BIRTH OUTCOMES OF ADVANCED MATERNAL AGE PREGNANCIES

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SUMMARY

Objective: Pregnancy at advanced maternal age has become more common over the last decades. Therefore, the study aimed to describe the characteristics and maternal and perinatal outcomes of women giving birth at advanced maternal age and very advanced age.

Methods: We conducted a retrospective cohort study of 2,300 singleton births that occurred in 2020–2021 at the Department of Gynaecology and Obstetrics of the Louis Pasteur University Hospital in Košice. The control (age 20–34 years), advanced maternal age (35–39 years), and very advanced maternal age (≥ 40 years) groups included 1,851, 382, and 67 women, respectively. Exclusion criteria were multiple pregnancies, maternal age less than 20 years, smoking and alcohol use, foetal malformation and intrauterine foetal death, and birth weight of 500 grams or less. Data on mothers and newborn infants have been reported from the birth book and the reports on mothers at childbirth. The data were analysed using IBM SPSS Statistics 23.0.

Results: Our results confirmed statistically significant differences regarding the rate of preterm birth ($p = 0.004$), very preterm birth ($p = 0.010$), caesarean delivery rate ($p < 0.001$), very low birth weight ($p = 0.027$), extremely low birth weight ($p = 0.001$), and Apgar score at 5 minutes < 7 ($p = 0.020$) between newborns in the compared maternal age groups.

Conclusion: Advanced maternal age is a prognostic factor for poor pregnancy outcomes. Women of advanced maternal age are at higher risk of adverse obstetric and perinatal outcomes.

Key words: birth outcomes, advanced maternal age, very advanced maternal age, risk factors, birth weight, preterm birth

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INTRODUCTION

Pregnancy at advanced maternal age (AMA) has become more common in both developed and developing countries over the last decades. Postponement of childbearing is a widespread phenomenon, with many countries exhibiting mean ages at birth well exceeding previous generations. A trend has developed worldwide for women to delay childbearing into their 30s and, in some cases, their 40s. The number of pregnancies among women in AMA continues to escalate. Whether or not the maternal age is considered advanced is affected by sociological, ethnic and cultural considerations as well. Women may choose to delay pregnancy to complete higher education, develop their careers, gain financial security, or for their own choice. Limited job-related policies (e.g., unavailability or limitations of childcare, low benefit levels, policies unfavourable to motherhood and career) are among other reasons for delaying motherhood. Education and job opportunities contribute to delaying motherhood until later in life (1–6).

It is difficult to define a specific age threshold for pregnancy outcomes, as the effects of increasing age on pregnancy outcomes seem to occur more as a continuum. No universal consensus on the definition of AMA exists. This terminology currently refers to the later years of a woman's reproductive life span and generally applies to women aged ≥ 35 years. Regardless of the age used to define AMA, pregnancies in women aged ≥ 35 years are considered at risk of both obstetric complications and interventions (1, 2, 7–12). Beyond that, maternal age above 40 is considered a very advanced maternal age (VAMA), and above 45, is an extremely advanced maternal age (EAMA) (2, 4, 8–10).

With advanced maternal age, we have to contend with the fact that women are more likely to have pre-existing health conditions. Pregnancy in older mothers is associated with increased risks of adverse pregnancy outcomes for both the pregnant mother and the foetus (13). Lower fertility, a greater need for assisted reproductive therapy, and an increase in comorbidities, such as hypertension and diabetes, are some of the reasons for the rise of adverse outcomes (7, 8). With aging, the prevalence of coexisting conditions (e.g., cancer, diabetes, obesity, cardiovascular, renal, and autoimmune diseases) increases considerably, putting pregnant women aged ≥ 35 years at high risk of experiencing higher rates of hospitalization, caesarean delivery, and other pregnancy-related complications (1, 13, 14).

The association between adverse perinatal outcomes and advanced maternal age has been a matter of controversy in several studies. While some researchers have noted an increased rate of adverse pregnancy outcomes in women older than 35 years, others have failed to find any association between advanced maternal age and adverse perinatal outcomes.

Therefore, in this study, we focused on the observation of perinatal and neonatal outcomes in mothers of advanced age in singleton pregnancies.

MATERIALS AND METHODS

The data in this study were obtained from January 2020 to December 2021. The collection of data took place in the context of the daily work of the Department of Gynaecology and Obstetrics of the Louis Pasteur University Hospital and the academic and research activity of the Faculty of Medicine of Pavol Jozef Šafárik University in Košice. Basic medical records on mothers and basic data on newborns were collected from the reports on mothers at childbirth. The study was approved by the Ethics Committee of the Louis Pasteur University Hospital.

Singleton pregnancies among women aged ≥20 years who delivered at 20 weeks of gestation or greater or birth weight larger than 500 g between 1 January 2020 and 31 December 2021 were included in this study.

Exclusion criteria were multiple pregnancies, maternal age less than 20 years, smoking and alcohol use, foetal malformation and intrauterine foetal death, and birth weight of 500 grams or less.

