Incidence of preeclampsia in 40-44 aged pregnancies was 2.37% and after age of 45 2.16%. They didn't find an increased risk of preeclampsia [7]. But they find an increase of developing severe preeclampsia by advancing maternal age.

Incidence of severe preeclampsia was 0.81%, 1.12% and 1.49% in 20-29 aged 40-44 aged and >45 aged pregnancies respectively [7].

Tendency to diabetes mellitus increases by advanced age [8,13,20,21]. Diminished insulin sensitivity and B cell function by age can be responsible for these increase [8,22]. Advanced maternal age is accepted a risk factor for GDM for many authors [6,8,12-14]. Gilbert et al and Tan et al and find prominent risk of developing gestational diabetes mellitus in advanced age pregnancies [12,22]. Consistent with these studies we find higher rate of GDM in advanced age pregnancies. We find nearly fourfold increased risk of developing gestational diabetes mellitus in women older than 40 years than younger women (6.6% versus 1.7%). Gilbert et al also confirmed four times greater risk of developing gestational diabetes mellitus in advanced age pregnancies [12]. In contrast to these reports Yun Wang et al didn't find an increase for GDM in advanced age pregnancies. They report GDM incidence 1.1% in advanced maternal age pregnancies and 1.4% in younger counterparts [9]. Driul et al. reported the incidence of gestational diabetes mellitus in pregnancies older than 40 years of age as 8%, and 2.35% in pregnancies younger than 40 years of age. They observed nearly 4 times greater incidence of GDM in advanced age pregnancies. But after correcting weight gain during pregnancy, BMI (Body Mass Index), tobacco smoking and risk factors that can be confounder for GDM they did not find an increased risk of GDM in advanced age pregnancies [17].

All of the studies in literature have consistently demonstrated an increased risk of caesarean delivery in advanced age pregnancies [4,6,8,9,10,13,17]. In agreement with these studies we also find higher caesarean section rate in advanced age pregnancies. Caesarean section rate is 46.8% ($n=333$) in study group and 25% ($n=333$) in control group. Caesarean section rate is higher in study group.

Studies appraising preterm labor in advanced age pregnancies declares conflicting results. Jacobsson et al, Tan et al, Joly et al Milner et al, Ezra et al, Lehmann and Chism, reports an increase in preterm labor with advancing maternal age [7,22-26]. In contrast to these studies; Yung Wang et al, Loranza Driul et al, Berkowits et al 1990, Smit et al [9,17,27,28], don't confirm this increase in preterm births associated with advanced maternal age. In agreement with Berkowits, Smit, Lorenza, and Yung Wan We did not find an increase in preterm birth rate in advanced age pregnan-

cies. In our research preterm birth rate is 8.2% in study group, 9.2% in control group. This difference is not statistically significant. Newborn-Cook CV carried out a systematic review of literature from 1985 to 2002 to resolve this dilemma. Although majority of reports they had assessed claimed an increase in preterm birth rate in advanced age pregnancies they could not demonstrate that advanced age is an independent risk factor for preterm birth [29]. This discrepancy stem from inability to control confounders related with preterm births. Potential confounders induce this dilemma can be listed as: socioeconomic status, parity, preexisting chronic disease, behavioral factors like smoking, inadequate prenatal care, genitourinary infections, antenatal complications and ethnicity.

Low birth weight infants and IUGR in advanced age pregnancies is another conflicting issue. Hansen et al, Jacobson et al, Dildy et al, Delbaere et al claimed an increase in SGA infants by advancing maternal age [3,7,20,30]. In contrast to these reports we did not find an increase in IUGR at advanced age pregnancies. Incidence of IUGR is 1.3% in our study group and 0.4% in our control group. And this difference is not statistically significant. In agreement with our findings Yun Wang et al Driul et al did not find an increase in low birth weight infants in advanced age pregnancies [9,17]. Probably this dilemma stem from the confounder factors which influences birth weight such as parity socioeconomic status, ethnicity, weight gain during pregnancy and smoking.

As a predictor of poor perinatal outcome in advanced age pregnancies we find higher Neonatal intensive care unit administration rate and lower first and fifth Minutes APGAR scores in study group. Although preterm birth rate, IUGR rate and mean birth weight are not statistically different between the study and control group (table 3,6) Neonatal intensive care unit administration rate is found to be 17.4% in study group, 7.9% in control group and this difference is statistically significant. In agreement with our findings Bianco et al reported higher neonatal intensive care admission and lower 1. Minute APGAR score in advanced age pregnancies [6]. Prysac et al also confirmed increased intensive care admission rate in advanced age mothers [18]. Jacobson also reported that poor perinatal outcome in advanced age pregnancies can not be attributed to pregnancy complications or underlying medical conditions [7]. In contrast to these studies Joly et al did not confirm an increase in neonatal intensive care admission rate in advanced age

pregnancies [23], and Yun Wang et al did not find an association between advanced age pregnancies and poor perinatal outcome [9].

In conclusion, advanced maternal age is related with increased pregnancy complications and poor perinatal outcome. Preeclampsia, GDM, chronic hypertension is seen more common in advanced age pregnancies. Neonatal intensive care administration is higher and APGAR scores are lower in advanced age pregnancies. Cesarean delivery is performed more common, and hospitalization time is longer in advanced age pregnancies.

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