

Risk factors in pregnant women older than 35 years at the General Hospital of Playa del Carmen.

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ABSTRACT

INTRODUCTION. A variety of maternal risks and complications can occur during pregnancy or delivery in women with advanced maternal age have been examined. These include an increased risk of developing diabetes, gestational hypertension, preeclampsia, eclampsia, and HELLP syndrome. The correlation of advanced maternal age with placental dysfunction such as placenta previa or placental abruption has also been frequently reported.

MATERIAL AND METHODS. A descriptive, observational, cross-sectional study was carried out in 52 patients aged 35 years and older attended during the period January 2022-December 2022 in the Gynecology and Obstetrics Service of the General Hospital Playa del Carmen.

RESULTS. Only the increase in cesarean sections was statistically significant, obesity as a risk factor, although refusal of family planning was also important, as well as obesity as a risk factor in this group of pregnant women. Gestational diabetes was not important in this group over 35 years of age.

DISCUSSION. During the last three decades, pregnancy at advanced maternal age has been increasing in frequency. According to a report from the Center for Disease Control and Prevention, the prevalence of births among women aged 35 years or older in the United States increased 23% (7% to 9%) between 2000 and 2014. From 2006 to 2015, the proportion of births increased 5% for women aged 35 to 39 years, 8%. Many studies have demonstrated increased risk of adverse outcomes in older patients. However, few studies stratified these risks by maternity older than 35 years, and few studies examined neonatal outcomes.

Keywords: gestational diabetes mellitus, advanced maternal age, preeclampsia pregnancy outcome.

INTRODUCTION

A variety of maternal risks and complications can occur during pregnancy or delivery in women with advanced maternal age have been examined. These include an increased risk of developing diabetes, gestational hypertension, preeclampsia, eclampsia, and HELLP syndrome. The correlation of advanced maternal age with placental dysfunction such as placenta previa or placental abruption has also been frequently reported. In addition, increased risks to the fetus, such as increased number of chromosomal aberrations, low or high birth weight and intrauterine fetal death are known to be correlated with advanced maternal age (1).

Gestational diabetes mellitus (GDM) is associated with an increased risk of perinatal mortality and morbidity and is a major public health problem. The prevalence of GDM has increased in recent decades in parallel with advancing age at conception and westernized lifestyles, accompanied by an economic boom. Worldwide, GDM is estimated to affect 14% of all pregnancies. It is also associated with ischemic heart disease and type 2 diabetes. Children of pregnant women with GDM are more likely to suffer pediatric problems, cardiovascular disease and metabolic problems in old age. A meta-analysis suggested that the prevalence of GDM was 21% in Asia and 15% in China. There has been an increasing trend in the prevalence of GDM worldwide (2).

In 2016, advanced pregnancies (age ≥ 35 years) accounted for approximately 31% of total pregnancies in China. This trend can be partly attributed to changes in social habits, such as higher education, careers, financial stability, late marriage, and con-

traceptive use. The Chinese government relaxed its family planning policy and implemented a universal two-child policy in 2015 to address the country's aging problem, which also contributes to advanced pregnancies. With increasing age, the aging of the human reproductive system is inevitable and the functions of the ovaries, uterus and other organs of older women are significantly reduced. Fertility, glucose and lipid metabolism decreased. The incidence rate of physical, surgical and gynecological diseases is increasing. The above risk factors increase adverse maternal and fetal pregnancy outcomes, including gestational diabetes mellitus, hypertensive disorder complicating pregnancy, placenta previa, placenta increta, fetal malformation, spontaneous abortion, preterm delivery, macrosomia, intrauterine growth restriction, and other pregnancy complications (3).

MATERIAL AND METHODS

A descriptive, observational, cross-sectional study was carried out in 52 patients aged 35 years and older attended during the period January 2022-December 2022 in the Gynecology and Obstetrics Service of the General Hospital Playa del Carmen, descriptive statistics were performed with measures of central tendency and dispersion, as well as number and percentages of other variables considered.

RESULTS

RESULTS. Only the increase in cesarean sections was statistically significant, as well as obesity as a risk factor, although refusal of family planning was also important. Gestational diabetes was not significant in this group over 35 years of age. On the other hand, weeks of gestation was important as a risk factor in this age group.

