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Comparison of pregnancy outcomes between women of advanced maternal age (≥35 years) versus younger women in a tertiary care center in Saudi Arabia

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BACKGROUND: Pregnancy in women aged 35 years or above is generally considered an advanced maternal age (AMA). AMA is associated with an increased rate of maternal and neonatal complications.

OBJECTIVES: Assess the effect of AMA on maternal and neonatal outcomes.

DESIGN: Analytical cross-sectional study of medical records.

SETTINGS: In-patient hospital tertiary care setting in Jeddah.

PATIENTS AND METHODS: All women who attended antenatal care and delivered at King Abdulaziz Medical City in Jeddah in the first half of 2018 were included in the study. Outcomes for women 35 years of age or older were compared with younger women. Significant factors in a univariate analysis were entered in a multiple logistic regression model to assess the association between AMA and outcomes.

MAIN OUTCOME MEASURES: Rates of maternal neonatal complications, analysis of factors associated with advanced maternal, gestational diabetes mellitus (GDM), cesarean delivery.

SAMPLE SIZE: 1586 women.

RESULTS: Of the 1586 women, 406 were 35 years of age or older (25.6%), and 1180 were younger than 35 years. The AMA group had a significantly higher proportion of GDM (32.0% versus 13.2%, *P*<.001). The adjusted odds ratio (OR) for GDM was 2.6 (95% CI 2-3.5, *P*<.001.) compared with younger women in the multivariate logistic regression analysis. Older women had a higher rate of cesarean delivery (43.6% versus 30.8%, *P*<.001). The adjusted OR for cesarean vs. vaginal delivery was 1.5 (CI 1.2-1.9, *P*=.002).

CONCLUSION: Pregnancy in women 35 years or older was associated with an increased risk of GDM and cesarean delivery.

LIMITATIONS: Cross-sectional design, small sample size, single hospital.

CONFLICT OF INTEREST: None.

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The term advanced maternal age (AMA) applies to childbearing women aged 35 years and older.[1] In recent decades, having children at an older age has been an increasing trend within developed countries.[2,3] Many factors, such as the presence of safe and effective contraception, higher education and demanding career opportunities, advances in assisted reproductive techniques, financial insecurity, and unstable relationships have contributed to the trend of delaying pregnancy.[3,4]

In the year 2013 in the United Kingdom, 20% of deliveries were among women aged 35 and older, and 4% were among women aged 40 years old and older compared with 6% and 1%, were respectively, in 1980.[2] This increase in AMA has also been observed in many parts of Asia and in Portugal.[5] In Saudi Arabia, the rate of AMA was 17% in 2017.[6] Pregnancy in women at an AMA is associated with an increased risk of miscarriage, preeclampsia, gestational diabetes (GDM), small for gestational age (SGA) neonates, placenta previa,[7] cesarean delivery[8] and severe maternal morbidity such as amniotic fluid embolism, obstetric shock, renal failure, complications of obstetric interventions, and intensive care unit admission. Similar associations were observed for fetal and infant outcomes.[9]

A study from the eastern province of Saudi Arabia that included 2517 primigravidas reported that only 8% of women were older than the age of 35 years. Women at an AMA had more diabetes mellitus, preterm labor, and cesarean deliveries. In addition, babies of older mothers had lower birthweights.[10] Our study aimed to determine the rate of AMA and the maternal and neonatal outcomes associated with AMA at King Abdulaziz medical city in Jeddah (KAMC-J), Saudi Arabia.

PATIENTS AND METHODS

This cross-sectional study included all pregnant women who attended antenatal care and delivered in KAMC-J, Saudi Arabia, in the 6-month period between January and June 2018. The study compared pregnant women who were aged 35 years or older at the time of delivery (AMA group) and the control group included pregnant women who were younger than 35 years (non-AMA group). After ethical approval was acquired from the Institutional Review Board of King Abdullah International Medical Research Center, data were collected from electronic medical records. The two groups were compared regarding their demographic data, medical history, and different maternal and neonatal outcomes. Demographic data included maternal age at delivery, body mass index (BMI), gravidity, and parity, pre-pregnancy maternal medical conditions (diabetes, hypertension, and hypothyroidism). Pregnancy outcomes included GDM, diagnosed according to the American Diabetes Association.[11] Hypertensive disorders in pregnancy were defined according to the American College of Obstetricians and Gynecologists[12] as placenta previa, induction of labor using prostaglandin or oxytocin, placental abruption, preterm labor, cesarean delivery, and postpartum hemorrhage.

