

# Pregnancy outcomes at advanced maternal age in a tertiary Hospital, Jeddah, Saudi Arabia

Ettedal A. AlJahdali, ABOG, SBOG, Nawal S. AlSinani, ABOG, SBOG.

## ABSTRACT

**الأهداف:** تقييم نتائج هذه المضاعفات أثناء الحمل والولادة للأم والجنين بين النساء ذوات السن المتقدم.

**المنهجية:** أجريت دراسة جماعية بأثر رجعي في مستشفى تعليمي بجدة المملكة العربية السعودية خلال 18 عاماً (يناير 2003م إلى ديسمبر 2020م). في هذه المستشفى أنجبت 79095 سيده، وأخذت منهن عينة عشوائية شملت 4318 سيده حامل في جنين واحد، من بينهن 2162 سيده تبلغ من العمر  $\leq 40$  عاماً. وتقييم العلاقة بين سن الأم المتقدم ونتائج الحمل والجنين.

**النتائج:** سن الأم المتقدم مرتبط بشكل مستقل بالعرق غير السعودي، وزن الأم 80-99 كجم، مرض البول السكري، وارتفاع ضغط الدم. الأمهات ذوات السن المتقدم أكثر عرضة لتمزق الغشاء الامنيوني السابق لاوانة، الولادة القيصرية، ونزيف ما بعد الولادة. مواليد السيدات ذات السن المتقدم معرضين لوزن أقل من 2500 غرام عند الولادة، و وزن المواليد 3600-4500 غرام، وانخفاض درجة أبعاد عند 5 دقائق، ودخول المواليد العناية المركزه.

**الخلاصة:** يشكل عمر الأم المتقدم عامل خطر مستقل بالنسبة للنتائج السلبية المتعلقة بولادة الأمهات، مثل الولادة القيصرية، والنزيف أثناء الحمل، ومرض السكري، وارتفاع ضغط الدم، والتمزق المبكر للغشاء الامنيوني، ونزيف ما بعد الولادة، ومضاعفات الجنين مثل انخفاض الوزن عند الولادة، وزيادة وزن الجنين، ودخول العناية المركزه للمواليد، والنشوهات الخلقية، وانخفاض درجة أبعاد عند الولادة. ويجب أن ينظر مقدمو الرعاية الأمومية بعناية في هذه النتائج لتحسين التردد السريري بشكل فعال.

**Objectives:** To evaluate obstetrical and fetal outcomes among advanced maternal age (AMA) women.

**Methods:** Retrospective cohort study carried out at a teaching hospital, Jeddah, Saudi Arabia, during 18 years period (from January 2003 until December 2020). A total of 79095 women gave birth, and randomized block was used to include 4318 singleton pregnancy women ( $>28$  gestational weeks), of them 2162 age  $\geq 40$  years. Associations between AMA and obstetrical and fetal parameters were assessed.

**Results:** Advanced maternal age independently associated with non-Saudi national, mother's weights 80-99 kg, diabetes mellitus, and hypertension. Advanced maternal age mothers were more liable to premature rupture of membranes (PROM), caesarean

(CS) deliveries, and postpartum hemorrhage. Newborn of AMA women were at high risk of birth weight  $<2500$  g, birth weight 3600-4500 g, decline Apgar score at 5 minutes, and neonatal intensive care unit (NICU) admissions.

**Conclusion:** Advanced maternal age is an independent risk factor for adverse obstetric hazards as CS, antepartum haemorrhage, diabetes mellitus, hypertension, PROM, postpartum hemorrhage, and fetal complications as low birth weight, macrosomia, NICU admission, congenital anomalies, and low Apgar score. These results must be carefully considered by maternal care providers to effectively improve clinical surveillance.

**Keywords:** advanced maternal age, fetal outcome, pregnancy outcome, obstetric complications, risk factors

*Saudi Med J* 2022; Vol. 43 (5): 491-499  
doi: 10.15537/smj.2022.43.5.20220023

From the Department of Obstetrics and Gynecology, Faculty of Medicine, King Abdulaziz University Hospital, Jeddah, Kingdom of Saudi Arabia.

Received 23rd January 2022. Accepted 18th March 2022.

Address correspondence and reprint request to: Dr. Ettedal A. AlJahdali, Associate Professor, Department of Obstetrics and Gynecology, Faculty of Medicine, King Abdulaziz University, Jeddah, Kingdom of Saudi Arabia. E-mail: dr.aljahdali@hotmail.com  
ORCID ID: <https://orcid.org/0000-0002-9858-8417>

Pregnancies at advanced maternal age (AMA) have steadily grown over a few previous decades. Women around the world are deferring birth until later in life, according to reports from both low- and high-income countries.<sup>1</sup> In China, birth rate in females aged from 35-39 years raised from 2004 (8.6%) to 2014 (17%), and in females aged from 40-44 years, birth rate elevated from 1.8-4%. Meanwhile, birth rate in women

of 25-29 years declined from 102.4% into 93.6%.<sup>2</sup> In 2016, advanced pregnancies ratio was 31.0% of total pregnancies.<sup>3</sup> In Saudi Arabia and other Middle Eastern countries, females still get children after 35 years, owing to a solid family financial situation in which the husband is the primary breadwinner and the desire to have large families.<sup>4</sup>

Many women delayed childbearing into their later reproductive life for various causes, including marriage postpone, late pregnancy because of infertility, career advancement and higher education, prolonged life expectancy, more effective contraceptive techniques, recent infertility therapy, the need for large family, and absence or ineffective family planning.<sup>5</sup> In contrast to developed countries, where AMA females were most likely primiparous, childbearing at AMA is the most common between multiparous women in developing countries due to ineffective family planning methods, a cultural preference for big families, and poverty.<sup>6</sup>

