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ORIGINAL ARTICLE / ARAŞTIRMA YAZISI

Obstetrics and Gynaecology/Kadın Hastalıkları ve Doğum

Pregnancy Outcomes in Advanced Maternal age: a Single Reference Institution Experience

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ABSTRACT

Objective: Advanced maternal age was shown to be associated with several adverse maternal and perinatal outcomes. The aim of this study to compare pregnancy complications and the outcome between pregnant women with and without advanced age.

Methods: This retrospective cohort study included a total of 2,889 women and was designed to compare pregnancy outcomes between women aged <40 years and those aged ≥40 years. Maternal and neonatal complications were systematically evaluated, and both crude and adjusted risk estimates were calculated. Multivariate analyses were performed to account for potential confounding factors, allowing for a more accurate assessment of the independent effect of advanced maternal age on pregnancy outcomes.

Results: Advanced age was shown to be associated with higher risk for neonatal intensive care unit admission [OR:3.1 (95% CI: 2.2-4.2), p<0.05], IUGR [OR:1.6 (95% CI: 1.1-2.5), p<0.05], preterm delivery [OR:8.9 (95% CI: 5.7-14.2), p<0.001] and preeclampsia [OR:1.8 (95% CI: 1.2-2.6), p<0.05] after adjustment for number of prenatal visits, pre pregnancy hemoglobin level, number of previous deliveries and gestational age at delivery.

Conclusion: Advanced maternal age is associated with a range of adverse pregnancy outcomes. These risks are independent of number of prenatal visits, pre-pregnancy hemoglobin level, number of previous deliveries and gestational age delivery.

Keywords: Advanced maternal age, pregnancy complications, preterm birth, preeclampsia, fetal growth retardation, intensive care units, neonatal

ÖZET

Amaç: İleri anne yaşının çeşitli olumsuz maternal ve perinatal sonuçlarla ilişkili olduğu gösterilmiştir. Bu çalışmanın amacı, ileri yaş ve ileri yaş olmayan gebe kadınlar arasında gebelik komplikasyonlarını ve sonuçlarını karşılaştırmaktır.

Yöntem: Bu retrospektif kohort çalışmada toplam 2.889 kadın dahil edilmiş olup, 40 yaş altı ve ≥40 yaş gebeler arasında gebelik sonuçları karşılaştırılmıştır. Maternal ve neonatal komplikasyonlar sistematik olarak değerlendirilmiş, hem ham hem de düzeltilmiş risk oranları hesaplanmıştır. Ayrıca, ileri anne yaşının gebelik sonuçları üzerindeki bağımsız etkisini daha doğru değerlendirebilmek amacıyla çok değişkenli analizler yapılarak olası karıştırıcı faktörler için düzeltme uygulanmıştır.

Bulgular: Doğum öncesi ziyaret sayısı, gebelik öncesi hemoglobin düzeyi, önceki doğum sayısı ve doğumdaki gebelik haftasına göre düzeltme yapıldıktan sonra, ileri yaşın yenidoğan yoğun bakım ünitesine yatış [OR:3,1 (%95 GA: 2,2-4,2), p<0,05], IUGR [OR:1,6 (%95 GA: 1,1-2,5), p<0,05], preterm doğum [OR:8,9 (%95 GA: 5,7-14,2), p<0,001] ve preeklampsi [OR:1,8 (%95 GA: 1,2-2,6), p<0,05] için daha yüksek riskle ilişkili olduğu gösterildi.

Sonuç: İleri anne yaşı, bir dizi olumsuz gebelik sonucu ile ilişkilidir. Bu riskler, doğum öncesi ziyaret sayısı, gebelik öncesi hemoglobin düzeyi, önceki doğum sayısı ve doğumdaki gebelik haftasından bağımsızdır.

Anahtar Kelimeler: İleri anne yaşı, gebelik komplikasyonları, preterm doğum, preeklampsi, fetal büyüme kısıtlılığı, yoğun bakım üniteleri, yenidoğan

Although commonly defined as pregnancy at or beyond age 35, advanced maternal age (AMA) has become increasingly frequent and is recognized to carry distinct risks for both the mother and fetus (1,2). Over recent decades, the proportion of births to women in this age group has risen steadily, making AMA a notable public health issue in developed nations. According to the American College of Obstetricians and Gynecologists, AMA constitutes an independent risk factor for adverse obstetric and perinatal events, with risk levels rising progressively at ages 40, 45 and 50 years (1,2).

