

## RESEARCH ARTICLE

# Advanced Maternal Age and Adverse Perinatal Outcomes – One Decade Analysis

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## Abstract

**Objective:** To appoint the risk of stillbirth and the other adverse maternal and perinatal outcomes in women of AMA (Advanced maternal age) that traditionally described as pregnancy in women aged 35 years or older.

**Methods:** Our study was a retrospective investigation of all women with singleton pregnancies who gave birth at > 20 weeks' gestation aged 35 - 39 years old (early advanced maternal aged group, group I, n=926), aged 40 - 49 years old (late advanced maternal aged group, group II, n=184) and aged 20 - 35 years old (control group, group III, n=1110) between January 2008 and January 2018. Parameters such as age, parity, fetal sex, fetal birth weight, birth pattern (cesarean and vaginal delivery) were examined. The variables investigated to determine perinatal outcomes were low birth weight, macrosomic fetus and stillbirth frequency.

**Results:** Advanced maternal aged birth ratio to all births was 4.5 %. 83.4% of the advanced age group were the early advanced maternal aged. The low birth weight rate was significantly higher in the AMA group (8.6 % - 5.9 %) (p=0.042). At the same time, the rate of macrosomia was significantly higher in the AMA group too. (9.5 % - 9.1 %) (p=0.042). The rate of caesarean delivery was significantly higher in AMA group (63.7 % - 56.4 %). The stillbirth rate was significantly higher in AMA group (1,6 % - 0,5 %) (p=0.005). In group II; male gender was lower (47.3 % - 55 %) (p=0.034), stillbirth rate was higher (3.8 % - 1.2 %) (p=0.019), birth weight was lower (3193 - 3287) (p=0.048).

**Conclusion:** The risk of stillbirth was significantly higher in the late advanced maternal aged group. Pregnancies over 35 years of age are high-risk pregnancies necessitating more careful antenatal follow-up in which follow-up of pregnancy must be done more carefully. National mother friendly health policies must focus more on AMA pregnancies. More research is needed to find suitable and well-timed interventions to decrease adverse maternal and also perinatal outcomes.

**Key words:** Advanced maternal age, stilbirth, high-risk pregnancies.

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## Introduction

In past three decades, modern industrial life has had prominent effects on women's reproductive life. Today women commonly postpone their pregnancies and childbearing. Therefore, advanced maternal age (AMA) and related problems are rapidly increasing. AMA is traditionally defined as pregnancy in women aged 35 years or older even though some researchers have used the age limits of 40 and insomuch as 45 years (Bianco et al.,1996; Fretts et al.,1997; Dulitzki et al.,1998; van Katwijk et al.,1998; Gilbert et al.,1999).

This trend in today's society is mostly attributed to older primigravid women who postpone childbearing by various reasons include late marriage, longer life expectancy and higher education career pursuit. And also, multiparous women continue childbearing. On the other hand, effective contraceptive methods and modern infertility treatment options encourage women to delay their pregnancies and childbearing (Guedes et al.,2014).

AMA is reported to be associated with maternal complications and adverse pregnancy outcomes (Cleary-Goldman et al.,2005). Preexisting comorbidities (pregestational hypertension and diabetes) and increased risk of Caesarean birth are related with higher risk of maternal complications. Fetal growth restriction, preeclampsia, placental decolman, preterm delivery is more common among AMA women but the strongest association with AMA is stillbirth according to many researches (Cleary-Goldman et al.,2005; Salihu et al.,2008; Bayrampour et al.,2010; Haines et al.,2011; Giri et al.,2012; Kenny et al.,2013; Khalil et al.,2013). Authors investigating the relation between AMA and stillbirth have chiefly focused on placental aging, dysfunction and insufficiency (Smith et al.,2007; Flenady et al.,2011; RCOG Compaining and opinions 2011).

In our study we aimed to investigate the efficacy of AMA on the rate of stillbirth in Ordu, Turkey. And we determined the other adverse maternal and perinatal outcomes in women of AMA that traditionally defined as pregnancy in women aged 35 years or older.

