



Second-trimester maternal lipid profiles predict pregnancy complications in an age-dependent manner

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Abstract

Purpose Our objective was to investigate the combinatorial effect of maternal age and second-trimester maternal lipid profiles for pregnancy complications.

Methods With 1:4 matching, this retrospective study selected 499 advanced maternal age women and 1996 younger controls. Logistic regression analysis was used to estimate the correlation between second-trimester lipid profiles [total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C)] and pregnancy complications [gestational diabetes mellitus (GDM), pregnancy-induced hypertension syndrome (PIH), preterm labor (PTL), and macrosomia]. Optimal cutoff points were determined by ROC curve analysis.

Results In women aged 20–34 years, TG are a risk factor for PIH (OR 1.54, 95% CI 1.16–2.04) and PTL (OR 1.34, 95% CI 1.04–1.72). LDL-C was positively associated with macrosomia (OR 1.25, 95% CI 1.04–1.50), while HDL-C was negatively associated with PIH (OR 0.45, 95% CI 0.21–0.93). The optimal cutoff points for TG predicting PIH and PTL were separately ≥ 2.135 and 2.305 mmol/L. The optimal cutoff point for HDL-C identifying PIH was ≤ 1.995 mmol/L and for LDL-C identifying macrosomia was ≥ 3.425 mmol/L. As for advanced maternal age, only TG was an independent risk factor for PIH (OR 1.60, 95% CI 1.01–2.54), and its optimal cutoff point was ≥ 2.375 mmol/L.

Conclusions Second-trimester lipid profiles might predict pregnancy complications varied by maternal age. This suggested that individualized prenatal care strategies should be established for women with advanced and normal maternal age to prevent pregnancy complications.

Keywords Advanced maternal age · Lipid profiles · Second trimester · Pregnancy complications · Correlation

Introduction

Advanced maternal age is defined as childbirth in women aged 35 years or older [1]. In recent years, with the development of society and medicine, maternal age is tending to be

older. The first birth rate for women aged 35 years or older in the United States has increased more than eight times over the past 4 decades [2]. A large contemporary cohort study consisting of 215,344 births in the UK showed a 18.18% prevalence of advanced maternal age [3]. A retrospective cohort study also found that the proportion of women giving birth over 35 years of age increased from 11.4 to 19.1% in an Asian population [4]. There is a clear trend worldwide towards increasing prevalence of advanced maternal age. In addition, as the implementation of the universal two-child policy, more and more women will give birth with advanced maternal age in China.

Advanced maternal age is considered as a high-risk factor for pregnancy complications and adverse perinatal outcomes, such as gestational diabetes mellitus (GDM), stillbirth, preterm labor (PTL), macrosomia, and so on [5]. A large number of studies suggested various organs, especially

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reproductive and neuroendocrine organs, will be functionally impaired with increasing maternal age. In addition, it will greatly increase the risk of severe adverse outcomes, coupling with the continuous accumulation of environmental effects. Women with advanced maternal age are more likely to have obstetric complications [6, 7].

Previous studies also indicated that maternal lipid, whose metabolism changed throughout gestation to meet the needs of fetal growth, played an important role on obstetric complications [8]. Clinically, maternal lipid profiles are usually measured by total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C). Catov et al. [9] reported that elevated early pregnancy TC and TG concentrations were associated with a more than twofold increased risk for spontaneous preterm birth. Furthermore, evidence has shown every unit increase in TG during early pregnancy was linearly associated with an increased risk of pregnancy-induced hypertension syndrome (PIH), preeclampsia, and PTL [10]. In addition, a large cohort study discovered that elevated TG levels throughout pregnancy contributed to a raised risk of PTL and macrosomia [11]. However, most of these researches targeted pregnant women without age stratification, while few focused on women with advanced maternal age alone.

Our study was aimed at investigating the associations between maternal lipid profiles of second trimester and adverse pregnancy outcomes in advanced maternal age and comparing with pregnant women in appropriate age, to explore the combinatorial effect of maternal age and lipid profiles for pregnancy complications. At the same time, we hoped to provide more reliable evidence for predicting perinatal outcomes and developing better perinatal care in an age-dependent manner.

