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Analysis of the characteristics of blood lipid metabolism in twin pregnancy

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ABSTRACT

To investigate the characteristics of blood lipid metabolism in twin pregnancy combined with gestational diabetes mellitus (GDM) or pregnancy-induced hypertension (PIH). This study retrospectively analyzed 96 cases of twin pregnancy and 232 cases of full-term singleton pregnancy. General data and blood lipid levels, including triglyceride (TG) and total cholesterol (TC), between twin and singleton pregnancies were compared. Blood lipid levels between GDM (PIH) and non-GDM (non-PIH) groups in twin pregnancy were compared. The TG level for twin pregnancy was higher than that for singleton pregnancy ($p<0.05$), while there was no significant difference in the TC level between them ($p>0.05$). The TG level in the GDM group was higher than that in the non-GDM group ($p<0.05$), while the TC level in the GDM group was not different from that in the non-GDM group ($p>0.05$). The TG level in the PIH group was higher than that in the non-PIH group ($p<0.05$), while there was no difference in the TC level between them ($p>0.05$). Logistic regression analysis showed that age was a risk factor for GDM and PIH in singleton and twin pregnancies. The lipid levels in twin pregnancy increased with the increase of gestational age, and the TG level in twin pregnancy complicated with GDM or PIH was higher than that in twin pregnancy without GDM or PIH, indicating that the blood lipid metabolism was related to the occurrence of GDM and PIH in twin pregnancy to some extent.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Compared with singleton pregnancy, twin pregnancy is a high-risk pregnancy and is more prone to bring about complications; increased blood lipid level in the twin pregnancy also increases the adverse pregnancy outcome.

WHAT THIS STUDY ADDS

⇒ We found that the triglyceride (TG) level of twin pregnancy was higher than that of singleton pregnancy, and the TG level increased with the increase of gestational age.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The blood lipid level should be monitored regularly during twin pregnancy. Ideally, blood lipid screening is recommended to be carried out before pregnancy.

INTRODUCTION

With the development of assisted reproductive technology, the probability of twin pregnancy is getting higher and higher.[1] However, compared with singleton pregnancy, twin pregnancy is a high-risk pregnancy, and is more prone to bring about complications such as high blood pressure, high blood glucose, infection, premature rupture of membranes, premature delivery, low weight, and asphyxia, thereby causing some adverse pregnancy outcomes, and affecting the safety of mothers and fetuses.[2–4] Previous studies have shown that maternal blood lipid level of singleton pregnancy under normal pregnancy conditions increases, but the abnormally elevated blood lipid is closely related to the adverse pregnancy outcome.[5–7] Similarly, the increased blood lipid level in twin pregnancy also increases the adverse pregnancy outcome.[8 9] Our study aimed to explore the changing characteristics of blood lipid level in different gestational weeks of twin pregnancy and twin pregnancy complicated with gestational diabetes mellitus (GDM) or pregnancy-induced hypertension (PIH).

MATERIALS AND METHODS

This study was conducted in accordance with the Declaration of Helsinki.

General information

This is a hospital-delivery population-based case–control study. Patients who were filed in our hospital, had undergone antenatal examination, and gave birth in the No 1 Hospital of Wuhan from March 2016 to March 2021 were selected. The data contain maternal characteristics, such as age, parity, height and weight, medical history, mental conditions, pre-pregnancy and prenatal examinations, and pregnancy complication; and fetal and neonatal characteristics, which were extracted from the medical record system of the No 1 Hospital of Wuhan by trained research assistants.

Inclusion criteria: (1) cases with complete data of demographic characteristics, medical history, pregnancy history, and lipid screening; (2) cases experiencing oral glucose tolerance

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test (OGTT) during pregnancy; (3) cases without serious organic diseases such as liver disease, kidney disease, etc.

Exclusion criteria: (1) cases who suffered from hypertension, diabetes, thyroid function or other metabolic diseases before pregnancy, primary aldosteronism or pheochromocytoma; (2) monochorionic twin pregnancy.