VARIABLES	X	S	p	N	%
AGE	37	1.5			
GESTA	3.7	1.5			
FOR	2.8	1.4			
CESAREAS	1.3	0.5	0.432		
SDG	33.9	92			
INTERGENERATIONAL PERIOD	5.9	3.0			
IHL:	3.8	1.3			
PRENATAL CARE					
				18	82
CESAREAS				18	82
OBESITY				14	64
WITHOUT FAMILY PLANNING				4	18
CARDIOPATHIES				4	18
PARTS				2	9
LUI				2	9
DM				2	9

DISCUSSION

Over the past three decades, pregnancy at advanced maternal age has been increasing in frequency. According to a report from the Center for Disease Control and Prevention, the prevalence of births among women aged 35 years and older in the United States increased 23% (7.4% to 9.1%) between 2000 and 2014. From 2006 to 2015, the proportion of births increased 5% for women aged 35 to 39 years, 8%. Many studies have demonstrated increased risk of adverse outcomes in older patients. However, few studies stratified these risks by maternity older than 35 years, and few studies examined neonatal outcomes. The risk of requiring a hysterectomy or blood transfusion was increased in older pregnant women, reaching a nearly 5-fold and 3-fold increased risk. Those aged 44 to 49 years also had an increased risk of placenta previa and PPH. Sheen et al. (4) demonstrated an increased risk of hysterectomy in these patients, reaching a rate of 103 hysterectomies per 10,000 deliveries in

patients aged 45 to 54 years. Other studies also reported elevated risks of placenta previa and antepartum hemorrhage in patients older than 45. These findings are likely explained by physicians' lower threshold for performing hysterectomies in AMA patients with PPH, especially in the presence of risk factors such as placenta previa. These risks should be communicated to AMA patients given the high morbidity and mortality associated with peripartum hysterectomies (5).

The shift in fertility toward higher ages during the last few decades comprises one of the most distinctive aspects of reproductive behavior in developed countries. Many studies have linked higher maternal age with adverse pregnancy outcomes, increased risks of preterm delivery and low birth weight, fetal death and unexplained fetal death, and an increasing proportion of cesarean deliveries. Increases in cesarean section (CS) rates have been observed globally in recent decades, and nearly doubled between 2000 and 2015: from 12 in 2000 to 21% of births in 2015. The same trends regarding fertility postponement and an increase in CS rates are evident in Czechia, where the process of fertility postponement began in the 1990s and has been particularly dynamic; the average age of women at delivery increased from 25 in 1990 to 30 in 2018, and the percentage of live births to mothers aged 35 and older increased from only 4% in 1990 to 22% in 2018. The CS rate doubled in this period: from 10% in 1994 to 24% in 2018 (6).

Pregnancies in older women are growing rapidly and are associated with aneuploidy, copy number variations, trophoblast cell function abnormalities, cardiovascular health and unfavorable pregnancy outcomes. A relationship between maternal age and chromosomal aneuploidy has been established in

previous studies. However, there are few studies on the association between maternal age and CNV copy number variation. The risk of sex or autosomal chromosomal aneuploidy increases significantly with maternal age, especially after 35 years. A previous study suggested that AMA is an independent indicator of pathological examination of the placenta. Due to the aging of oocytes per se in older women, chromosome segregation errors during meiotic division are becoming more common and easy to produce oocytes with an incorrect number of chromosomes, resulting in an increased risk of chromosomal aneuploidy. Maternal age negatively affects methylation and expression of imprinted genes in germ and somatic cells of the reproductive tract, contributing to reduced fertility in aging women. Interestingly, posttranslational modifications in ovarian oocytes in pregnant women lead to fetal chromosomal abnormalities. However, the frequency of abnormal CNV in offspring was not related to maternal age, and the risk of abnormal CNV remained constant throughout a woman's reproductive period (7).

Older pregnant women are at increased risk for complications including gestational diabetes and fetal death. Carnitine Palmitoyl Transferase (CPT) decreases with age in various tissues and is associated with poorer metabolic health. Mitochondrial CPT catalyzes the synthesis of acylcarnitine, which facilitates the oxidation of fatty acids as fuel (8).