Methods

Between 1 January 2014 and 31 December 2014, information of 14,909 pregnant women who attended regular prenatal health care and gave birth in Women's Hospital School of Medicine Zhejiang University was collected in the study. Inclusion criteria of pregnant women were: (1) maternal ages at delivery ≥ 20 years; (2) gestational weeks at delivery ≥ 28 weeks; (3) integrated medical records; (4) singleton pregnancy; and (5) no abnormal results of prenatal screening. Exclusion criteria of pregnant women were: (1) multiple pregnancy; (2) stillbirth; (3) received assisted reproductive techniques; (4) experienced infection on reproductive system during pregnancy; and (5) had diabetes mellitus, hypertension, thyroid diseases, autoimmune diseases, inherited metabolic diseases or other vital organ diseases before pregnancy. We selected 899 women with advanced

maternal age (≥ 35 years) and 8661 women with maternal age (20–34 years). With 1:4 matching about gravidity, parity, gestational weight gain (GWG) and pre-pregnancy body mass index (BMI), 2495 women were available for and included in the final analysis, of which 499 were in advanced maternal age group and 1996 in younger control group. We gathered demographic and medical information of all these participants, including maternal ages, gravidity, parity, height, pre-pregnancy weight, GWG, gestational weeks at birth, birth weight of newborns, pregnancy complications and maternal lipid profiles of second trimester. This study was approved by the hospital's ethics committee, and specific informed consent for inclusion was waived because of using anonymized patient records.

Macrosomia was defined as the birth weight equal to or greater than 4000 g in a newborn. In addition, women whose gestational weeks at birth were less than 37 weeks and more than 28 weeks were diagnosed as having PTL in China. As for GDM and PIH, they were diagnosed based on the recommendations from International Association of Diabetes and Pregnancy Study Groups [12] and International Society for the Study of Hypertension in Pregnancy [13], respectively.

The maternal lipid profiles were tested in the biochemical laboratory of Women's Hospital School of Medicine Zhejiang University. All the participants were drawn venous blood samples at second trimester (24–28 gestational weeks) after overnight fasting. Those blood samples were centrifuged (3500 rpm for 10 min at 4 °C) for serum samples, and they were assayed for lipid profiles using an Olympus AU400e chemistry immune analyzer (Tokyo, Japan).

BMI was calculated as pre-pregnancy weight in kilograms divided by the square of height in meters. According to the standard for Asian populations [14], pre-pregnancy BMI was categorized into underweight ($< 18.5 \text{ kg/m}^2$), normal weight ($18.5\text{--}22.9 \text{ kg/m}^2$), and overweight ($\geq 23 \text{ kg/m}^2$) groups. On the basis of recommendations from American Institute of Medicine [15], appropriate GWG with different pre-pregnancy BMI was defined as follows: 12.5–18 kg ($\text{BMI} < 18.5 \text{ kg/m}^2$), 11.5–16 kg ($18.5 \text{ kg/m}^2 \leq \text{BMI} < 25 \text{ kg/m}^2$), 7–11.5 kg ($\text{BMI} \geq 25 \text{ kg/m}^2$). In addition, falling below the thresholds was defined as inadequate GWG, while exceeding the thresholds was defined as excessive GWG. Besides, lipid profiles were divided into four different lipid categorization groups by quartiles.

Data were analyzed by SPSS version 20.0. The nonparametric test was used to compare basic information. Maternal lipid profiles were compared by *t* test, and the prevalence of pregnancy complications were evaluated by χ^2 test. Logistic regression analysis was applied to explore the associations between maternal lipid profiles and pregnancy complications, while controlling for potentially confounding variables (maternal ages, gravidity, parity, pre-pregnancy BMI, and GWG groups). In addition, to eliminate the effects between

Table 1 Obstetrical characteristics by maternal age groups

Characteristic	Age \geq 35 ($n=499$)	Age 20–34 ($n=1996$)	<i>p</i> value
Maternal age (years)	36.9 \pm 2.2	29.2 \pm 2.7	< 0.001
Gravidity	1.9 \pm 0.7	1.9 \pm 0.7	> 0.99
Parity			> 0.99
Nulliparous	268 (53.7)	1072 (53.7)	
Multiparous	231 (46.3)	924 (46.3)	
GWG (kg)	14.1 \pm 3.9	14.2 \pm 4.0	0.814
GWG groups			> 0.99
Appropriate	281 (56.3)	1124 (56.3)	
Inadequate	106 (21.2)	424 (21.2)	
Excessive	112 (22.4)	448 (22.4)	
BMI (kg/m ²)	21.2 \pm 2.5	21.1 \pm 2.6	0.416
BMI groups			0.558
Underweight	59 (11.8)	276 (13.8)	
Normal weight	331 (66.3)	1281 (64.2)	
Overweight	109 (21.8)	439 (22.0)	
Gestational weeks	38.7 \pm 1.7	39.4 \pm 1.3	< 0.001
Birth weight (g)	3259.2 \pm 499.3	3356.8 \pm 422.7	< 0.001