Although delayed childbearing and AMA effects on maternal and perinatal outcomes investigated, obstetric literature differs on what constitutes AMA. Maternal advanced age is traditionally described as being >35 years old at delivery time, although other authors utilized limitation age of 40 and even 44 years.<sup>7,8</sup> In spite of cutoff AMA is, pregnancies in females aged >35 years subjected to risk of both obstetric interventions and complications. While the majority of these studies found a strong link between age and pregnancy outcome, others came up with contradictory results.<sup>9</sup> Advanced maternal age is associated with raised risk of perinatal deaths, spontaneous abortions, complications of pregnancy as diabetes mellitus and hypertension; interventions as caesarean (CS) deliveries, labor induction, fetal complications as preterm birth, low birth weights, and congenital anomalies.<sup>10</sup>

Given the significant rise in number of older mothers and paucity of evidence in the literature, it is critical to figure out whether and how AMA affects the health of both mother and newborn. Currently, there is limited published information in Saudi Arabia that reveal associations between AMA ( $\geq 40$  years), obstetrical, and neonatal outcomes. This retrospective research aimed to evaluate obstetrical and newborn outcomes in association with AMA in females with singleton pregnancies at a tertiary teaching university hospital, Jeddah, Saudi Arabia.

**Methods.** This retrospective cohort research was carried out from January 2003 until December 2020 on females attended antenatal visits and delivered in the Department of Obstetrics and Gynecology, King Abdulaziz University Hospital, Jeddah, Saudi Arabia. Ethical approval was obtained from the Ethical Committee Broad of King Abdulaziz University Hospital. Study protocol was carried out according to Declaration of Helsinki.

Total numbers of deliveries during research duration of 18 years were 79095. In this study, randomized block method was used to include only 4318 singleton pregnancy. Block randomization is the most common used method in clinical research to decrease bias in selection of participants. This method elevates the probability that each arm of the research had almost the same numbers of individuals by sequencing participant assignments by block. In this study delivered women were divided into 2 groups, those <40 years and those  $\geq 40$  years and then participants of each group were selected followed by several blocks of participants and so on in each year to choose the appropriate sample size instead of a large number of delivered women during 18 years period of the study. The research group included females aged  $\geq 40$  years at delivery ( $n=2162$ ), while women of <40 years formed the comparison group ( $n=2156$ ). Females with singleton pregnancies that lasted >24 weeks and whose gestational age established by ultrasound scan were eligible to participate. Exclusion criteria were women <20 years, multiple pregnancies, pregnancy with reproductive aid methods, and having known physical and mental diseases (such as kidney, immune diseases, cancers, hepatitis, and sexually transferred diseases, so on). Major fetal abnormalities, multiple gestations, and microdeletions or aneuploidies verified by karyotype or array-comparative genomic hybridization were also excluded.

The data was obtained from department's computerized database and available hospital records over the 18-year period. The obstetrical characteristics and complications such as nationality, mother's weights, maternal age groups, mother's comorbidity, antipartum hemorrhage, gravidity, parity, numbers of vaginal or CS deliveries, delivery mode, amniotic membrane rupture mode, amniotic fluid status, total labor duration, post-partum complications such as retained placenta, and postpartum hemorrhage were assessed. The newborn data such as birth weights, Apgar score at 5 minutes, neonatal intensive care unit (NICU) admission, abnormality of newborn, and viability were collected.

**Disclosure.** Authors have no conflict of interests, and the work was not supported or funded by any drug company.

Vaginal bleeding due to placental abruption, placenta previa, pregnancy difficulties after 24 weeks, extra-uterine causes, and hemorrhage due to unknown origin were characterized as APH. When in late pregnancy edge of placenta covered or within 2 cm of internal cervical orifice, trans-vaginal ultrasonography was used to identify placenta previa. Premature rupture of amniotic fluid (PROM) is defined as amniotic membranes rupture before 37 weeks of gestation. Elective CS deliveries are made only for one or more and medical indications. Emergency CS deliveries such as CS is carried out after labor onset, suspected fetal distress, intrapartum or severe APH. Multiparity was considered when gravid was  $\geq 2$ . Postpartum hemorrhage described as loss of blood  $>500$  mL for vaginal birth or 1000 mL for CS birth, requiring hysterectomy or concentrated red cell transfusion. Gestational age was estimated referred to information from last menstrual cycle and first trimester ultrasound scan. Neonatal weight was divided into 4 categories: large for gestational age (birth weight  $>90^{\text{th}}$  percentile for gestation based upon local reference chart); small for gestational age (birth weight  $10^{\text{th}}$  percentile); macrosomia (birth weight  $>4500$  grams); and low birth weight (birth weight  $<2500$  grams). Preterm all births  $<37$  weeks and  $>27$  gestational weeks or  $<259$  days from day one of woman's last menstrual cycle. Miscarriage is spontaneous fetal loss  $<22$  week of gestation. Abortion is termination or initiation of termination of pregnancy before reaching viability (before 28 weeks of gestation or  $<1$  kg fetal weight). Intrauterine growth restriction defined as less than  $10^{\text{th}}$  percentile of normal neonatal weight. Stillbirth defined as fetal mortality happened beyond 28 weeks of pregnancy or when baby weighed  $>400$  grams at birth. A low Apgar score is score of less than 7 at 1 or 5 minutes. Prior researches carried out regarding obstetric and neonatal complications were searched on, using Google Scholar by searching key words versus subjects.

