

Effect of Very Advanced Maternal Age on Pregnant Women and Fetuses

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ABSTRACT

Objective: To compare the difference in the effect on pregnant women and fetuses between very advanced maternal age (age of or over 45 years) and other ages (age below 45 years).

Study Design: A descriptive study.

Place and Duration of Study: Changyi People's Hospital, China, from June 2017 and September 2020.

Methodology: Four-hundred singleton pregnancies were selected. One hundred and three pregnant women at age of or over 45 years (Group A) and 297 pregnant women at age below 45 years (Group B) were grouped by age. Serum total cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (HDL-C) and low density lipoprotein cholesterol (LDL-C), incidence of pregnancy complications and fetal outcomes were compared.

Result: Group A had higher TC and HDL-C than Group B at 12-week, 32-week pregnancy and 3 days after delivery (all $p < 0.001$); Group A had higher TG than Group B at 12-week, 32-week pregnancy and 3 days after delivery ($p = 0.003$, $p < 0.001$ and $p < 0.001$), respectively. Group A had higher incidence of gestational diabetes mellitus (GDM), pregnancy complicated with leiomyoma, gestational hypertension, placenta previa, placental abruption, anemia and postpartum hemorrhage than Group B (all $p < 0.001$). Group A had higher incidence of fetal distress and preterm birth than Group B (both $p < 0.001$). The difference in fetal weight and Apgar score of 5-min infants compared between the two groups was significant (both $p < 0.001$).

Conclusion: The incidence of gestational complications and adverse perinatal outcomes may be increased in very advanced maternal age singleton pregnant women aged over 45 years.

Key Words: Very advanced maternal age, Pregnant women, Pregnancy, Fetus, Complications.

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INTRODUCTION

The pregnant women of very advanced maternal age are those who give birth to their babies at the age of or over 45 years.¹ Most of existing studies take those with advanced maternal age of more than 35 years as a group.^{2,3} However, an increase in the number of very advanced maternal age (≥ 45 years) women brings more concerns on the pregnancy issues of the very advanced maternal age (≥ 45 years) women. Advanced maternal age pregnancies are considered to bring increased risks to both mothers and babies.^{4,5} Compared to younger women, women of advanced age (≥ 45 years) was related to greater risk for adverse birth outcomes.⁶

One study found that women of advanced age (≥ 45 years) had a significantly increased risk for preterm delivery, hypertension, diabetes, etc.⁷ Thirteen percent women aged 45 years had hypertensive disorders of pregnancy.⁸ Studies have found that very advanced maternal age women over 45 years have higher morbidity of complications during pregnancies and also increased prevalence of preterm birth.⁹ A study confirmed that women at ≥ 43 years had higher risks of adverse maternal and neonatal outcomes than the younger counterparts.¹⁰ But some scholars believed that there wasn't enough evidence to determine if older maternal age was an independent and direct risk factor for preterm birth and small-for-gestational-age birth.¹¹

The objective of this study was to compare the difference in the effect on pregnant women and fetuses between very advanced maternal age (pregnant women at age of or over 45 years) and other ages (pregnant women at age below 45 years).

METHODOLOGY

This study was approved by the Ethics Committee of Changyi People's Hospital, China, from June 2017 and September 2020. Four hundred singleton pregnancies were selected. One hundred and three pregnant women at age of or over 45 years (Group A) and 297 pregnant women at age below 45 years (Group B) were grouped by age.

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The inclusion criteria were that the pregnant women were singleton pregnancy, with informed consent, and with a complete set of prenatal examinations and postnatal follow-up visit information, age of or over 45 years and less than or equal to 53 years in Group A; age below 45 years and greater than or equal to 18 years in Group B. The exclusion criteria were twin or multiple pregnancies, coexistent hyperlipidemia, combined hypertension, renal disease, blood disease, mental and neurological diseases, communication dysfunction, or with familial hereditary diseases.

Fasting venous blood samples of the pregnant women at 12-week, 32-week pregnancy and 3 days after delivery were collected. The automatic biochemical analyser was used to determine the total cholesterol (TC), triglyceride (TG), high density lipoprotein cholesterol (HDL-C) and low density lipoprotein cholesterol (LDL-C).

The associated diseases and complications were collected. Postnatal follow-up visits were made and the pregnancy outcomes were recorded. The incidence of gestational diabetes mellitus (GDM), anemia, pregnancy complicated with leiomyoma, gestational hypertension, placenta previa, placental abruption and postpartum hemorrhage; the incidence of adverse pregnancy outcome (fetal distress, malformation, preterm birth and fetal death); and comparisons were made for fetal weight and Apgar score of 5-min infants between the two groups were observed and recorded.