Finally, 96 cases of twin pregnancy and 232 cases of full-term singleton pregnancy were randomly enrolled into this study. The first antenatal examination was performed at 5–11 weeks of gestation, and during the first antenatal examination, demographic characteristics, medical history, and pregnancy history were collected. The height and weight of each case were also recorded at the first antenatal examination, and the body mass index (BMI) of each case was also calculated at this examination and regarded as the early-pregnancy BMI (kg/m^2). Cases over 35 years old (including 35 years old) were divided into the advanced age group, and cases who were less than 35 years old were divided into the appropriate age group. Cases with early-pregnancy BMI <24.9 kg/m^2 were included into the normal weight group, and cases with early-pregnancy BMI >25 kg/m^2 were included into the overweight group. According to the presence or absence of GDM and PIH, they were divided into GDM group, non-GDM group, PIH group, and non-PIH group.

Among the 96 pregnant women with twin pregnancies, 55 were in the appropriate age group, 41 in the advanced age group, 72 in the normal weight group, and 24 in the overweight group; 62 cases experienced naturally conceived twins, and 34 cases experienced twin pregnancy by assisted reproductive technology. Among the 232 pregnant women with singleton pregnancy, 198 were in the appropriate age group, 34 cases in the advanced age group, 181 cases in the normal weight group, and 51 cases in the overweight group; 151 cases experienced naturally conceived singletons, and 81 cases experienced singleton pregnancy by assisted reproductive technology.

Diagnosis of GDM and hypertension

Diagnostic criteria for GDM: a 75 g OGTT was performed. The critical values of fasting blood glucose, 1-hour and 2-hour OGTTs were 5.1 mmol/L, 10.0 mmol/L and 8.5 mmol/L, respectively. If any of the above-mentioned three indicators was greater than or equal to its critical value, the case could be diagnosed with GDM.[10] Based on this, 22 of the 96 women with twins were diagnosed with GDM, and the incidence of GDM was 22.9%; 30 of 232 women with singleton pregnancy were diagnosed with GDM, and the incidence of GDM was 12.9%.

The diagnostic criteria of gestational hypertension are based on the 'Guidelines for Diagnosis and Treatment of Hypertension in Pregnancy 2015'.[11] In our study, of 96 women with twins, 18 had gestational hypertension, the incidence of PIH was 18.8%, and 6 cases both had GDM and PIH. Of 232 women with singleton pregnancy, 22 had gestational hypertension, the incidence of PIH was 9.5%, and 8 cases both had GDM and PIH.

A fully automated immunoassay analyzer and kit were used to detect triglyceride (TG) and total cholesterol (TC). All pregnant women fasted and did not drink water the night before visiting the hospital, and 6 mL of brachial vein blood was drawn after 8-hour fasting at the hospital in the early pregnancy (5–11 weeks), the second trimester (22–26 weeks), and the third trimester (33–37 weeks), respectively.

Statistical analysis

SPSS V.19.0 was used for statistical analysis of the data. The enumeration data were analyzed by $\chi 2$ test, and the measurement data were expressed by mean±SD. The comparison between the two groups was performed by independent-sample t-test. The comparison among multiple groups was performed by one-way analysis of variance, and the further comparison was performed by Student-Newman-Keuls q test. The risk factors were screened by binary logistic regression analysis. P<0.05 was considered a statistically significant difference.

RESULTS

General data

As shown in table 1, the age and BMI (kg/m^2) of pregnant women with twins were higher than those of pregnant women with singletons, and the difference was statistically significant (p<0.05); however, there was no significant difference in the gravidity, parity and method of conception between the two groups (p>0.05). For the pregnant women with twins, the BMI of those with GDM (23.56±1.91) was higher than that of those without GDM (22.97±2.83), the BMI of those with gestational hypertension (23.49±2.05) was higher than that of those without gestational hypertension (22.86±1.83), and the differences were statistically significant (p<0.05). The incidence of GDM and PIH between singleton and twin pregnancies had significant difference (p<0.05).