**Statistical analysis.** Statistical Package for the Social Sciences, version 23.0 (IBM Corp., Armonk, NY, USA) was utilized for analysis. Frequencies and percentages were utilized for categorical data. Categorical data compared utilizing  $\chi^2$  test (with Yates correction) or Fisher exact test. Association between mother age and obstetric and newborn factors were determined using cross tabulation ( $\chi^2$ ) to estimate odd's ratios (ORs) and 95% confidence interval (CI). Variations considered significant at a  $p$ -value of  $<0.05$ .

**Results.** Among all pregnancies, 2162 (51.1%) were women aged  $\geq 40$  years and 2156 (48.9%) were women

age  $<40$  years. Women aged  $\geq 40$  years were more non-Saudi, weigh 80-99 kg than women younger  $<40$  years ( $p<0.0001$ ). The percentages of Saudi mothers' weight (40-59 kg and  $>100$  kg) were significantly decreased in females aged  $\geq 40$  years versus younger age group ( $p<0.0001$ ). To identify AMA independent role on variable outcomes determined in cross tabulation analysis to calculate ORs and 95% CI were carried out for maternal and newborn variables. Advanced maternal age was independently linked with non-Saudi national (OR=1.600, 95% CI: [1.418-1.809]), mother's weight 80-99 kg (OR=2.420, 95% CI: [2.049-2.857]) (Table 1).

Females aged  $\geq 40$  years were more gravidity, parity, number of vaginal deliveries  $\geq 5$ , and once made CS than women aged  $<40$  years ( $p<0.0001$ ). Percentages of gravidity and parity 2-4, number of vaginal deliveries (0 and 2-4), and no CS were significantly decreased in females aged  $\geq 40$  years versus younger age group ( $p<0.0001$ ). Advanced maternal age was independently linked with gravity 1 and  $\geq 5$ , parity 0, 1, and  $\geq 5$ , number of vaginal deliveries  $\geq 5$ , and once CS than women aged  $<40$  years (Table 2).

Women aged  $\geq 40$  years had more diabetes mellitus and hypertension than women aged  $<40$  years ( $p<0.0001$ ). Advanced maternal age was independently linked with diabetes mellitus, and hypertension. Women aged  $\geq 40$  years were more in type of labor not available (N/A), membrane (premature rupture of amniotic membrane [PROM], spontaneous rupture of membranes [SROM]), meconium amniotic fluid, total duration of labor (N/A,  $<6$  hours, and 13-20 hours), CS, and postpartum hemorrhage (PPH) than women aged  $<40$  years ( $p<0.0001$ ). The percentages of type of labor (spontaneous, membrane, and none), clear amniotic fluid, total labor duration (6-12 hours), spontaneous vaginal delivery (SVD), instrument deliveries, and retained placenta were significantly decreased in females aged  $\geq 40$  years versus younger age group ( $p<0.0001$ ). Advanced maternal age was independently linked with labor N/A, PROM, and SROM, meconium amniotic fluid, total labor duration of N/A,  $<6$  hours, and 13-20 hours, CS, and PPH (Table 3).

Newborn of women aged  $\geq 40$  years were more birth weight  $<2500$  grams, 3600-4500 grams, abnormal Apgar score, and admission to NICU versus women aged  $<40$  years ( $p<0.0001$ ). The birth weight 2500-3560 kg, dead newborn, and still birth significantly decreased in females aged  $\geq 40$  years versus younger age group ( $p<0.0001$ ). Advanced maternal age was independently linked with birth weight  $<2500$  grams, birth weight 3600-4500 grams, abnormal Apgar score, and admission to NICU (Table 4).

**Table 1** - Sociodemographic characteristics in relation to maternal age (N=4318).

Characteristics	Total	Mother age <40 years	Mother age ≥40 years	Fisher's exact test	OR (95% CI)
<i>Nationality</i>					
Saudi	2302 (53.9)	1265 (58.7)	1037 (48.1)	<0.0001	0.625 (0.554-0.705)
Non-Saudi	1972 (46.1)	853 (40.3)	1119 (51.9)	<0.0001	1.600 (1.418-1.806)
<i>Mother's weight</i>					
40-59 kg	254 (10.6)	218 (19.2)	36 (2.9)	<0.0001	0.124 (0.086-0.179)
60-79 kg	944 (39.4)	461 (40.5)	483 (38.4)	0.295	0.914 (0.776-1.077)
80-99 kg	1061 (44.3)	376 (33.1)	685 (54.5)	<0.0001	2.420 (2.049-2.857)
>100 kg	136 (5.7)	82 (7.2)	54 (4.3)	0.003	0.577 (0.405-0.822)
<i>Age groups</i>					
<40 years	2156 (49.9)	2156 (100)	-	<0.0001	-
≥40 years	2162 (50.1)	-	2162 (100)	-	-
40-42 years	1020 (23.8)	-	1076 (49.8)	-	-
43-45 years	718 (16.7)	-	718 (33.2)	-	-
>45 years	368 (8.6)	-	368 (17.0)	-	-

The values presented as number and percentages (%). Fisher's exact test utilized to see whether there was a significant difference between groups. OR: odds ratio, CI: confidence interval