Data from large population-based cohorts and meta-analyses consistently indicate that AMA is linked to higher frequencies of gestational diabetes, hypertensive disorders (including preeclampsia), cesarean delivery, postpartum hemorrhage and maternal death. For women aged 35 years and older, the likelihood of developing gestational diabetes or hypertensive complications is almost twice that of younger women, and this probability continues to increase with age. Fetal and neonatal risks also rise, encompassing greater rates of miscarriage, chromosomal anomalies, congenital defects, preterm birth, intrauterine growth restriction (IUGR), low Apgar scores, neonatal intensive care unit (NICU) admission and stillbirth. In particular, women aged 40 years or older face a two-fold higher risk of stillbirth and perinatal death compared to their younger counterparts, and for those older than 45 years the maternal mortality risk ratio may exceed 10 (2-5).

These associations remain significant even after controlling for confounders such as parity, socioeconomic background and coexisting medical conditions, suggesting that age per se is a key contributor. The underlying mechanisms are multifactorial and include age-related alterations in reproductive and vascular physiology, a higher prevalence of chronic diseases, and increased utilization of assisted reproductive techniques. Current guidelines from the American College of Obstetricians and Gynecologists advocate for individualized preconception counseling, early and thorough prenatal screening (e.g., genetic testing and detailed fetal anatomy scans), and risk-reduction measures such as low-dose aspirin for preeclampsia prophylaxis in eligible patients (6-9).

A growing body of evidence underscores the necessity of tailored antenatal care and close surveillance for AMA pregnancies in order to optimize outcomes for both mother and newborn. Additional fetal monitoring and consideration of earlier induction of labor may be justified, as these strategies have been shown to lower perinatal mortality without raising operative delivery rates or short-term complications. Moreover, postpartum follow-up is essential because women with AMA are at greater risk for postpartum depression and long-term cardiovascular morbidity following hypertensive disorders of pregnancy (9,10).

Collectively, the available data support a heightened awareness and vigilant clinical approach to pregnancies in women of advanced maternal age, with individualized risk assessment being crucial to minimize adverse outcomes (10). The present study was therefore designed to compare pregnancy complications and neonatal outcomes between women with and without advanced maternal age.

Materials and Methods

From an initial dataset of 44,752 deliveries, women meeting the inclusion criteria were selected, resulting in a final study population of 2,889 women (1,585 in the <40 years group and 1,304 in the ≥40 years group). Women were categorized into two groups: <40 years (reproductive age) and ≥40 years (advanced maternal age). The ages were stratified, there were 455 (34.2%) women at age 40, 604 (45.4%) women aged between 41 and 42, 254 (19.1%) women aged between 43 and 45, and there were 17 (1.3%) women between 46 and 47 years. In this retrospective cohort study, the data was obtained from the hospital database of the Zeynep Kamil Women and Children's Health Training and Research Hospital.

Inclusion in the study group was solely restricted to women between 20 and 50 years of age (mean: 29.9 years).

Maternal age was defined as the completed age of the mother (in years) at the time of delivery. Gestational age at birth was calculated as number of weeks from the first day of the last menstrual cycle until the delivery date. Adverse maternal outcomes were determined according to various pregnancy complications, i.e. preeclampsia, cesarean delivery (CS), preterm premature rupture of membranes (PPROM), preterm delivery (PD), and intrauterine growth restriction (IUGR). Maternal morbidity is defined as the death of a woman while pregnant or within 42 days after delivery from any cause related to, or aggravated by, the pregnancy or its management. The variables used

to determine the perinatal outcomes were LBW (birth weight < 2500 g at birth), PD (deliveries before 37 weeks' gestation), small for gestational age (birth weight < 10th percentile at birth), fetal death (delivery of infant at or after 20 weeks' gestation without cardiac activity).