Table 1 Comparison of general data between twin pregnancy and singleton pregnancy

Groups	Cases	Age (y $\bar{X}$±s)	Gravidity ($\bar{X}$±s)	Parity ($\bar{X}$±s)	BMI (kg/m^2)	Conception method		GDM (n)		PIH (n)	
						Naturally	Assisted reproductive technology	Yes	No	Yes	No
Singleton pregnancy	232	28.62±3.41	3.15±0.62	0.82±0.56	21.54±2.76	151	81	30	202	22	210
Twin pregnancy	96	30.83±4.10	3.21±0.64	0.81±0.63	23.12±3.05	62	34	22	74	18	78
t/χ^2		4.927	1.847	1.050	4.750	0.008		5.075		5.446	
P value		0.000	0.066	0.295	0.000	0.931		0.031		0.026	

BMI, body mass index; GDM, gestational diabetes mellitus; PIH, pregnancy-induced hypertension.

Table 2 Changes of the TG level and the TC level in the first, second and third trimesters of twin pregnancy (mmol/L, $\bar{x}\pm s$)

	TG	TC
The first trimester	1.46±0.30	4.29±0.07
The second trimester	3.19±1.11	6.31±1.32
The third trimester	3.58±1.10	6.47±1.30
F	146.287	109.410
p1	0.000	0.000
p2	0.004	0.347
p3	0.000	0.000

Note: p1 meant comparison between the first trimester and the second trimester; p2 meant comparison between the second trimester and the third trimester; p3 meant comparison between the first trimester and the third trimester.
TC, total cholesterol; TG, triglyceride.

The gradual increase of TG and TC in twin pregnancy with the increase of gestational age

Among 96 women with twin pregnancy, the TG level in the third trimester was higher than that in the second trimester, the TG level in the second trimester level was higher than that in the first trimester, and the differences were statistically significant ($p<0.05$). The TC level in the second trimester and the third trimester was higher than that in the first trimester ($p<0.05$), but there was no statistically significant difference in the TC level between the second trimester and the third trimester ($p>0.05$; see table 2).

Comparison of the TG level and the TC level between twin pregnancy and singleton pregnancy

The TG level between singleton and twin pregnancies had statistically significant difference in the first, second and third trimesters ($p<0.05$), while the TC level between singleton and twin pregnancies had no statistically significant difference in the first, second and third trimesters ($p>0.05$; see table 3).

Comparison of the TG level and the TC level between GDM group and non-GDM group in twin pregnancy

Among 96 cases with twin pregnancy, 22 were in the GDM group and 74 were in the non-GDM group. The TG level in the GDM group was higher than that in the non-GDM group in the first, second and third trimesters ($p<0.05$), while the difference of the TC level between the GDM group and the non-GDM group in the first, second and third trimesters was not statistically significant ($p>0.05$; see table 4).

Comparison of the TG level and the TC level between the PIH group and the non-PIH group in twin pregnancy

Among 96 cases with twin pregnancy, 18 were in the PIH group and 78 were in the non-PIH group. The TG level in the PIH group was higher than that in the non-PIH group in the first, second, and third trimesters ($p<0.05$), while the difference of the TC level between the PIH group and the non-PIH group in the first, second and third trimesters was not statistically significant ($p>0.05$; see table 5).

Analysis of risk factors of GDM and PIH in women with twin and singleton pregnancies

Among the 96 twin pregnancies, 22 were in the GDM group, 74 in the non-GDM group, 18 in the PIH group, and 78 in the non-PIH group. GDM and PIH were used as dependent variables, respectively; age, early-pregnancy BMI, and blood lipid levels of different trimesters were used as independent variables for logistic regression analysis; and the results showed that age was a risk factor for GDM and PIH in pregnant women with twin pregnancies (OR=0.68, 95% CI: 0.61 to 0.74; OR=0.73, 95% CI: 0.67 to 0.79). In the same way, in the group of 232 pregnant women with singleton pregnancy, logistic regression analysis showed that age also was a risk factor for the occurrence of GDM and PIH in singleton pregnancy (OR=0.57, 95% CI: 0.51 to 0.64; OR=0.66, 95% CI: 0.60 to 0.71).