**Table 2** - The association between obstetrics histories and maternal age (N=4318).

Pregnancy related characteristics	Total	Mother age <40 years	Mother age ≥40 years	Fisher's exact test	OR (95% CI)
<i>Gravidity</i>					
1	49 (1.1)	5 (0.2)	44 (2.0)	<0.0001	8.937 (3.537-22.582)
2-4	466 (10.8)	315 (14.6)	151 (7.0)	<0.0001	0.439 (0.358-0.538)
≥5	3803 (88.1)	1836 (85.2)	1967 (91.0)	<0.0001	1.758 (1.455-2.124)
<i>Parity</i>					
0	51 (1.2)	5 (0.2)	46 (2.1)	<0.0001	9.352 (3.709-23.582)
1	97 (2.2)	38 (1.8)	59 (2.7)	0.020	1.564 (1.036-2.361)
2-4	1108 (25.7)	769 (35.7)	339 (15.7)	<0.0001	0.335 (0.290-0.388)
≥5	3062 (70.9)	1344 (62.3)	1718 (79.5)	<0.0001	2.338 (2.041-2.678)
<i>Number of previous vaginal deliveries</i>					
0	640 (14.8)	388 (18.0)	252 (11.7)	<0.0001	0.601 (0.507-0.713)
1	94 (2.2)	49 (2.3)	45 (2.1)	0.678	0.914 (0.607-1.376)
2-4	876 (20.3)	578 (26.8)	298 (13.8)	<0.0001	0.436 (0.374-0.510)
≥5	2708 (62.7)	1141 (52.9)	1567 (72.5)	<0.00001	2.343 (2.064-2.659)
<i>Number of previous caesarian section</i>					
0	3436 (79.6)	1816 (84.2)	1620 (74.9)	<0.0001	0.560 (0.481-0.651)
1	495 (11.5)	152 (7.1)	343 (15.9)	<0.0001	2.486 (2.033-3.040)
2-4	349 (8.1)	163 (7.6)	186 (8.6)	0.219	1.151 (0.927-1.433)
≥5	38 (0.9)	25 (1.2)	13 (0.6)	0.052	0.516 (0.263-1.011)
<i>Type of previous labors</i>					
N/A	551 (12.8)	166 (7.7)	385 (17.8)	<0.0001	2.598 (2.142-3.150)
Spontaneous vaginal delivery	3509 (81.3)	1861 (86.3)	1648 (76.2)	<0.0001	0.508 (0.434-0.595)
Induction delivery	258 (6.0)	129 (6.0)	129 (6.0)	1.000	0.997 (0.775-1.282)

The values presented as number and percentages (%). Fisher's exact test utilized to see whether there was a significant difference between groups. N/A: not available, OR: odds ratio, CI: confidence interval

**Discussion.** Data from this research revealed that Saudi females aged <40 years were significantly higher than those ≥40 years. While, in non-Saudi women aged ≥40 years were significantly more versus <40 years. These results reflected social status in the Saudi world where women married early and delivered early in age.<sup>11</sup>

Most women aged ≥40 years recruited in this study had body weight 80-99 kg. While those <40 years

had body weight mostly 60-79 kg. Previous research linked AMA to increase in frequency of overweight and obesity among Saudi women.<sup>12</sup> Maternal obesity linked with elevated risk of CS deliveries, gestational diabetes mellitus (GDM), macrosomia, and stillbirth.<sup>13</sup> In this study, women with AMA had 91.0% gravidity and 79.5% parity ≥5. In this regard, Fayed et al<sup>4</sup> found that roughly 90% of women aged 40 had a high parity rate.

**Table 3 -** The association between maternal outcomes and mothers age.

Variables	Total	Mother age <40 years n (%)	Mother age ≥40 years	Fisher's exact test	OR (95% CI)
<b>Comorbidity</b>					
None	3460 (80.1)	1995 (92.5)	1465 (67.8)	<0.0001	0.170 (0.141-0.204)
Diabetes mellitus	553 (12.8)	159 (7.4)	394 (18.2)	<0.0001	2.799 (2.303-3.401)
Hypertension	33 (6.9)	14 (0.5)	285 (13.2)	<0.0001	23.325 (13.59-40.028)
Antepartum hemorrhage	49 (1.1)	-	49 (2.3)	-	-
<b>Membrane</b>					
None	3996 (92.5)	2039 (94.6)	1957 (90.5)	<0.0001	0.548 (0.433-0.693)
PROM	156 (3.6)	39 (1.8)	117 (5.4)	<0.0001	3.106 (2.151-4.485)
SRAM	127 (2.9)	39 (1.8)	88 (4.1)	<0.0001	2.030 (1.572-3.374)
ARM	39 (0.9)	39 (1.8)	-	-	-
<b>Amniotic fluid</b>					
Clear	3917 (90.7)	2029 (94.1)	1888 (87.3)	<0.0001	0.431 (0.346-0.537)
Meconium	401 (9.3)	127 (5.9)	274 (12.7)	<0.0001	2.319 (1.862-2.888)
<b>Delivery outcomes</b>					
Spontaneous vaginal delivery	3399 (78.7)	1789 (83.0)	1610 (74.5)	<0.0001	0.598 (0.516-0.694)
Instrument	32 (0.7)	31 (1.4)	1 (0.01)	<0.0001	0.032 (0.004-0.233)
Caesarian section	887 (20.5)	336 (15.6)	551 (25.5)	<0.0001	1.853 (1.592-2.155)
<b>Total duration of labor</b>					
N/A	626 (14.5)	237 (11.0)	389 (18.0)	<0.0001	1.777 (1.493-2.114)
<6 hours	2252 (52.2)	975 (45.2)	1277 (59.1)	<0.0001	1.748 (1.549-1.972)
6-12 hours	1405 (32.5)	938 (43.5)	467 (21.6)	<0.0001	0.358 (0.313-0.409)
13-20 hours	35 (0.8)	6 (0.3)	29 (1.3)	<0.0001	4.872 (2.019-11.758)
<b>Post-partum complications</b>					
None	4236 (98.1)	2137 (99.1)	2099 (97.1)	0.599	0.296 (0.177-0.497)
Post-partum hemorrhage	67 (1.6)	4 (0.2)	63 (2.9)	<0.0001	16.148 (5.867-44.442)
Retained placenta	21 (0.5)	15 (0.7)	6 (0.3)	0.050	0.397 (0.154-1.026)