Advanced maternal age (AMA) is defined as a maternal age of 35 years or older at the time of delivery. Over the past three decades, the percentage of AMA has increased rapidly in many developed countries and high-income countries, reaching 23% in the United States in 2014 and up to 33% in Korea in 2019. However, aging, as an inevitable biological progress, comes with the accumulation of organ functional impairment and cellular damage, such as impaired cardiovascular homeostasis, systemic inflammation, mitochondrial dysfunction and so on. Investigation of the human plasma proteome revealed nonlinear changes during the aging process, with a remarkable peak of changes in protein expression around age 34. In fact, AMA is well recognized as a major risk factor for various pregnancy complications and adverse pregnancy outcomes, including preeclampsia, diabetes mellitus, miscarriage and preterm delivery (9).

Kim et al (10) Investigated the association between maternal age and severe maternal morbidity (SMM) in a Korean population. The data from delivery cases between 2003 and 2019. The primary outcome was MMS, determined using the Center for Disease Control and Prevention algorithm. A generalized estimation was performed equation modeling with a logarithmic link for the relationship between MMS and maternal age adjusting for covariates. MMS occurred in 40,959/2,113,615 (2%) of cases. Adolescents and women aged 35 years or older had an increased risk of MMS in nulliparous and multiparous cases (15 to 19 years: relative risk (RR) 1.32, 95 % confidence interval (CI) 1.15 to 1.46; 35 to 39 years: RR 1.24, 95 % CI 1.21-1.28; 40-44 years: RR 1.57, 95 % CI 1.50-1.64; In nulliparous and multiparous cases, adolescent girls and women aged 35 years and older were at particularly high risk of SMM. This is consistent with our results.

The postponement of childbearing has been one of the most prominent demographic developments in wealthy countries in recent decades, with the median maternal age at childbearing rising to >30 years

in the 2010s in most member countries of the Organization for Economic Cooperation and Development (OECD). This trend may have important spillover effects to other life domains; advanced maternal age, defined as age 35 years, is considered a risk marker for poorer pregnancy and perinatal health outcomes, which, in turn, have been linked to lower cognitive ability and poorer health in later life of offspring. At the same time, maternal age at childbearing reflects a variety of physiological and social processes, some of which may have positive implications for the well-being of offspring (11).

Preeclampsia and GDM are common and significant complications of maternal pregnancy worldwide, posing a serious threat to maternal morbidity, neonatal morbidity and mortality. The world prevalence of preeclampsia is reported to be between 2 and 4%. In addition, it is associated with about 46,000 maternal deaths annually, especially in countries with poor income distribution (12).

A processed dietary pattern refers to behaviors that favor salty, fried and processed foods, food products containing high levels of saturated fats, free sugars, sodium and trans fats, such as baked goods, salty snacks, sauces, dressings and condiments that have a negative effect on an individual's health and may also negatively affect the birth weight of infants. In Taiwan, as in other countries, socioeconomic changes are related to changes in dietary patterns that are associated with a reduction in daily calorie intake, increased consumption of unsaturated fats, added sugars and processed foods, and lower consumption of fruits and vegetables. This dietary pattern is of concern at all stages of life and especially during pregnancy, where it is associated

with poor health and compromises fetal growth and development. Lack or excess of nutrients during pregnancy can lead to morbid complications for both mother and fetus and can affect the health of a child later in life (13).

GDM is defined as the occurrence of glucose intolerance and glucose levels are lower than those diagnosed with overt diabetes outside pregnancy. In recent decades, the incidence of GDM has increased significantly, especially among women of advanced maternal age (>35 years). Worldwide, GDM affects approximately 14% of pregnancies and the prevalence of GDM in high-risk population reaches almost 27%. Furthermore, the prevalence of GDM increases with gestational age from 25% at 23 weeks of gestation to 33% in the third trimester of pregnancy. GDM poses significant short-term consequences and long-term threat to the mother and her offspring (14).