Neonatal outcomes included SGA, defined as birth weight less than 2.5 kg, neonatal mortality, 1- and 5-minute Apgar scores, admission to intensive care unit, intrauterine fetal death (IUFD), and congenital anomalies. Patients who did not have antenatal care in KAMC-J or were not screened for GDM were excluded from the study.

Statistical analysis was performed using IBM SPSS software (version 24, IBM, Armonk, NY: IBM Corp). The chi-square test was used to assess the association between different pregnancy outcomes and AMA as a categorical variable. Pregnancy outcomes that were significantly associated with AMA were tested using multiple logistic regression.

RESULTS

Of 1677 women who had antenatal care and gave birth at KAMC-J, Saudi Arabia, 1586 women met the inclusion criteria. Ninety-one women were excluded because they did not have antenatal care at KAMC-J. Twenty-five percent (25.6%) of the study population was 35 years of age or older. The median ages were 37.5 years (range, 35-48) for the older women and 27 years (range, 17-34) for the younger women (P<.001). BMI was 31 kg/m^2 (range, 14-62) for the older women and 28 kg/m^2 (range, 15-65) for the younger women (P<.001). According to BMI at the time of delivery, most women were overweight or obese: 83% and 70% in the study group and control group, respectively (**Table 1**). Only 6% of the women in the AMA group were pregnant for the first time while 38% of the younger group was pregnant for the first time. Type II diabetes, chronic hypertension, and hypothyroidism were more prevalent in the study group (**Table 2**).

Pregnancy in women of AMA was more likely to be complicated by GDM. Older women were more likely to have a cesarean delivery than younger women. Other maternal outcomes such as hypertensive disease of pregnancy, placental abruption, placenta previa, oligohydramnios, and polyhydramnios were not statistically significant between the two groups. Neonatal complications such as low 1- and 5-minute Apgar scores, SGA, IUFD, neonatal disease, malformation, and admission to NICU were similar in the two groups (**Table 3**).

Table 1. Maternal characteristics of 1586 women in the study.

Characteristics	AMA (n=406)	Non-AMA (n=1180)	P value
Median age (range)	37 (35-48)	27 (17-34)	.001[a]
Body mass index (kg/m^2)			
Underweight (<18.5)	3 (1.0)	30 (2.5)	
Normal (18.5-24.9)	59 (14.5)	335 (28.4)	.001[a]
Overweight (25-29.9)	113 (27.8)	413 (35.0)	
Obese (≥30)	225 (55.4)	397 (33.6)	
Parity			
Median	4	1	
Nulli	25 (6.2)	448 (38.0)	<.001
Multi	381 (93.8)	732 (62.0)	
Thyroid function			
Normal	360 (88.7)	1111 (94.1)	<.001
Low	46 (11.3)	69 (5.8)	
Diabetes			
Non-diabetic	383 (94.3)	1173 (99.4)	
DM II	19 (4.7)	3 (0.3)	<.001[a]
DM I	4 (1.0)	4 (0.3)	
Chronic hypertension	11 (2.7)	7 (0.6)	<.001

Data are number (%) unless otherwise noted. [a]Fisher Exact test.

Table 2. Maternal pregnancy outcomes.

Outcome	AMA (n=406)	Non-AMA (n=1180)	P value
Gestational diabetes	130 (32)	156 (13.2)	<.001
Hypertensive disease of pregnancy			
Gestational	4 (1.0)	15 (1.0)	.99[a]
Preeclampsia	9 (2.2)	38 (3.0)	
Antenatal complications			
Abruption	1 (0.2)	7 (0.6)	.8[a]
Placenta previa	5 (1.2)	11 (0.9)	
Oligohydramnios	1 (0.2)	4 (0.3)	
Polyhydramnios	3 (0.7)	9 (0.8)	
Induced labor	57 (14.0)	225 (19.1)	.02
Cesarean delivery	177 (43.6)	363 (30.8)	<.001
Postpartum hemorrhage	43 (10.6)	103 (8.7)	.3

Data are number (%). [a]Fisher exact test.