The values presented as number and percentages (%). Fisher's exact test utilized to see whether there was a significant difference between groups. PROM: premature rupture of amniotic membrane, SRAM: spontaneous rupture of membranes, ARM: artificial rupture of the membrane, OR: odds ratio, CI: confidence interval, N/A: not available

**Table 4 -** Characteristics of fetal outcomes.

Variables	Total	Mother age <40 years n (%)	Mother age ≥40 years	Fisher's exact test	OR (95% CI)
<b>Birth weight</b>					
<2500 g	792 (18.3)	308 (14.3)	484 (22.4)	<0.0001	1.731 (1.479-2.026)
2500-3599 g	2271 (52.6)	1314 (60.9)	957 (44.3)	<0.0001	0.509 (0.451-0.574)
3600-4500 g	1202 (27.8)	534 (24.8)	668 (30.9)	<0.0001	1.358 (1.188-1.552)
>4500 g	53 (1.2)	-	53 (2.5)	-	-
<b>NICU admission</b>					
Yes	256 (5.9)	72 (3.3)	184 (8.5)	<0.0001	2.693 (2.036-3.560)
No	4062 (94.1)	2084 (96.7)	1978 (91.5)	0.096	0.371 (0.281-0.491)
<b>Apgar score</b>					
Normal	4161 (96.4)	2087 (96.8)	2074 (95.9)	0.840	0.779 (0.565-1.074)
Abnormal	110 (2.5)	25 (1.2)	85 (3.9)	<0.0001	3.488 (2.224-5.471)
<b>Abnormality</b>					
None	4004 (92.7)	2015 (93.5)	1989 (92.0)	0.681	0.805 (0.639-1.013)
Down syndrome	15 (0.3)	-	15 (0.7)	-	-
Others	299 (6.9)	141 (6.5)	158 (7.3)	0.326	1.127 (0.890-1.426)
<b>Viability</b>					
Live birth	4271 (98.9)	2112 (98.0)	2159 (99.9)	0.472	14.993 (4.648-48.359)
Still birth	47 (1.1)	44 (2.0)	3 (0.1)	<0.0001	0.067 (0.021-0.215)

The values presented as number and percentages (%). Fisher's exact test utilized to see whether there was a significant difference between groups. OR: odds ratio, CI: confidence interval, NICU: neonatal intensive care unit

The results of this research supported findings of other studies that AMA was linked with prenatal complications. In this study, 18.2% of our AMA women group had diabetes mellitus and 13.2% had hypertension. In line with our results many researcher carried out in Saudi Arabia and in different areas had revealed similar findings.<sup>4,14</sup> Previous researches in Saudi Arabia reported that age >35 years was a risk factor for preeclampsia and GDM.<sup>4</sup> This contributed to ovaries aging process and inadequate maternal cardiovascular adaptations during pregnancy. Furthermore, trophoblast cells' ability to invade underlying decidua is limited due to decidua response impairment and changes in microvillus architecture. Moreover, an ischemic placenta may cause greater oxidative stress reactions, resulting in increased syncytiotrophoblast apoptosis and immunological reactions, increasing likelihood of pregnancy problems.<sup>15</sup>

Mothers with AMA are liable to have diabetes mellitus versus younger women.<sup>16</sup> With increasing age, pancreatic B-cell function and insulin sensitivity decline, and up to 16% of AMA women had an abnormal glucose tolerance test. This could be related to a link between aging and progressive arterial endothelial destruction, or it could be owing to rising prevalence of obesity as people become older, which is linked to decreased insulin sensitivity.<sup>16</sup> Due to gradual compliance loss, decrease in vascular responsiveness to endothelium-dependent vasodilators, myocardial compliance loss, and aortic flow loss during diastole, normal hemodynamic alterations in pregnancy appear to be in the opposite direction from those seen with aging, making pregnancy adaptation more difficult. Preeclampsia, intrauterine growth restriction, and placental abruption are all more likely in women who have prior hypertension.<sup>16</sup> These findings point to necessity for more rigorous prenatal monitoring and management. In our study, antepartum hemorrhage (APH) occurred in 2.3% of our mothers with AMA. Ngowa et al<sup>17</sup> reported that APH was 10-fold more in AMA primiparous women versus their younger counterparts and 2-fold higher in AMA multiparous women versus their younger counterparts.