Values are given as mean \pm SD or number (percentage) unless stated otherwise

complications, women with multiple complications were excluded from the correlation analysis. ROC curve analysis was conducted to determine the optimal cutoff point of lipid profiles for predicting adverse outcomes. Each optimal cutoff point was assessed via searching for the maximum value of Youden index (sensitivity + specificity-1). AUC was calculated to evaluate the predictive powers. $p < 0.05$ was considered to be statistically significant.

Results

Overall, 499 women aged \geq 35 years and 1996 women aged 20–34 years were included in our study. Mean maternal age of two groups were 36.9 \pm 2.2 and 29.2 \pm 2.7 years, respectively ($p < 0.001$). The gestational weeks at delivery in advanced maternal age group were significantly less than those in control group (38.7 \pm 1.7 vs 39.4 \pm 1.3; $p < 0.001$), and the same for birth weight of newborns (3259.2 \pm 499.3 g vs 3356.8 \pm 422.7 g; $p < 0.001$). Moreover, others revealed no significant differences between the two groups (Table 1).

In terms of second-trimester maternal lipid profiles, TC and TG levels were, respectively, 6.28 \pm 1.00 mmol/L and 2.42 \pm 0.90 mmol/L, which were significantly higher in women aged \geq 35 years (both $p < 0.05$), while HDL-C level was lower (2.29 \pm 0.49 mmol/L; $p = 0.023$). As for LDL-C, there was no significant difference between the two groups (Table 2).

The analysis in prevalence of pregnancy complications revealed that GDM, PIH and PTL were more likely to occur in advanced maternal age than in younger controls (24.2% vs

Table 2 Second-trimester lipid profiles by maternal age groups

Lipid profiles ^a	Age \geq 35	Age 20–34	<i>p</i> value
TC	6.28 \pm 1.00	6.18 \pm 1.05	0.046
TG	2.42 \pm 0.90	2.24 \pm 0.84	< 0.001
HDL-C	2.29 \pm 0.49	2.34 \pm 0.50	0.023
LDL-C	3.42 \pm 0.80	3.41 \pm 0.84	0.575

Values are given as mean \pm SD mmol/L unless stated otherwise

^aDeleting extreme values or using Ln conversion to ensure the normal distribution of data

Table 3 Pregnancy complications by maternal age groups

Pregnancy complications	Age \geq 35 ($n=499$)	Age 20–34 ($n=1996$)	<i>p</i> value
GDM	121 (24.2)	297 (14.9)	< 0.001
PIH	38 (7.6)	57 (2.9)	< 0.001
PTL	46 (9.2)	72 (3.6)	< 0.001
Macrosomia	35 (7.0)	141 (7.1)	0.969

Values are given as number (percentage) unless stated otherwise

14.9%, 7.6% vs 2.9%, 9.2% vs 3.6%; all $p < 0.001$). However, the prevalence of macrosomia between two groups was not statistically different (Table 3).

Figure 1 showed that the prevalence of GDM, PIH, PTL and macrosomia were significantly higher in pregnant women with TG above 75th% and HDL-C below 25th% (all $p < 0.05$). However, there was no significant difference