De novo gestational hypertension, chronic hypertension, preeclampsia-eclampsia, and chronic hypertension with superimposed preeclampsia have an incidence of 5-12% among pregnant women. PE is elevated blood pressure and proteinuria after 20 weeks of gestation, which can cause multiorgan damage (renal, hepatic, neurologic, and hematologic complications), and fetal growth restriction. Active detection of women at high risk of PE and early preventive measures should be validated to define a precise indication. Since hypercoagulability is the underlying pathology with the highest level of evidence for the occurrence of PE, it is urgent to monitor indicators of hypercoagulability starting in the first trimester (15).

Delaying childbearing until later in life can carry

significant risks for women and their babies. Previous studies have explored which factors are related to prenatal health behaviors. A meta-analysis study of pregnant women and their health behavior, age, employment, income, education, parity, maternal-fetal attachment, stress, depression, and social support as predictors. Obstetric characteristics, such as type of current conception, gestational age, parity, and abortion experience, are related to prenatal health behavior: more pregnant women in the third trimester than in the second trimester, and younger pregnant women than older pregnant women engaged in less healthy behaviors. Meanwhile, some studies have considered psychosocial factors, as these components might otherwise be improved through interventions compared to demographic and obstetric characteristics (21).

Women who are older than 35 years at delivery have higher rates of gestational diabetes (16), preterm delivery [17], fetal death, cesarean delivery, preeclampsia [18], and maternal and neonatal morbidity and mortality. These risks become even more pronounced with further increases in maternal age. In fact, a recent report from the Centers for Disease Control cited maternal mortality rates of 107.8/100,000 in women over 40 compared with 22.8/100,000 for women aged 25-39 years. A particularly strong association is between advanced maternal age and the risk of developing hypertensive disorders of pregnancy (HDP), which includes gestational hypertension, chronic hypertension, preeclampsia-eclampsia and hemolysis, elevated liver enzymes and low platelet Hellp syndrome. Although HDP complicates between 2 and 8% of pregnancies in general, it affects 18% of pregnancies in women aged 35 to 44 years and 35% in women older than 45 years. More importantly, however, HDP handles up to 30% of maternal mortality due to stroke, eclampsia, disseminated intravascular coagulopathy, and renal failure (19, 20).

It is necessary to explore which characteristics are related to the health behavior of pregnant women in the EMA. Older pregnant women perceived pregnancy as more threatening than younger women did and tended to engage in healthier behaviors (13). Therefore, applying the results of studies on pregnant women of all ages to pregnant AMA women may make understanding the factors influencing prenatal health behaviors difficult. In addition, compared with other countries, pregnant women in Korea are under much social pressure, which is natural given their role as mothers to behave for the health of their fetus.

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REFERENCES

1. Ratiu D, Sauter F, Gilman E, et al. Impact of Advanced Maternal Age on Maternal and Neonatal Outcomes. *In vivo*, 2023; 37: 1694-702. Doi:10.21873/invivo.13256
2. Li G, Wei T, Ni W, Zhang A, Zhang J, Xing Y and Xing Q Incidence and Risk Factors of Gestational Diabetes Mellitus: A Prospective Cohort Study in Qingdao, China. *Front Endocrinol*, 2020; 11:636. Doi: 10.3389/fendo.2020.00636.
3. Shen J, Song J, Zeng F, Sun J. The effect of maternal age and duration of labor on perinatal and neonatal outcomes: a retrospective cohort study. *Ann Transl Med*, 2022; 10(20):1138. Doi: 10.21037/atm-22-4404.