SPSS version 25 was used for data analysis. Kolmogorov-Smirnov test was used to test the normality of measurement data. The measurement data that did not conform to the normal distribution were expressed by median and interquartile interval (IQR: 25th percentile-75th percentile), the comparison between groups was performed by non-parametric Mann-Whitney U-test. Count data was expressed by n (%), and Chi-square test or Fisher Exact test was used for comparison between the groups. A p value less than 0.05 was considered statistically significant.

RESULTS

One hundred and three pregnancies in Group A were aged 49.00 years (48-50) and at the gestational age of 39.00 w (35-41); there were 68 (66.02%) women with two or fewer pregnancies and 35 (33.98%) women with more than 2 pregnancies.

Two hundred and ninety-seven pregnancies in Group B were aged 30.00 years (26-34.50) and at the gestational age of 39.00 w (38-42); there were 197 (66.33%) women with two or fewer pregnancies and 100 (33.67%) women with more than 2 pregnancies.

Group A had higher TC and HDL-C than Group B at 12-week, 32-week pregnancy and 3 days after delivery (all $p < 0.001$, Table I); Group A had higher TG than Group B at 12-week, 32-week pregnancy and 3 days after delivery ($p = 0.003$, $p < 0.001$, and $p < 0.001$, respectively, Table I); the difference in LDL-C

compared between the two groups at 12-week, 32-week pregnancy and 3 days after delivery was not statistically significant ($p = 0.870$, $p = 0.203$, and $p = 0.105$, respectively, Table I).

Group A had higher incidence of GDM, pregnancy complicated with leiomyoma, gestational hypertension, placenta previa, placental abruption, anemia and postpartum hemorrhage than Group B (all $p < 0.001$, Table II).

There were no maternal or neonatal deaths in both groups. Group A had higher incidence of fetal distress and preterm birth than Group B (both $p < 0.001$, Table III). There was no significant difference in malformation between the two groups ($p = 0.164$, Table III). The difference in fetal weight and Apgar score of 5-min infants compared between the two groups was statistically significant (both $p < 0.001$, Table III).

DISCUSSION

Delaying childbirth of women has adverse effects on mothers and babies, and it also brings a series of issues like decline of population quality. It was shown in this study that Group A had significantly higher TG than Group B at 32-week pregnancy and 3 days after delivery; Group A had higher TC and HDL-C than Group B for the entire perinatal period. It was a sign that a majority of AMA pregnant women were with lipid and glucose metabolic abnormalities, and higher potential risks of vascular disease.

Studies have shown that AMA pregnant women in singleton pregnancy aged over 40 years have the risk of GDM 1.34 times as high as that of those in AMA singleton pregnancy aged 35-39 years.¹²

It was found in this study that Group A had higher incidence of GDM than Group B. It may be related to the decline in the function of insulin β cell and lower serum adiponectin level of AMA pregnant women.^{13,14} It was further found that Group A had higher incidence of the gestational hypertension than Group B. It may be a result of the fact that very advanced maternal age pregnant women do less exercise and take in excessive nutrition, and this leads to higher weight and frequent occurrence of gestational hypertension. Placenta previa and placental abruption are one of the main causes of hemorrhage in pregnancy. They are severe complications in pregnancy and may be a threat to maternal and fetal life.^{15,16}

Group A had higher incidence of pregnancy complicated with leiomyoma, placenta previa, anemia, placental abruption and postpartum hemorrhage than Group B. Previous studies have also shown that AMA pregnant women have higher incidence of uterine fibroids.¹⁷ Decline of uterine function in very advanced maternal age pregnant women, especially the damage of uterine fiber function and relatively increased connective tissue, can lead to physical tiredness and uterine inertia in delivery and be prone to postpartum hemorrhage.

A meta-analysis showed that the increased age of pregnant women was a key factor of fetal growth restriction.¹⁸

Table I: Comparison in the changes of perinatal serum markers between the two groups.