Using multiple logistic regression to adjust for confounder that may affect the rate of GDM and cesarean delivery such as BMI, multiparity, hypothyroidism, SGA, preterm labor, hypertensive diseases of pregnancy and labor induction, GDM and cesarean delivery were significantly associated with AMA (**Table 4**). The factors associated with GDM were BMI more than 25 kg/m^2. In other words, women aged 35 years or older with BMI ≥25 kg/m^2 were 70% more likely to have GDM, and multiparous women of AMA during pregnancy were 80% more likely to have GDM (**Table 5**). Factors associated with cesarean delivery were BMI more than 25 kg/m^2, GDM, and SGA. Induction of labor decreased the risk of cesarean delivery (**Table 6**).

DISCUSSION

The rate of AMA in this study (25.6%) was higher than the 17% rate reported in the northern region of Saudi Arabia[13] but consistent with 23% found by a large demographic study done in Riyadh,[14] and another study in the USA.[15] Although there is a rising trend to delay childbearing secondary to improving access to education, career opportunities, contraception and assisted reproductive techniques,[8] only 6.2% of women of AMA in this study were pregnant the first time. This finding is in agreement with the finding of Fayed et al.[14] They found 3.4% of their AMA population were primigravida and 70% were para five or more. This means Saudi women choose to have children after the age of 35 years to complete their family rather than delaying the onset of motherhood.

The rate of obesity was high in the whole cohort (56% in the AMA group and 33% in the younger group). In a population-based study including 10735 Saudi participants aged 15 years or older,[16] there were high rates of obesity across all segments of the population, reaching 33.5% of women and 24.1% of men. Among women, the risk of obesity increased with age, being married, having been diagnosed with a chronic condition, being hypertensive, and having less education.

The rate of GDM in the AMA group was high, reaching 32% in comparison to the rate of 22% in Korea and 14% in the US.[17,18] This high rate is most likely related to the high rate of obesity and ethnic background.[19] The estimated risk of GDM was 2.6 times higher than younger women in our study, which is higher than risk estimated by a large retrospective study in the UK by Khalil et al[8] (OR 1.88, 95% CI: 1.55-2.29; P<.001), but similar to the OR of 2.85 estimated by a meta-analysis of 28 studies looking at cesarean delivery as a secondary outcome in AMA.[2]

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As expected, the incidence of cesarean delivery was higher in the AMA group (44% versus 31% in the Non-AMA group). This rate is similar to the rate of 40% found in central Saudi Arabia by a recent cross-sectional study published by Alshehri et al.[20] After adjusting for confounders such as parity, obesity, gestational age at the time of delivery, induction of labor, and GDM, women of AMA are 50% more likely to have cesarean delivery than younger women (OR 1.5, P<.003, CI 1.1-1.9). This risk is similar to the estimated risk by Japanese population-based study published by Ogawa et al[7] reported a relative risk of 1.18, 1.4 and 1.53 for women 35-39, 40-44, and 45-49 years of age, respectively.

In women of AMA, induction of labor decreased the risk of cesarean delivery by 30% in our study (OR 0.7, CI 0.5-0.9, P<.03). However, a recent meta-analysis of of six randomized clinical trials including 958 patients with low heterogeneity, comparing induction of labor with expectant management in singleton pregnancies at term in women of AMA, showed no significant difference;[21] The pooled odds ratio was 0.97 (95 % CI=0.86-1.1). Most likely the estimate from the meta-analysis is more accurate.[20] The finding of our study that induction of labor decreases the risk of cesarean delivery may well be due to type I error (i.e, the statistically significant difference is due to chance and not due to real difference).

A recent cross-sectional study[22] including 3942 women found a higher rate of preeclampsia in AMA (5.1% in comparison to younger women 3.7% OR 1.4 (95% CI 1.1-1.9, P=.03). Our data did not find a difference between the two groups. The rate of preeclampsia in our population was low (3%) which is in agreement with Subki et al[23] study done in the same region. They looked into the rate of preeclampsia among 9493 deliveries and reported a rate of 2.4%.

Our study did not find a difference in the selected neonatal outcome, most likely due to the small sample size. The incidence of fetal anomalies was high in both groups: 13% in the AMA group and 12% in the non-AMA group. This rate is higher than the reported incidence of 4.5% in Riyadh.[24] We expect the reason for this high incidence is the fact KAMC-J is the largest referral center for fetal anomalies in the Western province of Saudi Arabia.

The strength of this study includes the use of electronic hospital medical records, accurate assessment of gestational age, the examination of a wide range of adverse pregnancy outcomes, and the use of multivariable logistic regression analysis to control for risk factors associated with each adverse outcome. The limitation of our study is the small sample size from a single hospital.