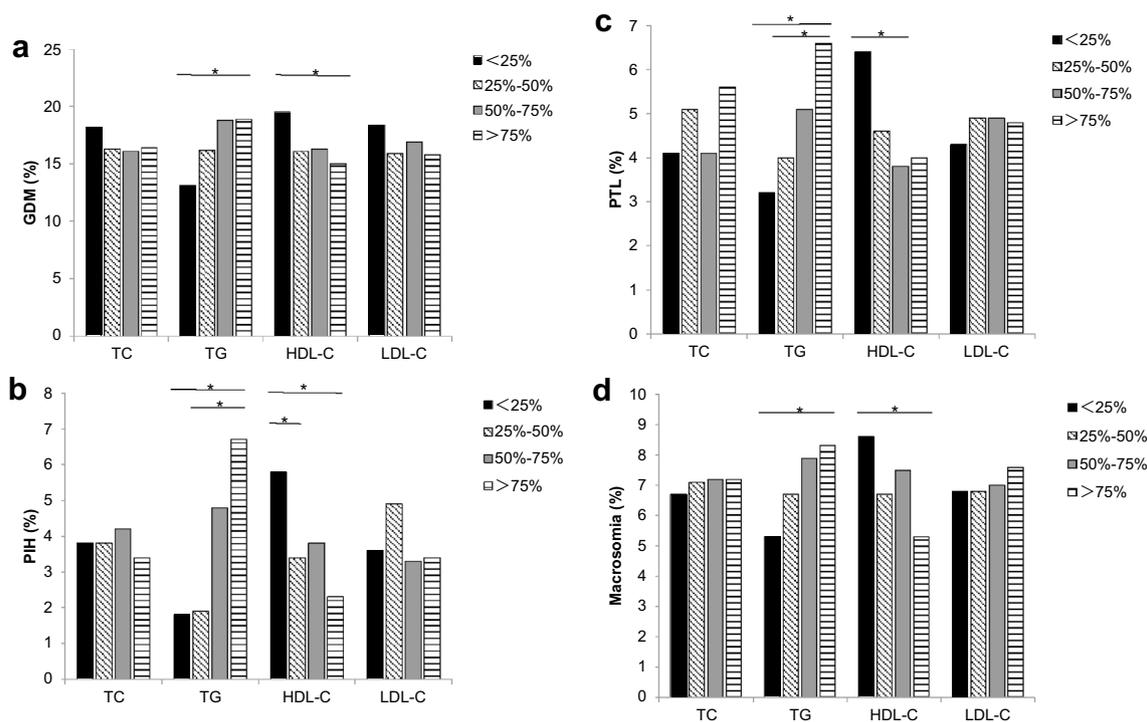


Fig. 1 Pregnancy complications according to second-trimester lipid profiles. Asterisk indicates a significant difference between groups, $p < 0.05$

about prevalence of pregnancy complications when TG in 50–75th% and above 75th%. Similar result was also found in HDL-C.

The associations between second-trimester maternal lipid profiles and pregnancy complications were displayed by Table 4. In women aged 20–34 years, we observed every unit elevation in TG level was associated with an increased risk of PIH (OR 1.54, 95% CI 1.16–2.04) and PTL (OR 1.34, 95% CI 1.04–1.72). In addition, high LDL-C level

was associated with a 1.25-fold increased risk of macrosomia (OR 1.25, 95% CI 1.04–1.50). Additionally, significant negative association was found between HDL-C level and PIH (OR 0.45, 95% CI 0.21–0.93). In contrast, there was no significant association between TC levels and all pregnancy complications. Interestingly, the results were different in advanced maternal age. We only found high TG level was an independent risk factor for PIH in women aged ≥ 35 years (OR 1.60, 95% CI 1.01–2.54).

Table 4 Associations between second-trimester lipid profiles and pregnancy complications in an age-dependent manner

Pregnancy complications	TC		TG		HDL-C		LDL-C	
	OR (95% CI)	<i>p</i> value						
Age ≥ 35 ($n = 459$)								
GDM	1.21 (0.95–1.54)	0.118	1.01 (0.77–1.32)	0.964	1.01 (0.82–1.25)	0.932	1.20 (0.90–1.62)	0.221
PIH	1.03 (0.64–1.67)	0.900	1.60 (1.01–2.54)	0.047	0.58 (0.21–1.64)	0.307	0.99 (0.55–1.79)	0.980
PTL	1.12 (0.78–1.61)	0.551	1.14 (0.79–1.66)	0.487	0.79 (0.37–1.67)	0.535	1.02 (0.64–1.60)	0.945
Macrosomia	0.91 (0.58–1.42)	0.673	1.28 (0.79–2.07)	0.323	0.59 (0.22–1.59)	0.296	0.95 (0.54–1.65)	0.845
Age 20–34 ($n = 1935$)								
GDM	0.89 (0.78–1.02)	0.090	1.00 (0.85–1.18)	0.988	0.95 (0.75–1.20)	0.668	0.86 (0.73–1.01)	0.058
PIH	0.95 (0.70–1.29)	0.739	1.54 (1.16–2.04)	0.003	0.45 (0.21–0.93)	0.032	0.90 (0.61–1.33)	0.593
PTL	1.00 (0.86–1.16)	0.975	1.34 (1.04–1.72)	0.024	0.71 (0.41–1.23)	0.225	1.03 (0.78–1.37)	0.842
Macrosomia	1.04 (0.94–1.15)	0.467	0.93 (0.72–1.20)	0.566	0.85 (0.57–1.27)	0.426	1.25 (1.04–1.50)	0.018