Statistical Analysis

Adverse pregnancy outcome rates were calculated for each maternal age cohort. Crude odds ratios (OR) with a 95% confidence interval (CI) were calculated to assess the association between each maternal age group and the identified adverse pregnancy outcomes. Adjusted odds ratios were obtained using logistic regression models. The estimates have been adjusted to account for the following potential confounding variables: gravidity, frequency of prenatal visits, gestational age at birth, and pre-pregnancy hemoglobin concentration. These variables were selected primarily based on **c**linical relevance and evidence from prior literature regarding factors known to influence pregnancy outcomes in advanced maternal age. All analyses were conducted using the SPSS 11 software package (SPSS Inc, Chicago, Ill). The Mann-Whitney U test or independent samples t-test was employed to examine continuous variables, the chi-square test was utilized for categorical variables, and binary logistic regression analyses were conducted to determine the adjusted odds ratios. This study was approved by the Ethics Committee of Zeynep Kamil Women and Children's Diseases Training and Research Hospital, Istanbul, Turkey (Date: 30.12.2020, Decision No: 195) and conducted in accordance with the Declaration of Helsinki.

Results

Baseline maternal and clinical characteristics of the study groups are presented in **Table 1**. Statistically significant differences were observed between the groups in terms of maternal age, gravidity, number of prenatal visits, birth weight, gestational age at delivery, and pre-pregnancy hemoglobin levels (all p<0.001). Compared to the younger group, women in the advanced maternal age group had significantly higher gravidity and a greater number of prenatal visits, while mean birth weight and gestational age at delivery were significantly lower (all p<0.001).

Table-1: Comparison of some demographic and clinical characteristics of groups with and without advanced age

	Groups	N	Mean	Std. Deviation	P Value
Maternal age (Years)	RA	1585	20.25	.430	
	AA	1304	41.41	1.419	***< 0.001****
Gravidity	RA	1585	1.31	.574	
	AA	1304	3.15	1.603	***< 0.001****
Number of prenatal visits	RA	1585	5.55	4.213	
	AA	1304	12.40	13.189	***< 0.001****
Birth weight (gr)	RA	1585	3095.55	620.950	
	AA	1304	2927.30	978.128	***< 0.001****
GA at delivery (Weeks)	RA	1585	38.16	2.372	
	AA	1304	36.64	4.792	***< 0.001****
Pre-pregnancy Hgb level (gr/dl)	RA	1585	9.96	1.227	
	AA	1304	10.38	1.446	***< 0.001****

GA:Gestational age, Hgb:Hemoglobin, RA: reproductive age, AA: advanced maternal age

Maternal and neonatal outcomes are summarized in **Table 2**. There was no significant difference between the groups in terms of PPROM and post-term delivery rates (p>0.05). Preterm delivery rates were significantly higher in the advanced maternal age group compared to the younger group (11.3% vs. 2.2%, p<0.001).

Table-2: Maternal and neonatal outcomes of groups with and without advanced age			
	Reproductive age <40 years (n=1585)	**Advanced maternal age ≥40 years (n=1304)**	**P value**
PPROM rate	8.6%	8.3%	>0,05
PD rate	2.2%	11.3%	***<0,001****
Post term delivery rate	8.8%	7.3%	>0,05
Stillbirth rate	2.7%	1.3%	***<0,05****
IUGR	7.9%	5.4%	***<0,05****
NICU admission	26.3%	10%	***<0,001****
PPROM= preterm premature rupture of membranes, PD= preterm delivery, IUGR= intrauterine growth retardation, NICU= neonatal intensive care unit.			

In contrast, stillbirth rates were significantly higher in the younger group compared to the advanced maternal age group (2.7% vs. 1.3%, p<0.05). Similarly, the rates of IUGR (7.9% vs. 5.4%, p<0.05) and NICU admission (26.3% vs. 10%, p<0.001) were significantly higher in the younger group. Episiotomy was performed more frequently in the younger group compared to the advanced maternal age group (98% vs. 42%, p<0.001). The primary cesarean section rate was significantly higher in the advanced maternal age group (41.1% vs. 23.8%, p<0.001).

The rate of low birth weight (LBW) was significantly higher in the advanced maternal age group compared to the younger group (23.4% vs. 13.1%, p<0.001). Likewise, macrosomia was more frequent in the advanced maternal age group (8.1% vs. 3.8%, p<0.001). Female fetal sex was identified as a risk factor for IUGR in the younger age group (6.7% vs. 4.2%, p<0.05; OR: 1.6, 95% CI: 1.1–2.5).