Increasing maternal age also linked with higher risk of CS and instrumental deliveries.<sup>18</sup> The results of this study revealed that CS was significantly higher 25.5% for women aged  $\geq 40$  years versus 15.6% for women aged <40 years ( $p < 0.0001$ ). While, spontaneous vaginal (74.5%) and instrumental deliveries (0.01%) were significantly lower for women aged  $\geq 40$  years versus women aged <40 years ( $p < 0.0001$ ). Premature rupture of amniotic membrane (5.4%) and SROM (4.1%)

were significantly higher for women aged  $\geq 40$  years versus women aged <40 years ( $p < 0.0001$ ). Meconium in amniotic fluid was significantly higher in 12.7% for females aged  $\geq 40$  years versus 5.9% females aged <40 years ( $p < 0.0001$ ). Duration of labor <6 hours (59.1%) and 13-20 hours (3.1%) were significantly higher in women aged  $\geq 40$  years compared with women aged <40 years ( $p < 0.0001$ ). Another study with a total of 24032 pregnancies of women <40 years, reported a greater probability of surgical delivery (caesarean, forceps, and vacuum), 61.0% of older nulliparous women compared to 35.0% of younger nulliparous women, despite decreased birth weight and gestational age.<sup>19</sup> In retrospective cohort analysis of mothers aged 45 years, CS rate 49.0% versus 23.0% in 20-29 years aged group ( $p < 0.0001$ ).<sup>20</sup> Despite parity, frequencies and hazards of primary CS increased with age in cohort analysis in the United States of 78880 singleton births, which excluded from the study cases with previous CS surgery.<sup>21</sup> Researches in American countries, European, and Asian revealed that CS rate in females >35 varied from 53.3-91.8%.<sup>22,23</sup> In Beijing, a research recruited 15 hospitals, recorded that rate of CS was 74.8% in females  $\geq 40$  years old and 66.3% in females of 35-39 years old.<sup>24</sup> Londero et al<sup>25</sup> reported that in older women, there was a reduced prevalence of labor and spontaneous birth, as well as a greater rate of CS. The causes of operative delivery high rate in older women were controversial. Labor dystocia reported to be more in AMA due to inefficient uterine actions.<sup>26</sup> Because of decreased oxytocin receptors numbers and inability of aged myometrium to contract, CS may be an easy choice for doctors as well. Fetal discomfort, multiple gestations, non-vertex presentation, placenta previa, macrosomia, constricted pelvis, and repeated CS deliveries are all age-related contributing factors.<sup>16</sup> Only link to emergency CS could be explained in this way. Instead, it has been argued that unexpectedly high incidence of elective CS births between older females was due to disparities in care and maternal preferences.<sup>27</sup> Women >40 years old more were likely to have elective CS without medical reasons.<sup>28</sup>

The postpartum complications reported in this study were PPH and retained placenta. Postpartum hemorrhage rate in mothers with AMA (2.9%) was significantly higher than those with younger age (0.2%), with an OR of 16.148; 95% CI: (5.867-44.442), ( $p < 0.0001$ ). Meanwhile, retained placenta (0.3%) was significantly lower in AMA than those with younger age (0.7%) with an OR of 0.397; 95% CI: (0.154-1.026), ( $p = 0.050$ ). Our results are in line with

previous researches carried out in the United Kingdom, Nigeria, and America, AMA was linked with PPH risk.<sup>29</sup> Meanwhile, Chinese studies showed a decline in odds of PPH with increasing mother age.<sup>29</sup> Chinese government took precautions to control PPH rate.<sup>22</sup> Higher rates of CS birth among older women are most likely to blame for some of the increased risk of PPH.<sup>30</sup>

The results of this study revealed number of low-birth-weight newborns (<2500 grams) of AMA women were significantly higher than those of younger women ( $p < 0.0001$ ). They had 1.7-fold increased risk than younger women. This can be explained by intrauterine growth retardation (IUGR) that may occur due to insufficient placenta. Also, number of newborns with macrosomia (>4500 grams) of AMA women were significantly higher than those of younger women ( $p < 0.0001$ ). They had 1.4-fold increased risk than younger women. This can be explained by women with AMA having more diabetes mellitus that led to macrosomia. In this respect, Ratnasiri et al<sup>31</sup> considered mother's elevated age as an indirect risk factor for low birth weight neonate. The results of this research showed that newborns of AMA women had higher rate of NICU admissions and low Apgar score at 5 minutes than younger women ( $p < 0.0001$ ). They had 2.693- and 3.488-fold increased risk than younger women in NICU admissions and low Apgar score at 5 minutes. This may be explained by high incidence of congenital anomalies, low Apgar score, low birth weight, IUGR, and prematurity among newborn of AMA mothers. Previous researches in Saudi Arabia reported that age >35 years was a risk factor for adverse neonatal outcomes specifically low birth weight, still birth, neonatal death, and NICU admissions.<sup>4</sup> Also, newborns of AMA women had Down syndrome (0.7%) and other congenital anomalies (7.3%). Others reported that women of AMA were at increased risk factors for low birth weight, low Apgar score, and preterm labor.<sup>17</sup> Pregnancy at  $\geq 35$  and  $\geq 40$  years old of age added 1.0% and 2.5% to risk of non-chromosomal abnormalities versus baseline risk of 3.5% in females aged <25 years.<sup>32</sup> Those included cardiac anomalies (2x), clubfoot (3x), hernia of diaphragm (10.5x), cleft palate, spina bifida, limb anomalies, syndactyly, and male genital abnormalities.<sup>33</sup> In this study, only 3 (0.1%) cases in AMA women were still birth that was significantly lower than younger women that reported 44 (2.0%) cases. These results can be explained by good antenatal care received by AMA group. A Scottish research showed that women aged  $\geq 40$  had higher than 2-fold, raised risk of delivery related perinatal mortality.<sup>34</sup> All of 4 stillbirths in Shan et al's<sup>29</sup> research were in mothers aged

$\geq 40$ . Advanced maternal age was linked with adverse pregnancy outcomes as pre-term birth, stillbirth, low birth weight, and unexplained fetal death.<sup>35</sup> When AMA women versus mothers aged 20-34 years in a large scale research undertaken by World Health Organization in 29 countries from Latin America, Africa, Asia, and Middle East, odds of stillbirths, preterm birth, and low birth weight were shown to be greater in AMA mothers.<sup>36</sup> Findings from European and American countries also demonstrated that AMA women had less neonatal unfavorable outcomes, with some even finding an inverse link.<sup>22,37</sup> One cause could be self-regulatory maternal behavior. After infertility and miscarriage, the survival of better embryos or foetuses in AMA women could be the second cause.<sup>38</sup> In AMA women, natural selection has resulted in only better embryos surviving and avoiding negative pregnancy outcomes.<sup>38</sup> Older women reported less psychosocial stress than younger women, who were going through a societal revolution and may be under a lot of stress and have mood swings. Psychosocial stress was linked to an increased preterm birth risk.<sup>39</sup> Neonatal outcomes improved as coping mechanisms and socioeconomic support improved. During labour, especially in individuals over age of 40, intensive monitoring and sufficient preparation are required.