DISCUSSION

During the normal pregnancy, in order to meet the needs of fetal growth and development, childbirth preparation and postpartum breast feeding, a series of changes occur in the mother's endocrine, thereby affecting its overall metabolism, and changes in blood lipid metabolism are one of them.[12] Studies in recent years have shown that the changes in TG and cholesterol in blood lipids during pregnancy are the most obvious.[13] Under normal circumstances, from the

Table 3 Comparison of the TG level and the TC level between twin pregnancy and singleton pregnancy (mmol/L, $\bar{x}\pm s$)

		TG		TC	
		Elderly group	Age group	Elderly group	Age group
The first trimester	Singleton	1.21±0.51 (n=34)	1.13±0.42 (n=198)	4.20±0.68 (n=34)	4.18±0.73 (n=198)
	Twin	1.49±0.48 (n=41)	1.42±0.57 (n=55)	4.31±0.65 (n=41)	4.28±0.71 (n=55)
	t	6.273	6.352	1.453	1.298
	P value	0.000	0.000	0.268	0.347
The second trimester	Singleton	2.32±0.86 (n=34)	2.25±0.73 (n=198)	6.27±1.77 (n=34)	6.14±2.21 (n=198)
	Twin	3.47±1.09 (n=41)	3.06±1.24 (n=55)	6.32±1.96 (n=41)	6.25±1.13 (n=55)
	t	7.426	7.683	1.372	1.012
	P value	0.000	0.000	0.386	0.272
The third trimester	Singleton	3.08±0.98 (n=34)	2.94±1.06 (n=198)	6.38±1.43 (n=34)	6.33±1.71 (n=198)
	Twin	3.59±1.12 (n=41)	3.52±1.04 (n=55)	6.47±1.02 (n=41)	6.43±1.39 (n=55)
	t	3.287	4.652	0.572	0.546
	P value	0.000	0.000	0.482	0.516

TC, total cholesterol; TG, triglyceride.

Table 4 Comparison of the TG level and the TC level between the GDM group and the non-GDM group in twin pregnancy

		The first trimester		The second trimester		The third trimester	
Groups	Cases	TG	TC	TG	TC	TG	TC
The GDM group	22	1.58±0.39	4.37±0.67	3.85±1.13	6.18±1.09	4.13±1.24	6.59±1.28
The non-GDM group	74	1.42±0.28	4.27±0.67	2.99±1.03	6.35±1.38	3.41±1.00	6.43±1.31
t		2.323	0.621	3.324	0.530	2.795	0.525
P value		0.020	0.523	0.001	0.597	0.006	0.601

GDM, gestational diabetes mellitus; TC, total cholesterol; TG, triglyceride.

early pregnancy on, the levels of TG and TC in the maternal blood gradually increase with the increase of gestational week, reach the highest peak in the third trimester, remain at this level until childbirth, rapidly decline after delivery, and return to the normal level after around 4–6 weeks.[14] It has been reported that TG and TC increase about 2–3 times compared with non-pregnancy.[15] In twin pregnancy, the mother and fetuses need more nutrients for growth and development, and blood lipids also increase accordingly, which is a physiological change in adaptation to growth and development; but if the blood lipids exceed a certain limit, the risk of adverse pregnancy outcomes will increase.

In our present study, it was found that for both singleton pregnancy and twin pregnancy, TG and TC increased with the increase of the gestational age. The TG level of women with twin pregnancy was significantly higher than those of women with singleton pregnancy, while there was no significant difference in the TC level between them, which is consistent with the research by Wei *et al*.[16]

At present, there is no consensus on the normal level of blood lipids during pregnancy. Studies have shown that dyslipidemia during pregnancy is related to adverse pregnancy outcomes,[17] and dyslipidemia during pregnancy is related to the onset of gestational diabetes and hypertension.[18] The main pathogenesis of gestational diabetes is insulin resistance and insufficient pancreatic β-cell function. Pregnant women with gestational diabetes not only have disorders of glucose metabolism, but also have abnormal lipid metabolism. Even if pregnant women with gestational diabetes have satisfactory blood glucose control, they have higher levels of insulin resistance and blood lipid than healthy pregnant women.[19] Abnormal lipid metabolism may be one of the reasons for insulin resistance and impaired pancreatic β-cell function, thereby promoting the occurrence of gestational diabetes. Our present study suggested that the TG level in twin pregnancy was higher than that in singleton pregnancy, and for the twin pregnancy, the TG level in the GDM group was higher than that in non-GDM group, indicating that GDM cases of twin pregnancy had much more serious lipid metabolism disorders.