OR were adjusted for maternal ages, gravidity, parity, pre-pregnancy BMI, and GWG groups (use the appropriate GWG group as the reference category)

The optimal cutoff points proposed by ROC curve analysis for maternal second-trimester lipid profiles in predicting pregnancy complications were presented in Table 5. Among them, TG predicting PIH in normal maternal pregnant women had the largest AUC [0.651 (95% CI 0.560–0.743)] and its optimal cutoff point was ≥ 2.135 mmol/L, while higher cutoff point was found in advanced maternal age (≥ 2.375 mmol/L). Besides, the optimal cutoff points for TG predicting PTL were ≥ 2.305 mmol/L. The optimal cutoff point for HDL-C identifying PIH was ≤ 1.995 mmol/L and for LDL-C identifying macrosomia was ≥ 3.425 mmol/L in women aged 20–34 years.

Discussion

In this retrospective study, we included 499 women aged ≥ 35 years as study group and 1996 aged 20–34 years as control group. Then, we compared their maternal and neonatal characteristics, levels of second-trimester lipid profiles, prevalence of pregnancy complications and associations between second-trimester lipid profiles and pregnancy complications. There is no significant difference in gravidity, parity, BMI and GWG, which was mainly due to matching of these confounders to eliminate their influence on subsequent analysis. A decrease of gestational age and birth weight was observed in advanced maternal age, which generally resulted from higher prevalence of pregnancy complications, and clinicians tend to help delivery in advance to reduce impact on both mother and fetus.

Previous study indicated second-trimester lipid profiles were correlated to age, and TG had significantly positive relationship while HDL-C had negative one. Additionally, TC and LDL-C had no significant relationship with age [16]. Similarly, our results showed TC and TG levels increased and HDL-C decreased in the women with advanced maternal

age, while no statistically significant difference was found in LDL-C levels. Consequently, second-trimester lipid profiles were higher among advanced maternal age women, which possibly results from organ failure and downtrend of metabolism function with increasing maternal age. In addition, compared with non-pregnant women, higher maternal lipid levels in pregnant women may be due to metabolic changes during pregnancy [17]. Nevertheless there is no accurate definition of normal pregnancy lipid range nowadays, and clinicians usually evaluate them by normal non-pregnant lipid criteria, which may increase unnecessary clinical interventions. Thus, the normal lipid reference values in pregnant women are urgently needed to be determined by epidemiological studies with a large sample size, and our results demonstrated that it should differ between advanced maternal age and younger pregnant women. Only in this way can we provide correct guidance for pregnant women especially those aged ≥ 35 years and it would also be beneficial to subsequent studies related to maternal lipid.

Comparing the prevalence of pregnancy complications between two groups, we found pregnant women aged ≥ 35 years had a significantly higher incidence of GDM, PIH and PTL and there is no significant difference on macrosomia. Consequently, advanced maternal age increased the prevalence of pregnancy complications. A study found the prevalence of GDM increased as maternal age increased and peaked at the age of 40 years [18]. Function of islet and insulin sensitivity declined and secretion of hyperglycemic hormone increased during pregnancy, which resulted in insulin resistance and then occurrence of GDM. Moreover, insulin secretion and its receptor affinity further reduced as maternal age increased. A cohort study showed a fivefold increased risk of gestational hypertension in advanced maternal age [19], which was similar with our findings and may result from progressive damage of vascular endothelial with age. Advanced maternal age also increased the prevalence of

Table 5 Optimal cutoff points of second-trimester lipid profiles for predicting pregnancy complications in an age-dependent manner