### Methods

This case control study was conducted after receiving approval from the ethics committee (Ordu University Clinical Research Ethics Committee, 26/04/2018, 2018-91). Our study was a retrospective investigation of all women with singleton pregnancies who gave birth at > 20 weeks' gestation aged 35 - 39 years old (early advanced maternal aged group, group I, n=926), aged 40 - 49 years old (late advanced maternal aged group, group II, n=184) and aged 20 - 35 years old (control group, group III, n=1110) at the clinic between January 2008 and January 2018. The control group was randomly formed aged 20 - 35 years old women from 24560 births in the last decade. Adolescent pregnant women (<19 years old) were excluded from the study for not to affect the pregnancy risks of control group. Maternal age was defined as the completed age of the pregnant at the time of delivery.

We separate these groups (named early and late advanced maternal age) because of significance was increasing statistically and also from social aspect maternal age bigger than 40's is increasing much more than maternal age of 35 years old. And we think that late advanced maternal aged pregnant women will increase at the next decades because marriage ages of women will increase due to social reasons especially in developed and developing countries.

Parameters such as age, parity, fetal sex, fetal birth weight, birth pattern (cesarean and vaginal delivery) were examined from hospital registry system and file scanning. The variables used to determine the perinatal outcomes were low birth weight (birth weight < 2500 gr), macrosomic fetus (birth weight > 4000 gr) and stillbirth (delivery of infant > 20 weeks' gestation or > 500 gram weight without cardiac activity) prevalences were investigated and compared between groups.

Statistical analyses were performed with the SPSS 20.0 program package. Mann Whitney-U test or independent samples-t test were used to equate continuous variables, chi square test was used to compare categorical variables.

### Results

The records of 24560 patients who delivered between January 2008 and January 2018 were reviewed. Advanced maternal aged birth ratio to all births was 4.5 % (1110/24560). The mean age of advanced maternal aged pregnancies (> 35 years old) was  $37.3 \pm 2.2$  (35 - 49). 83.4 % of the 1110 advanced age group (926/1110) were the early advanced maternal aged (group I), 16.6 % (184/1110) were the late advanced maternal aged group (group II). As control group, 1110 pregnant women aged 20 - 35-year-old who gave birth at our hospital between the same dates participated in the study (group III). Comparison of mean age among the groups were given in table 1.

There was a statistically significant difference between the groups according to parity. The average of parity was 3.19 (1-9) in the advanced maternal aged groups whereas 2.17 (1-7) in control group (p=0.000).

Birth weight was not significantly different between the groups. The average of birth weight was  $3272 \pm 593$  in the advanced maternal aged group whereas  $3316 \pm 529$  in control group (p=0.61).

**Table 1.** Mean age

	Number	%
<b>Group I (age 35-39)</b>	926/1110	83.4
<b>Group II (age 40-49)</b>	184/1110	16.6
<b>Group III (age 20-35)</b>	1110	

The low birth weight rate was significantly higher in the AMA group (8.6% - 5.9%) ( $p=0.042$ ). At the same time, the rate of macrosomia was significantly higher in the AMA group too. (9.5% - 9.1%) ( $p=0.042$ ).

The rate of caesarean delivery was significantly higher in the AMA group (63.7% - 56.4%). We attributed this to high parity in advanced age pregnancies, birth complications and an increased demand for tubal ligation.

There was no significant difference between the fetal sexes (53.7% - 53%) ( $p=0.383$ ).

The stillbirth rate was significantly higher in advanced age pregnancies (1.6% - 0.5%) ( $p=0.005$ ).

Comparison of variables among the groups were given in table 2.

**Table 2.** Comparison of Variables Between AMA and Control Group

	<b>Group AMA (age 35-49)</b>	<b>Group Control (age 20-35)</b>	
<b>Parity</b>	3.19 (1-9)	2.17 (1-7)	$P=0.000$
<b>Low birth weight rate</b>	8.6	5.9	$P=0.042$
<b>Macrosomia rate</b>	9.5	9.1	$P=0.042$
<b>Stillbirth rate</b>	1.6	0.5	$P=0.005$

There was statistically significant difference between Group I and Group II. In group II; male gender was lower (47.3% - 55%) ( $p=0.034$ ), stillbirth rate was higher (3.8% - 1.2%) ( $p=0.019$ ), birth weight was lower (3193 - 3287) ( $p=0.048$ ).

Comparison of variables among the AMA group I and II were given in table 3.