We categorized them into three groups: 20–34 years, 35–39 years, and ≥40 years. VAMA was defined as women aged ≥40 years at delivery. The age of mothers at the time of delivery was calculated based on the date of birth indicated in the reports on mothers at childbirth and delivery date.

A total of 2,300 women met the study criteria, of which 1,851 were assigned to the control group (aged 20–34 years), whereas 382 formed the advanced maternal age (35–39 years) and 67 very advanced maternal age (40 years or more) groups.

The main adverse birth outcomes included gestational diabetes, preterm delivery, post-term delivery, and caesarean delivery. Gestational diabetes mellitus (GDM) was diagnosed based on a positive 75-g oral glucose tolerance test result, according to the one-step diagnostic approach between 24 and 28 weeks of gestation. Preterm deliveries were in turn divided into preterm deliveries (<37 weeks), very preterm deliveries (<32 weeks), and extremely preterm deliveries (below 28 weeks). Caesarean delivery was defined as a surgical procedure for the delivery of a foetus by an abdominal route.

The main adverse neonatal outcomes included were low birth weight and low Apgar score (<7 at 1st and 5 mins.). Birth weight was categorized as low birth weight (less than 2,500 g), very low birth weight (less than 1,500 g), extremely low birth weight (less than 1,000 g), and macrosomia (birth weight greater than 4,000 g).

The data were analysed using Statistical Product and Service Solutions (IBM SPSS Statistics for Windows, Version 23.0. IBM Corp., Armonk, NY, USA). Maternal demographic characteristics and clinical factors were compared among the three age groups. Categorical variables were described by counts and percentages. Chi-square tests or Fisher's exact tests were performed for categorical data. Differences were considered significant when p-values were <0.05.

RESULTS

During the study period, 2,926 singleton deliveries occurred at the Department of Gynaecology and Obstetrics of the Louis Pasteur University Hospital in Košice. Of these, 2,300 met the study criteria for analysis, 80.5% were aged 20–34 years, 16.6% 35–39 years, and 2.9% were aged ≥40 years. The demographic characteristics of the study population are summarized in Table 1.

Preterm delivery, very preterm delivery, and caesarean delivery rates were higher in the very advanced maternal age group than in the advanced maternal age and control groups, and the differences are statistically significant. There were no significant differences in gestational diabetes mellitus, spontaneous preterm delivery before 28 weeks of gestation and post-term delivery rates between the groups. The frequencies of complications according to maternal age group are described in Table 2.

Our results confirmed statistically significant differences regarding the rate of very low birth weight, extremely low birth weight, and Apgar score at 5 minutes <7 between newborns in the compared maternal age groups. The neonatal outcomes are shown in Table 3.

Table 1. *Maternal characteristics*

Maternal characteristics	Maternal age groups			p-value
	20–34 years n (%)	35–39 years n (%)	≥40 years n (%)	
Education				
Primary school	194 (13.7)	17 (6.0)	5 (9.1)	**0.001**
High school	659 (46.4)	126 (44.2)	31 (56.4)	
Graduated or higher	566 (39.9)	142 (49.8)	19 (34.5)	
Marital status				
Single	425 (28.7)	43 (14.2)	10 (17.9)	**<0.001**
Married	1040 (70.2)	242 (79.9)	39 (69.6)	
Divorced/widowed	17 (1.1)	18 (5.9)	7 (12.5)	

Numbers in bold indicate statistically significant values.

Table 2. *Birth outcomes according to maternal age group*

Perinatal outcomes	Maternal age groups			p-value
	20–34 years n (%)	35–39 years n (%)	≥ 40 years n (%)	
Gestational diabetes mellitus	16 (0.9)	5 (1.3)	1 (1.5)	0.647
Preterm delivery (< 37 weeks)	230 (12.4)	59 (15.4)	17 (25.4)	**0.004**
Very preterm delivery (< 32 weeks)	67 (3.6)	20 (5.2)	7 (10.4)	**0.010**
Extremely preterm delivery (< 28 weeks)	23 (1.2)	9 (2.4)	1 (1.5)	0.249
Post-term delivery	4 (0.2)	1 (0.3)	0 (0.0)	0.914
Caesarean delivery	464 (25.1)	136 (35.6)	27 (40.3)	**< 0.001**

Numbers in bold indicate statistically significant values.

Table 3. *Neonatal outcomes according to maternal age group*

Neonatal outcomes	Maternal age groups			p-value
	20–34 years n (%)	35–39 years n (%)	≥ 40 years n (%)	
Low birth weight (< 2,500 g)	229 (12.4)	50 (13.1)	14 (20.9)	0.118
Very low birth weight (< 1,500 g)	77 (4.2)	22 (5.8)	7 (10.4)	**0.027**
Extremely low birth weight (< 1,000 g)	28 (1.5)	10 (2.6)	5 (7.5)	**0.001**
Macrosomia (> 4,000 g)	110 (5.9)	21 (5.5)	5 (7.5)	0.814
Apgar score at 1st min. < 7	153 (8.3)	24 (6.3)	9 (13.4)	0.115
Apgar score at 5 mins. < 7	71 (3.8)	6 (1.6)	5 (7.5)	**0.020**

Numbers in bold indicate statistically significant values.