Pregnancy complications	AUC (95% CI)	Sensitivity (%)	Specificity (%)	Youden index	Cutoff point (mmol/L)
Age ≥ 35 ($n=459$)					
TG					
PIH	0.622 (0.492–0.751)	73.7	59.3	0.330	2.375
Age 20–34 ($n=1935$)					
TG					
PIH	0.651 (0.560–0.743)	73.0	54.2	0.272	2.135
PTL	0.569 (0.493–0.644)	55.0	63.8	0.187	2.305
HDL-C					
PIH	0.630 (0.533–0.727)	77.2	45.9	0.231	1.995
LDL-C					
Macrosomia	0.538 (0.479–0.597)	52.9	55.3	0.082	3.425

PTL and probably related to placental and uterine vascular lesions [20, 21]. In addition, because of high incidence of other pregnancy complications in advanced maternal age, it is necessary for them to give birth in advance to reduce impact on both mother and fetus in clinical, which led to high prevalence of iatrogenic preterm delivery. Kenny et al. [3] found that advanced maternal age was a risk factor of macrosomia, and associated with an increased incidence of obesity and GDM during pregnancy. But we found no significant difference on macrosomia between two groups, which might relate to correct nutrition guidance and tight glucose control during pregnancy. Furthermore, a decrease of gestational age and birth weight was observed in women aged ≥ 35 years which possibly result from iatrogenic preterm delivery, might also be the cause of our result.

Our study showed that lipid levels and prevalence of pregnancy complications increased in women with advanced maternal age, and women with high lipid levels ($> 75\text{th}\%$) had higher prevalence of pregnancy complications. On the basis of these results, we hypothesized their high second-trimester lipid levels were associated with high prevalence of pregnancy complications. We observed an increasing level of TG led to higher prevalence of PIH in both women with normal and advanced maternal age, which indicated that TG was an independent risk factor for PIH regardless of maternal age. In addition, an increasing trend in prevalence of PIH with HDL-C level decreasing was found in pregnant women aged 20–34 years while no trend in pregnant women aged ≥ 35 years. Researchers have explored associations between pregnancy lipid profiles and PIH previously. Enquobahrie et al. [22] found early pregnancy dyslipidemia was associated with an increased risk of preeclampsia. A prospective longitudinal cohort study conducted in China showed maternal TG concentrations were higher in PIH across the three trimesters and high TG elevation from the first to third trimesters was associated with increased risk of PIH [23]. In addition, Mudd et al. [24] reported positive association between TG and PTL, which was similar to results in maternal age women while no significant correlation was found in women with advanced maternal age. Other studies indicated that TC level and LDL-C/HDL-C ratio in early pregnancy were risk factors for PTL [9, 25]. However, our study found no associations between TC or HDL-C or LDL-C level and PTL. Moreover, a population-based study recently showed low middle and late pregnancy HDL-C levels and high late pregnancy TG level were all risk factors for macrosomia and late pregnancy LDL-C level was unrelated with macrosomia [26]. But in our study, only positive association between LDL-C level and macrosomia in younger controls were found.

Generally, these results of our study demonstrated that second-trimester lipid profiles might predict pregnancy complications both in pregnant women aged ≥ 35 years and

women aged 20–34 years, but associations between them in pregnant women aged ≥ 35 years were weaker than in women aged 20–34 years, which was inconsistent with our hypothesis. Actually, instead of maternal lipid profiles, we found BMI, GWG and gravidity were strongly associated with pregnancy complications in advanced maternal age. Inadequate GWG was a risk factor for GDM (OR 1.79, 95% CI 1.02–3.13), while overweight was for PIH (OR 1.30, 95% CI 1.09–1.54). Besides, gravidity and excessive GWG were positively correlated with PTL (OR 2.12, 95% CI 1.18–3.81) and macrosomia (OR 4.54, 95% CI 1.71–12.06), respectively. Possible causes were as follows: (1) although highest prevalence of pregnancy complications was found in high lipid levels, women with lipid levels in 50–75th% and above 75th% had similar pregnancy complication prevalence. In addition, women in advanced maternal age were more likely to have higher lipid levels, which were too high to have a significant effect on the occurrence of pregnancy complications and on the contrary other factors such as BMI, GWG might play major roles. (2) Our study had no record about education, smoking and other possible factors, which might affect results. (3) Small sample size of study group might influence the accuracy of results.