Parameter	Time	Group A (n=103)	Group B (n=297)	p-value
TC (mmol/L)	At 12-week pregnancy	6.55 (6.34-6.75)	6.28 (6.10-6.41)	<0.001
	At 32-week pregnancy	6.81 (6.59-7.02)	6.43 (6.25-6.56)	<0.001
	At 3 days after delivery	6.72 (6.50-6.93)	6.38 (6.20-6.51)	<0.001
TG (mmol/L)	At 12-week pregnancy	2.62 (2.54-2.70)	2.57 (2.50-2.62)	0.003
	At 32-week pregnancy	3.05 (2.96-3.14)	2.78 (2.70-2.83)	<0.001
	At 3 days after delivery	3.64 (3.53-3.75)	2.87 (2.79-2.92)	<0.001
HDL-C (mmol/L)	At 12-week pregnancy	3.38 (3.28-3.48)	2.39 (2.32-2.43)	<0.001
	At 32-week pregnancy	3.51 (3.41-3.61)	2.47 (2.41-2.52)	<0.001
	At 3 days after delivery	3.55 (3.45-3.65)	2.36 (2.30-2.41)	<0.001
LDL-C (mmol/L)	At 12-week pregnancy	3.56 (3.45-3.67)	3.56 (3.47-3.63)	0.870
	At 32-week pregnancy	3.66 (3.55-3.77)	3.63 (3.54-3.70)	0.203
	At 3 days after delivery	3.57 (3.46-3.68)	3.60 (3.51-3.67)	0.105

Table II: Comparison in perinatal gestational associated diseases of pregnant women between the two groups.

Parameter	Group A (n=103)	Group B (n=297)	p-value
GDM [n (%)]	20 (19.42)	15 (5.05)	<0.001
Pregnancy complicated with leiomyoma [n (%)]	25 (24.27)	11 (3.70)	<0.001
Gestational hypertension [n (%)]	49 (47.57)	37 (12.46)	<0.001
Placenta previa [n (%)]	28 (27.18)	8 (2.69)	<0.001
Placental abruption [n (%)]	31 (30.10)	42 (14.14)	<0.001
Anemia [n (%)]	15 (14.56)	9 (3.03)	<0.001
Postpartum hemorrhage [n (%)]	38 (36.89)	42 (14.14)	<0.001

Table III: Comparison of fetal outcomes between the two groups.

Parameter	Group A (n=103)	Group B (n=297)	p-value
Fetal distress [n (%)]	40 (38.83)	43 (14.48)	<0.001
Fetal malformation [n (%)]	2 (1.94)	1 (0.34)	0.164
Fetal preterm birth [n (%)]	31 (30.10)	20 (6.73)	<0.001
Fetal weight (Kg)	2.98 (2.89-3.07)	3.31 (3.22-3.40)	<0.001
Apgar score of 5-min infants	9.05 (8.77-9.20)	9.44 (9.26-9.67)	<0.001

One study found that advanced maternal age was independently associated with specific adverse perinatal outcomes.¹⁹ It was found in this study that Group A had higher incidence of fetal distress and preterm birth than Group B. The difference in fetal weight and Apgar score of 5-min infants compared between the two groups was statistically significant, indicating that there will be a further increase in the incidence of gestational complications such as GDM and hypertension, and adverse pregnancy outcomes like fetal distress and preterm birth of very advanced maternal age singleton pregnant women aged over 45 years. On this account, pregnancy care for very advanced maternal age pregnant women aged over 45 years should be strengthened. Strengthened prenatal monitoring, active measures in prevention and treatment of pregnancy complications should be made to reduce the occurrence of adverse pregnancy outcomes of mothers and babies. Dietl *et al.* confirmed that when the timely treatment of pre-existing chronic diseases in pregnant women were obtained, pregnancy complications were controlled, regular prenatal check-ups and a healthy lifestyle were received, delivery in a perinatal centre, there was no significant difference in gestational complications and adverse perinatal outcomes between pregnant women aged over 40 years and younger women.²⁰

CONCLUSION

The incidence of gestational complications and adverse perinatal outcomes may be increased in very advanced maternal age singleton pregnant women aged over 45 years. The perinatal care for very advanced maternal age

pregnant women aged over 45 years should be highly stressed. Obstetricians should be conscientious in screening high risk diseases such as gestational hypertension, GDM and preterm birth. Early diagnosis and treatment of pregnancy complications should be made, and the monitoring should be strengthened.

ETHICAL APPROVAL:

This study was approved by the Ethical Committee of Changyi People's Hospital, Shandong Province, China.

PATIENTS' CONSENT:

All subjects accepted the study with informed consent.

CONFLICT OF INTEREST

The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:

MZ: Literature search, manuscript writing, result interpretation, discussion and final approval.

YW: Data collection and analysis.

XQ: Research design and conception.

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