DISCUSSION

The incidence of insulin resistance and diabetes mellitus increases with age, and it is thus not surprising that the incidence of GDM also increases with AMA. Women of advanced maternal age (35–40 and > 40 years) have a higher probability of GDM. Preexisting diabetes is associated with increased risks of congenital anomalies and perinatal mortality and morbidity (1).

A retrospective study by Khalil et al. (15) describes an increased GDM incidence of 1.62 (95% CI: 1.43–1.83, $p < 0.001$) and 2.1 (95% CI: 1.74–2.55, $p < 0.001$) at AMA and VAMA, respectively, compared to women under the age of 35 years (8, 15, 16). In our study, the GDM rate was higher in the very advanced maternal age group (1.5%) than in the advanced maternal age (1.3) and control groups (0.9%), but the differences were not statistically significant. A higher probability of GDM in older pregnant women was also confirmed by Bianco et al. (17).

The main complication of gestational diabetes is macrosomia (1, 16). However, in our study, the differences in the prevalence of macrosomia were not confirmed as statistically significant between individual age groups of mothers.

The highest prevalence of preterm and very preterm births was in the oldest age group. Between the age groups of women, statistical differences in the number of preterm deliveries ($p = 0.004$), and in the number of very preterm deliveries ($p = 0.010$) were confirmed. Similarly, a contemporary large retrospective study found that pregnancy at VAMA increase the risk of preterm labour by 1.2 (95% CI: 1.06–1.36) as compared to pregnancy at 30–34 years of age (18). According to the results of Frederiksen et al. (19), pregnant women aged 40 years or older had a higher risk of delivery before the 34th week of pregnancy compared to women aged 20–34 years.

There were no statistically significant differences in spontaneous extremely preterm delivery before 28 weeks of gestation and post-term delivery rates between the groups.

The risk for caesarean delivery increases dramatically with age, which is consistent with previous studies (12, 20). A retrospective cohort study demonstrated that the primary caesarean delivery incidence for 25 to 34 years (reference group) was 20.0%, the incidence for the AMA group was 25.9%, and the incidence for the VAMA group was 30.9%. The EAMA incidence was 35.7%, and, in women above the age of 50 years, the caesarean delivery incidence was 60.7% (20).

According to a cohort study of 78,000 singleton births, the caesarean delivery rate in women aged 25–34 years was 20%, and rose gradually to 36% for women aged 45–49 years, reaching as high as 61% for women aged over 50 years (1, 21, 22).

In our study, the caesarean delivery rate in women aged 20–34 years was 25.1%, 35.6% in women aged 35–39 years, and, in women above the age of 40 years, the caesarean delivery incidence was 40.3%. The rising rate of caesarean sections can be attributed to several factors: the age-related weakening of the myometrium, a decrease in the number of oxytocin receptors, a lower clinical threshold for obstetric interventions, and higher incidences of maternal systemic diseases and obstetric complications (10).

In a cross-sectional study from Japan, the authors did not find a difference in low Apgar scores (5 mins. < 7) among women with AMA, VAMA and EAMA (23). Similarly, Kahveci et al.

(10) examined the impact of advanced maternal age on neonatal outcomes in Turkey and found no significant differences regarding Apgar scores among women with AMA and VAMA. Our results confirmed statistically significant differences in the Apgar score at 5 minutes <7 among women with AMA, VAMA and EAMA.

Delbaere et al. (24) found increased rates of low birth weight (adjusted OR 1.69, 95% CI: 1.47–1.94), very low birth weight (aOR 1.62, 95% CI: 1.15–2.28), and extremely low birth weight (aOR 2.14, 95% CI: 1.29–3.56) in primiparas of advanced maternal age. Our study confirms statistically significant differences in the incidence of very low birth weight and extremely low birth weight between the maternal age groups.

Limitations of the Study

The conclusions of this study should be considered with an awareness of the limitations in the dataset and study design. Notably, the study cannot fully account for factors like exposure to infections and drug use, which may vary between the groups. The study did not look at whether the woman was a first-time mother.

CONCLUSIONS

Advanced maternal age is a prognostic factor for poor pregnancy outcomes. Women of advanced maternal age are at higher risk of adverse obstetric and perinatal outcomes. Poorer outcomes are more common in the oldest group, suggesting that poorer outcomes are more common with increasing age. Most of the adverse outcomes can be explained through the physio-pathological changes related to the female reproductive system that come with aging and its inherent co-morbidities.

Women of advanced maternal age should be encouraged to enhance their health in preparation for pregnancy. This includes quitting smoking and alcohol consumption, starting a regular exercise routine, reaching a healthy body weight, taking folic acid supplements, and managing any existing health conditions.

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Conflicts of Interest

None declared

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