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4. Sheen JJ, Wright JD, Goffman D, et al. Maternal age and risk for adverse outcomes. *Am J Obstet Gynecol* 2018; 219(4):390.e1-390.e15. <https://doi.org/10.1016/j.ajog.2018.08.034>
 5. Machado-Gedeon A, Badeghiesh A, Baghlaif H, Dahan MH. Adverse pregnancy, delivery and neonatal outcomes across different advanced maternal ages: A population-based retrospective cohort study. *Eurox*, 2023; 17: 100180.
 6. Štastná A, Fait T, Kocourková J, Waldaufová E. Does Advanced Maternal Age Comprise an Independent Risk Factor for Caesarean Section? A Population-Wide Study. *Int J Environ Res Public Health*, 2023; 20: 668. <https://doi.org/10.3390/ijerph20010668>
 7. Cao L, Dong W, Wu Q, et al. Advanced maternal age: copy number variations and pregnancy outcomes. *Front Genet*, 2023; 14:1206855. Doi: 10.3389/fgene.2023.1206855
 8. Yong HEJ, Watkins OC, Mah TKL, et al. Increasing maternal age associates with lower placental CPT1B mRNA expression and acylcarnitines, particularly in overweight women. *Front. Physiol*, 2023; 14:1166827. Doi: 10.3389/fphys.2023.1166827
 9. Hua L, Chen W, Meng Y, et al. The combination of DNA methylome and transcriptome revealed the intergenerational inheritance on the influence of advanced maternal age. *Clin Transl Med*, 2022; 12:e990. <https://doi.org/10.1002/ctm2.990>
 10. Kim J, Nam JY, Park E-C. Advanced maternal age and severe maternal morbidity in South Korea: a population-based cohort study, *Sci Rep*, 2022; 12:21358. <https://doi.org/10.1038/s41598-022-25973-x>.
 11. Aradhya S, Tegunimataka A, Kravdal Ø, et al. Maternal age and the risk of low birth weight and pre-term delivery: a pan-Nordic comparison. *Int J Epidemiol*, 2023; 156-64 <https://doi.org/10.1093/ije/dyac211>
 12. Sun M, Luo M, Wang T, et al. Effect of the interaction between advanced maternal age and pre-pregnancy BMI on pre-eclampsia and GDM in Central China. *BMJ Open Diab Res Care* 2023; 11:e003324. Doi: 10.1136/bmjdr-2023-003324.
 13. Chen TL, Cheng SF, Gau ML, Lin LL. Processed Dietary Patterns during Pregnancy are Associated with Low Birth Weight at Term among Women of Advanced and Non-Advanced Age. *Nutr*, 2022; 14: 3429. <https://doi.org/10.3390/nu14163429>.
 14. Deng L, Ning B, Yang H. Association between gestational diabetes mellitus and adverse obstetric outcomes among women with advanced maternal age. A retrospective cohort study. *Med*, 2022; 101:40.
 15. Yali Deng, Lifei She, Xiaoye Li, et al. Monitoring hypertensive disorders in pregnancy to prevent preeclampsia in pregnant women of advanced maternal age: Trial mimicking with retrospective data. *Open Med*, 2022; 17:1840-8 <https://doi.org/10.1515/med-2022-0560>
 16. Lopian M, Kashani-Ligumsky L, Many AA. Balancing Act: Navigating Hypertensive Disorders of Pregnancy at Very Advanced Maternal Age, from Preconception to Postpartum. *J Clin Med*, 2023; 12: 4701. <https://doi.org/10.3390/jcm12144701>.
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17. Vounzoulaki E, Khunti K, Abner SC, Tan BK, Davies MJ, Gillies C. Progression to type 2 diabetes in women with a known history of gestational diabetes: systematic review and meta-analysis. *BMJ*, 2020; 369, m1361.
 18. Esposito G, Maura PA, Cipriani S, et al. The role of maternal age on the risk of preterm birth among singletons and multiples: A retrospective cohort study in Lombardy, Northern Italy. *BMC Pregnancy Childbirth* 2022; 22:234, Erratum in *BMC Pregnancy Childbirth* 2022, 22, 366.
 19. Vandekerckhove M, Guignard M, Civadier MS, Benachi A, Bouyer J. Impact of maternal age on obstetric and neonatal morbidity: A retrospective cohort study. *BMC Pregnancy Childbirth* 2021; 21: 732.
 20. Gao L, Li S, Yue Y, Long G. Maternal age at childbirth and the risk of attention deficit/hyperactivity disorder and learning disability in offspring. *Front Public Health*, 2023; 11:923133. Doi: 10.3389/fpubh.2023.923133.
 21. Haakstad LAH, Voldner N, Bø K. Pregnancy and advanced maternal age-the associations between regular exercise and maternal and newborn health variables. *Acta Obstet Gynecol Scand*, 2020; 99:240-8. Doi: 10.1111/aogs.13738.