After adjustment for potential confounders, advanced maternal age remained significantly associated with an increased risk of NICU admission (OR: 3.1, 95% CI: 2.2–4.2, p<0.05), IUGR (OR: 1.6, 95% CI: 1.1–2.5, p<0.05), preterm delivery (OR: 8.9, 95% CI: 5.7–14.2, p<0.001), and preeclampsia (OR: 1.8, 95% CI: 1.2–2.6, p<0.05), after adjustment for the number of prenatal visits, pre-pregnancy hemoglobin levels, parity, and gestational age at delivery. Advanced maternal age was also associated with an increased risk of macrosomia (OR: 2.6, 95% CI: 1.6–4.1, p<0.001), whereas the association with LBW was not statistically significant after adjustment.

Discussion

The present large-scale cohort analysis revealed that advancing maternal age is associated with a stepwise increase in several perinatal complications, including higher rates of episiotomy, preterm delivery, macrosomia, IUGR, lower mean birth weight and primary cesarean section.

In a previous investigation by our group, we examined pregnancy outcomes among early adolescent, late adolescent and adult women. That study demonstrated that adolescent pregnancy, particularly in the early-middle period, was independently linked to a higher risk of adverse outcomes after adjusting for prenatal visit frequency. Preterm deliveries, PPROM and NICU admissions were most frequent in the early-adolescent group, whereas the highest cesarean rates were observed in adults (11). These findings suggest that while age may influence the number of prenatal visits, variations in visit frequency do not fully offset age-dependent pregnancy risks. In the current population, women of advanced age attended significantly more prenatal visits. A previous study encompassing 308,149 singleton pregnancies, which used a 35-year cut-off, reported that after adjustment, the risks of maternal near-miss, maternal death, severe maternal morbidity and adverse perinatal outcomes (preterm birth, stillbirth, early neonatal death, perinatal death, low birth weight, NICU admission) were all elevated in the AMA group (12). In our data, low birth weight was more common in the AMA group but became statistically non-significant after multivariate adjustment.

Another large investigation of 37,327 pregnancies found that age ≥40 years was correlated with increased operative deliveries and higher rates of maternal diabetes, hypertensive disorders and extended hospitalization, especially when the fetus was male. Conversely, shoulder dystocia and neonatal respiratory problems were more frequent in male newborns of younger mothers.

In contrast, our results identified female fetal sex as a significant risk factor for IUGR among younger women (6.7% vs. 4.2%, p<0.05, OR 1.6, 95% CI 1.1–2.5) (13). We also evaluated the distribution of pregnancy and neonatal complications by fetal sex, and unlike the earlier report, only female sex emerged as a risk factor for IUGR in the younger age group (6.7% vs. 4.2%, p<0.05, OR:1.6 [1.1-2.5]).

A study of 110,450 pregnancies similarly reported that women aged ≥40 years had higher frequencies of uterine fibroids, pregestational diabetes, chronic hypertension, gestational diabetes, preeclampsia, preterm birth, postpartum hemorrhage, placenta previa, placental abruption, cesarean section, macrosomia and perinatal death compared with women aged 25–29 years (14). This study has several limitations. Due to its retrospective design, certain potentially important confounding variables, including maternal body mass index (BMI), use of assisted reproductive technologies, and pre-existing chronic conditions, were not available in the dataset. The absence of these variables may have influenced the observed associations, and therefore the findings should be interpreted with caution.

Although previous reports have employed varying definitions of advanced maternal age, few have directly contrasted outcomes between women above and below 40 years in such a large sample. Therefore, the primary objective of the present work was to evaluate pregnancy outcomes in women >40 years relative to younger controls within a comprehensive population-based cohort.

Conclusion

Advanced maternal age (> 40 years) is associated with a range of adverse pregnancy outcomes including lower rate of episiotomy requirement, higher rate of preterm deliveries, IUGR, macrosomia, lower mean birth weight and high primary cesarean section rate. These risks remained significant after adjustment for selected confounders, including the number of prenatal visits, pre-pregnancy hemoglobin levels, parity, and gestational age at delivery.

Declarations

Funding

No external funding was used for this study.

Conflicts of interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

Ethics approval

This study was approved by the ethics committee of Zeynep Kamil Research and Training Hospital (date: 30.12.2020, decision no: 195). The study was conducted in accordance with the Declaration of Helsinki.

Availability of data and material

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Authors' contributions

EDK: Concept, design, data analysis, writing – original draft

RK: Data collection, methodology, writing – review & editing

ÇK: Supervision, writing – review & editing

MNCK: Data interpretation, writing – review & editing

EBE: Supervision, project administration, writing – review & editing

All authors read and approved the final manuscript.

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