There is also a certain relationship between the blood lipid levels and hypertension during pregnancy. Studies have shown that the risk of hypertension during pregnancy in twin pregnancy is 4 times than that in singleton pregnancy.[20] Studies have confirmed that hypertension during pregnancy is related to vascular endothelial damage, and abnormal lipid metabolism can damage vascular endothelial cells, thereby resulting in the occurrence of hypertension in pregnancy.[21–23] Our present study found that for 96 women with twin pregnancy, the TG level of those with hypertension during pregnancy was higher than that in those without hypertension during pregnancy, indicating that the TG level during pregnancy might have a certain relationship with the occurrence of hypertension in twin pregnancy.

In this study, after adjusting for pre-pregnancy BMI, it was found that age was a risk factor for GDM and PIH in pregnant women with singleton pregnancy and twin pregnancy. Compared with normal pregnant women, pregnant women with GDM or PIH had abnormal blood lipid metabolism, so it is speculated that advanced age might be related to abnormal blood lipid metabolism.

In addition, there are some limitations in our present study. First, there are unequal sample sizes in different groups, and thus in the future study, we will keep equal sample size among different groups as possible as we can, so that the comparisons among groups are more convincing. Second, we did not analyze the supplementation of progesterone which may elevate lipids, especially TC in our present study, and thus in the future study, we will consider the influence of supplementation of progesterone and do the relevant analysis. Third, we also did not investigate the low-density lipoprotein cholesterol (LDL-C) as a key factor in cardiovascular disease, and thus in the future study, we will collect the LDL-C data and do the relevant analysis. Fourth, power calculation was not done for estimation of sample size selected for this study, and thus in the future,

Table 5 Comparison of the TG level and the TC level between the PIH group and the non-PIH group in twin pregnancy (mmol/L, $\bar{x}$±s)

		The first trimester		The second trimester		The third trimester	
Groups	Cases	TG	TC	TG	TC	TG	TC
The PIH group	18	1.62±0.35	4.34±0.85	3.92±1.09	6.24±1.12	4.18±1.19	6.61±1.35
The non-PIH group	78	1.45±0.34	4.33±0.79	2.95±1.05	6.32±1.27	3.39±1.09	6.41±1.26
t		2.465	0.637	3.453	0.542	2.378	0.486
P value		0.002	0.496	0.005	0.568	0.004	0.592

PIH, pregnancy-induced hypertension; TC, total cholesterol; TG, triglyceride.

we will do this power calculation before conducting the research in the future.

In summary, we found that the TG level in twin pregnancy was higher than that in singleton pregnancy, and the TG level increased with the increase of gestational age. For the twin pregnancy, the TG level of cases with gestational diabetes was higher than that of cases without gestational diabetes, and the TG level of cases with gestational hypertension was higher than that of cases without gestational hypertension. These results implied that compared with singleton pregnancy, there was more serious lipid metabolism disorder for twin pregnancy, and the lipid metabolism disorder was most obvious in twin pregnancy with gestational diabetes or hypertension. Therefore, the blood lipid level should be monitored regularly during twin pregnancy. Ideally, blood lipid screening is recommended to be carried out before pregnancy. If the blood lipid screening is not performed before pregnancy, considering that dyslipidemia might lead to adverse pregnancy outcomes, regularly monitoring the blood lipid during pregnancy should also be carried out. If abnormalities are found, diet and exercise intervention should be used as soon as possible to control weight and improve lipid metabolism, thereby reducing the risk of adverse pregnancy outcomes.

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