**Strengths and limitations.** The vast number of patients included in this trial, all of whom were thoroughly controlled in single institution, the meticulous data collecting, and detailed interest data on maternal and neonatal outcomes are only a few of the study's advantages. Because it was a single-center trial, a selection bias could not be ruled out, but this dependable database allowed for accurate and consistent retrospective analysis. Absence of collected data regarding patients' socioeconomic condition, inability to get information on former preterm delivery for multivariable logistic regression analysis in prematurity, kind of conception and other preexisting or underlying gynaecological disorders were limitations of this study.

In conclusion, CS birth, PROM, unclear amniotic fluid, prenatal illnesses as diabetes mellitus, hypertension, APH, longer delivery period, and postpartum hemorrhage were all linked to maternal age. Also, AMA was linked with many newborn complications such as low birth weight, macrosomia, low Apgar score at 5 minutes, and NICU admission, more congenital anomalies but less still birth. These findings have implications for obstetric and neonatal service planning and delivery in places where a growing number of females want to delay having their first child until later in life. Given the well-established and

continuing trend of postponing childbearing, maternal care providers should carefully consider these findings in order to adequately inform mothers, provide evidence-based data to support their procreation choices, and improve clinical surveillance aimed at identifying early manifestations of poor outcomes. Thus, in these patients, preconception evaluation and treatment of existing medical issues would be recommended prior to pregnancy.

**Acknowledgment.** *The authors gratefully acknowledge Oxford Science Editing Ltd. (www.oxfordscience.org) for English language editing.*