Moreover, it is known that different complications could interact with each other. For example, GDM was associated with elevated risk of giving birth to a macrosomia [27, 28]. In our study, we found the prevalence of macrosomia was significantly higher both in diabetic women with advanced maternal age (11.6% vs 5.6%; $p < 0.05$). In addition, for those women with GDM, HDL-C was significantly lower in macrosomia (1.97 ± 0.51 mmol/L vs 2.34 ± 0.55 mmol/L; $p = 0.020$). The AUC for HDL-C predicting macrosomia in advanced maternal age women with GDM was 0.739 (95% CI 0.596–0.882) and its optimal cutoff points were ≤ 2.275 mmol/L, which was higher than in those women without GDM (≤ 1.825 mmol/L). These results indicated that we should manage HDL-C more strictly for diabetic pregnancies to prevent macrosomia in advanced maternal age women. Furthermore, the results above also remind us the necessity to exclude the effects between different complications when exploring the relationship between lipid profiles and pregnancy complications.

There were several strengths in our study. We provided some prospective evidence suggesting that dyslipidemia during pregnancy might lead to pregnancy complications both in advanced and normal maternal age. To our knowledge, most previous studies focusing on the associations between lipid levels and pregnancy complications were conducted in pregnant women with no age restriction and almost no research was conducted in women with advanced maternal age. Our findings indicated that second-trimester maternal lipid profiles were differently predictive for pregnancy complications in an age-dependent manner, and it is necessary

for pregnant women aged ≥ 35 years to pay more attention on BMI and GWG besides lipid levels. Furthermore, we focused on second-trimester lipid levels rather than first or third trimester. Since first-trimester lipid levels were easily affected by other factors and hard to maintain throughout the pregnancy, while most adverse outcomes or complications had occurred in third trimester and lipid levels were difficult to adjust. In our study, we eliminated the influence of gravidity, parity, BMI and GWG on both groups by means of matching, which made the results more intuitional and credible. Besides, screening for single complications also contributed to the accuracy of the study. In addition, the optimal cutoff points proposed by ROC curve analysis provided sufficient basis for maternal second-trimester lipid profiles predicting pregnancy complications in different maternal age groups, which might help manage lipid profiles better.

However, there were still some limitations in our study. First of all, the age stratification in our study was rough, and comparison between subgroups of appropriate maternal age group might give more information. Considering this point, we divided pregnant women into 20–24 years, 25–29 years, 30–34 years and ≥ 35 years groups and found that difference of second-trimester maternal lipid profiles and prevalence of pregnancy complications were not significant between 20–24 and 30–34 years while significant between ≥ 35 years and 25–29 years (Table S1, S2). Consequently, we considered it might be more meaningful to compare between women with advanced and normal maternal age. Second, small sample size of women with advanced maternal age led to small amount of pregnancy complications, which might affect accuracy and reliability of our results. Third, although we collected maternal lipid profiles at second trimester (24–28 gestational weeks), we did not record precise data of gestational weeks. However, lipid levels may change constantly through gestational weeks. Finally, this study was a hospital-based retrospective study and our sample lacked population diversity. Moreover, there were controversies regarding association between lipid levels and pregnancy complications. Therefore, a multicenter study with larger sample size and more rigorous design could be more representative.

In conclusion, second-trimester lipid profiles might predict pregnancy complications varied by maternal age, which meant individualized antenatal care strategies should be established for women with advanced and normal maternal age. Our findings suggested advanced maternal age women need strict lipid regulation as well as normal maternal age women, especially TG in women aged ≥ 35 years and TG, HDL-C, LDL-C in women aged 20–34 years. And besides maternal lipid, more attention must be paid to weight control before and during pregnancy in advanced maternal age women and develop better prenatal care through diet and exercise management to reduce prevalence of pregnancy complications.

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Author contribution statement QW and LXZ: project development, data collection, data analysis, data interpretation, and manuscript writing. LH, YL and LC: data analysis and manuscript revision. ZXL, MLZ, HX, YMZ and FW: data collection and manuscript revision. DQC: project development, data interpretation, and manuscript revision.

Compliance with ethical standards

Conflict of interest The authors declare that there is no duality of interest associated with this manuscript.

Informed consent In this study, we confirm that patient privacy was not compromised, which was approved by the hospital's ethics committee. And specific informed consent for inclusion was waived because of using anonymized patient records.

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