**Table 3.** Comparison of Variables Between AMA Group I and II

	<b>Group I (age 35-39)</b>	<b>Group II (age 40-49)</b>	
<b>Birth weight</b>	3193	3287	$P=0.048$
<b>Fetal sexes (male)</b>	55	47.3	$P=0.034$
<b>Stillbirth rate</b>	1.2	3.8	$P=0.019$

## Discussion

In the past three decades, a growing number of women delay childbearing up to advanced ages of their lives. In 2013, 20 % of births in England and Wales were to women advanced maternal aged, compared to 6% in 1980 (RCOG Compaining and opinions 2011, ONS statistical bulletins 2014). According to a multi country data, the prevalence of AMA varied greatly from 2.8% in Nepal to 31.1 % in Japan. The overall prevalence of 29 countries (include 308 149 women) was found 12.3 %. And the highest prevalence of 9.5% was observed in women aged 35 - 39 years (Laopaiboon et al., 2014). In our study we have founded the prevalence 4.5 % below the world average. We also have seen that the early advanced maternal age group ratio to all advanced maternal aged group was 83.4 % whereas 77.2 % in the world average.

Women over age 35 are at increased maternal and perinatal complications when compared to younger women. Such that for no other reason being > 35 years old is associated with high risk pregnancy (Ihab et al., 2008).

Several studies have showed the association between increased fetomaternal adverse outcomes and AMA. Decreased fecundity, high risk of miscarriage, negative impact on in vitro fertilization are affecting the success in conception and pregnancy maintenance. In the antepartum and intrapartum period congenital anomalies, multiple gestation, preeclampsia, gestational diabetes, placental abruption, placenta previa, preterm delivery, low birth weight, macrosomia, malpresentation are important concerns that increasing the severe maternal adverse outcomes including maternal near miss, severe maternal outcome and maternal death and perinatal adverse outcomes. In the postpartum period hemorrhage and also depression is thought to be more prevalent among AMA women (Ihab et al., 2008; Laopaiboon et al., 2014).

Low birth weight may be due to age-related changes in the uterine vasculature, poorer placental perfusion. Multiparity, maternal obesity, smoking and maternal preexisting comorbidities (pregestational hypertension and gestational diabetes) are more common among the older pregnant and increases the adverse perinatal outcomes (Godfrey et al., 1999; Ihab et al., 2008). According to our study birth weight was significantly lower in the > 40 years old group (3193 vs 3287 and 3316). And the low birth weight rate was significantly higher in each AMA groups (8.6 % - 5.9 %).

Maternal obesity and gestational diabetes are also occurring macrosomia. In the recent study the rate of macrosomia was significantly higher in the AMA groups (9.5 % - 9.1 %).

Male: female fetus ratio is bigger than one in the young mothers. But female fetus dominance come up in the AMA women. That advanced aged women miscarry more male fetuses has been used to provide a comment for this observation. In the study male gender was lower in the > 40 years old group (47.3 % vs 55 % and 53 %).

Despite of the recommendations of World Health Organization the cesarean delivery rate has risen rapidly worldwide in recent years that is a important health concern. Because the proportion of advanced maternal aged women is growing, and intercalarily, the cesarean delivery rate is increasing. Several studies have found that advanced maternal age is a risk factor for cesarean delivery (Bayrampour et al.,2010). The rate of caesarean birth was significantly higher in the AMA group (63.7 % vs 56.4 %). We attributed this to high parity, birth complications and an increased demand for tubal ligation. Some authors identified maternal request as one of the factors subscribing to the increasing cesarean birth rate among primiparous women who had in vitro fertilization pregnancy (Roberts et al.,2002; Lin et al.,2004; O'Leary et al.,2007).

There are also some limitations in our article. We designed the study as a retrospective case control study. Prospective studies that including more women (like country studies) can give more information about this growing health concern.

### Conclusion

The prevalence of ten years results of advanced aged pregnancies was 4.5 % in our study. Cesarean delivery, low birth weight and macrosomic fetus rate was found to be higher than control group. The risk of stillbirth was significantly higher in the over 40-year-old group compared to the control group. This data has showed that increase in adverse outcomes present from age 35 years but gains speed after 40 years.

Pregnancies over 35 years of age are high-risk pregnancies necessitating more careful antenatal follow-up in which follow-up of pregnancy must be done more carefully. AMA pregnant should referred to centers, including neonatal intensive care units.

**Ethics Committee Approval:** Ethics committee approval was received for this study from Clinical Research Ethics Committee of Ordu University Medical Faculty.

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