## References

- Attali E, Yogev Y. The impact of advanced maternal age on pregnancy outcome. *Best Pract Res Clin Obstet Gynaecol* 2021; 70: 2-9.
- Cao G, Yang L, Liu L, Ma Z, Wang J, Bi J. Environmental incidents in China: lessons from 2006-2015. *Sci Total Environ* 2018; 633: 1165-1172.
- Fu Y, Schwebel DC, Hu G. Physicians' workloads in China: 1998-2016. *Int J Environ Res Public Health* 2018; 15: 1649.
- Fayed AA, Wahabi H, Mamdouh H, Kotb R, Esmail S. Demographic profile and pregnancy outcomes of adolescents and older mothers in Saudi Arabia: analysis from Riyadh Mother (RAHMA) and baby cohort study. *BMJ Open* 2017; 7: e016501.
- Claramonte Nieto M, Meler Barrabes E, Garcia Martínez S, Gutiérrez Prat M, Serra Zantop B. Impact of aging on obstetric outcomes: defining advanced maternal age in Barcelona. *BMC Pregnancy Childbirth* 2019; 19: 342.
- Solanke BL, Salau OR, Popoola OE, Adebisi MO, Ajao OO. Socio-demographic factors associated with delayed childbearing in Nigeria. *BMC Res Notes* 2019; 12: 374.
- Keskin S. Advanced maternal age and adverse perinatal outcomes - one decade analysis. *Middle Black Sea J of Health Sci* 2019; 5: 11-15.
- Kim YN, Choi DW, Kim DS, Park EC, Kwon JY. Maternal age and risk of early neonatal mortality: a national cohort study. *Sci Rep* 2021; 11: 814.
- Li Y, Ren X, He L, Li J, Zhang S, Chen W. Maternal age and the risk of gestational diabetes mellitus: a systematic review and meta-analysis of over 120 million participants. *Diabetes Res Clin Pract* 2020; 162: 108044.
- Mehari MA, Maeruf H, Robles CC, Woldemariam S, Adhena T, Mulugeta M, et al. Advanced maternal age pregnancy and its adverse obstetrical and perinatal outcomes in Ayder comprehensive specialized hospital, Northern Ethiopia, 2017: a comparative cross-sectional study. *BMC Pregnancy Childbirth* 2020; 20: 60.
- Almalki S, Ganong L. Family life education in Saudi Arabia. *Springer Cham* 2018: 381-396.
- Wahabi H, Esmail S, Fayed A. Maternal prepregnancy weight and pregnancy outcomes in Saudi women: subgroup analysis from Riyadh mother and baby cohort study (RAHMA). *Biomed Res Int* 2021; 2021: 6655942.
- Moussa HN, Alrais MA, Leon MG, Abbas EL, Sibai BM. Obesity epidemic: impact from preconception to postpartum. *Future Sci OA* 2016; 2: FSO137.
- Frederiksen LE, Ernst A, Brix N, Braskhoj Lauridsen LL, Roos L, Ramlau-Hansen CH, et al. Risk of adverse pregnancy outcomes at advanced maternal age. *Obstet Gynecol* 2018; 131: 457-463.
- Munira S, Ivy R, Ashraf F, Khalil MI. Adverse pregnancy outcome among different maternal age group - a comparative study. *Sch Int J Obstet Gynec* 2020; 3: 163-169.
- Correa-de-Araujo R, Yoon SSS. Clinical outcomes in high-risk pregnancies due to advanced maternal age. *J Womens Health (Larchmt)* 2021; 30: 160-167.
- Ngowa JD, Ngassam AN, Dohbit JS, Nzedjom C, Kasia JM. Pregnancy outcome at advanced maternal age in a group of African women in 2 teaching hospitals in Yaounde, Cameroon. *Pan Afr Med J* 2013; 14: 134.
- Maoz-Halevy E, Pariente G, Sheiner E, Wainstock T. Perinatal outcomes of women aged 50 years and above. *Am J Perinatol* 2020; 37: 79-85.
- Londero AP, Rossetti E, Pittini C, Cagnacci A, Driul L. Maternal age and the risk of adverse pregnancy outcomes: a retrospective cohort study. *BMC Pregnancy Childbirth* 2019; 19: 261.
- Robson SJ, de Costa CM. Thirty years of the World Health Organization's target caesarean section rate: time to move on. *Med J Aust* 2017; 206: 181-185.
- Richards MK, Flanagan MR, Littman AJ, Burke AK, Callegari LS. Primary cesarean section and adverse delivery outcomes among women of very advanced maternal age. *J Perinatol* 2016; 36: 272-277.
- Diel A, Cupisti S, Beckmann MW, Schwab M, Zollner U. Pregnancy and obstetrical outcomes in women over 40 years of age. *Geburtshilfe Frauenheilkd* 2015; 75: 827-832.
- Ben-David A, Glasser S, Schiff E, Zahav AS, Boyko V, Lerner-Geva L. Pregnancy and birth outcomes among Primiparae at very advanced maternal age: at what price? *Matern Child Health J* 2016; 20: 833-842.
- Wang C, Wang XY, Yang HX. [Effect of maternal age on pregnancy outcomes in Beijing]. *Zhonghua Fu Chan Ke Za Zhi* 2017; 52: 514-520. [in Chinese]
- Londero AP, Rossetti E, Pittini C, Cagnacci A, Driul L. Maternal age and the risk of adverse pregnancy outcomes: a retrospective cohort study. *BMC Pregnancy Childbirth* 2019; 19: 261.
- Waldenström U, Ekéus C. Risk of labor dystocia increases with maternal age irrespective of parity: a population-based register study. *Acta Obstet Gynecol Scand* 2017; 96: 1063-1069.
- Herstad L, Klungsoyr K, Skjærven R, Tanbo T, Eidem I, Forsén L, et al. Maternal age and elective cesarean section in a low-risk population. *Acta Obstet Gynecol Scand* 2012; 91: 816-823.
- Muto H, Ishii K, Nakano T, Hayashi S, Okamoto Y, Mitsuda N. Rate of intrapartum cesarean section and related factors in older nulliparous women at term. *J Obstet Gynaecol Res* 2018; 44: 217-222.
- Shan D, Qiu PY, Wu YX, Chen Q, Li AL, Ramadoss S, et al. Pregnancy outcomes in women of advanced maternal age: a retrospective cohort study from China. *Sci Rep* 2018; 8: 12239.
- Başer E, Seçkin KD, Erkilinç S, Karlı MF, Yeral IM, Kaymak O, et al. The impact of parity on perinatal outcomes in pregnancies complicated by advanced maternal age. *J Turk Ger Gynecol Assoc* 2013; 14: 205-209.

31. Ratnasiri AWG, Parry SS, Arief VN, DeLacy IH, Halliday LA, DiLibero RJ, et al. Recent trends, risk factors, and disparities in low birth weight in California, 2005-2014: a retrospective study. *Matern Health Neonatol Perinatol* 2018; 4: 15.
32. Schummers L, Hutcheon JA, Hacker MR, VanderWeele TJ, Williams PL, McElrath TF, et al. Absolute risks of obstetric outcomes by maternal age at first birth: a population-based cohort. *Epidemiology* 2018; 29: 379-387.
33. Dakhoir A, Pelu IEA, Ferricha D. Contextualization of the Use of Zakat in Reducing Stunting: Evidence from Indonesia. *Int J Entrep* 2021; 25: 242-246.
34. Pasupathy D, Wood AM, Pell JP, Fleming M, Smith GC. Advanced maternal age and the risk of perinatal death due to intrapartum anoxia at term. *J Epidemiol Community Health* 2011; 65: 241-245.
35. Vijayaletchumi T, Shuhaila A, Abdul Manaf MR, Nor Azlin MI. Detection of foetal anomaly in advanced maternal age. *Med J Malaysia* 2021; 76: 833-836.
36. Laopaiboon M, Lumbiganon P, Intarut N, Mori R, Ganchimeg T, Vogel JP, et al. Advanced maternal age and pregnancy outcomes: a multicountry assessment. *BJOG* 2014; 121: 49-56.
37. Kanungo J, James A, McMillan D, Lodha A, Faucher D, Lee SK, et al. Advanced maternal age and the outcomes of preterm neonates: a social paradox? *Obstet Gynecol* 2011; 118: 872-877.
38. Waldenström U, Cnattingius S, Vixner L, Norman M. Advanced maternal age increases the risk of very preterm birth, irrespective of parity: a population-based register study. *BJOG* 2017; 124: 1235-1244.
39. Shapiro GD, Fraser WD, Frasch MG, Séguin JR. Psychosocial stress in pregnancy and preterm birth: associations and mechanisms. *J Perinat Med* 2013; 41: 631-645.