In conclusion, the rate of AMA was 25.6% in women who gave birth at our center. Pregnancy in women 35 years or older was associated with an increased risk of GDM and cesarean delivery. Future population-based studies powered to assess risk related to the induction of labor and neonatal outcome are recommended.

Table 3. Fetal outcomes.

Outcome	AMA (n=406)	Non-AMA (n=1180)	P value
Preterm labor	37 (9.0)	112 (9.5)	.8
Small for gestational age	47 (12.0)	159 (14.0)	.3
Intrauterine fetal death	2 (0.5)	14 (1.2)	.3[a]
1 minute Apgar score less than 7	23 (6.0)	65 (6.0)	.9
5 minute Apgar score less than 7	8 (2.0)	22 (2.0)	.9
Admission to NICU	29 (7.0)	70 (6.0)	.4
Neonatal disease[b]	110 (27.0)	333 (29.0)	.6
Syndromes			
Down	3 (0.7)	2 (0.2)	
Sanjad Sakati	0	1 (0.1)	
Noonan	0	1 (0.1)	
Malformations			
Musculoskeletal	30 (7.4)	74 (6.3)	
Cardiac	6 (1.5)	20 (1.7)	
Central nervous system	1 (0.3)	4 (0.4)	
Genital	9 (2.2)	25 (2.1)	
Renal	1 (0.3)	5 (0.4)	
Gastrointestinal	2 (0.5)	5 (0.4)	
Multiple	3 (0.7)	8 (0.7)	
Total	52 (13.0)	141 (12.0)	
Syndrome and malformations	55 (14.0)	145 (12.0)	.6

Data are number (%). [a]Fisher's Exact test. [b]Respiratory distress syndrome, transient tachypnea of newborn, neonatal jaundice and polycythemia

Table 4. Multivariate logistic regression with advanced maternal age as the dependent variable (n=1545).

Variables	Unadjusted			Adjusted		
	Odds ratio	*P* value	95% C.I.	Odds ratio	*P* value	95% C.I.
Body mass index (≥25 kg/m²)	2.5	.001	1.8-3.3	1.7	.001	1.3-2.4
Multiparity	9.3	.001	6.1-14	7.8	.001	5-12
Hypothyroidism	2.1	.001	1.4-3.0	2.0	.001	1.3- 3.2
Labor induction	0.7	.02	.5-.9	.9	.6	.6-1.3
Cesarean delivery	1.7	.001	1.4-2.2	1.5	.002	1.2-1.9
Gestational diabetes	3.4	.001	2.6-4.4	2.6	.001	2-3.5

Model summary: -2 log likelihood:1521.81, Cox and Snell R square: .152, Nagelkerke R square: .225

Table 5. Multivariate logistic regression with gestational diabetes as the dependent variable (n=1545).

Predictors	Unadjusted			Adjusted		
	Odds ratio	*P* value	95% C.I.	Odds ratio	*P* value	95% C.I.
Body mass index (≥25 kg/m²)	2.1	.001	1.5-2.9	1.7	.003	1.2-2.4
Multiparity	2.6	.001	1.9-3.7	1.8	.002	1.2-2.5
Advanced maternal age	3.4	.001	2.6-4.4	2.7	.001	2 -3.6

Model summary: -2 log likelihood: 1408.84, Cox and Snell R square: .057, Nagelkerke R square: .093

Table 6. Multivariate logistic regression with cesarean delivery as the dependent variable (n=1522).

Predictors	Unadjusted			Adjusted		
	Odds ratio	*P* value	95% C.I.	Odds ratio	*P* value	95% C.I.
Body mass index (≥25 kg/m²)	1.5	**.002**	1.1-1.9	1.4	**.01**	1.1-1.8
Advanced maternal age	1.7	**.001**	1.4-2.2	1.5	**.002**	1.1-1.9
Gestational diabetes	1.7	**.001**	1.4-2.3	1.5	**.003**	1.1-2
Small for gestational age	2.6	**.001**	2.0-3.5	2.3	**.001**	1.6-3.3
Preterm labor	2.2	**.001**	1.6-3.1	1.3	.2	0.8-2
Labor induction	.7	**.01**	.5-.9	0.7	**.02**	.5-.9
Hypertensive disorders of pregnancy	1.9	**.01**	1.2-3.1	1.6	.1	.9-2.7

Model summary: -2 log likelihood:1925.380, Cox and Snell R square: .055, Nagelkerke R square: .076

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