Analysis of the characteristics of blood lipid metabolism in twin pregnancy

Yanqin Lou
The No. 1 Hospital of Wuhan

Pei He
The No. 1 Hospital of Wuhan

Huijun Jiang
The No. 1 Hospital of Wuhan

Li Xiang
The No. 1 Hospital of Wuhan

Xuemei Gao (gaoxm_218046@163.com)
The No. 1 Hospital of Wuhan

Research Article

Keywords: blood lipid metabolism, twin pregnancy, gestational diabetes mellitus, pregnancy induced hypertension, triglyceride, total cholesterol

Posted Date: June 16th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1714540/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License. Read Full License
Abstract

Objective:

This study aimed to investigate the characteristics of blood lipid metabolism in twin pregnancy and its combined with gestational diabetes mellitus (GDM) or pregnancy-induced hypertension (PIH).

Methods:

This study retrospectively analyzed 96 cases of twin pregnancy and 232 cases of full-term singleton pregnancy, and they were filed in our hospital, undergone antenatal examination and gave birth from March 2016 to March 2021. Among 96 cases of twin pregnancy, 22 cases had GDM, and 18 cases had gestational hypertension. Comparison of general data and blood lipid levels, including triglyceride (TG) and total cholesterol (TC), between twin pregnancy and singleton pregnancy was performed. Comparison of blood lipid levels between GDM group and non-GDM group in twin pregnancy was performed. Comparison of blood lipid levels between the PIH group and the non-PIH group in twin pregnancy was performed.

Results

For the twin pregnancy, the TG level in the third trimester was higher than that in the second and first trimester, and the TG level in the second trimester was higher than that in the first trimester (P < 0.05). For the twin pregnancy, the TC level in the second and third trimester was higher than that in the first trimester (P < 0.05), but there was no difference in the TC level between the second and third trimesters (P > 0.05). The TG level of twin pregnancy was higher than that of singleton pregnancy in the first, second and third trimesters (P < 0.05), but there was no difference in the TC level between twin pregnancy and singleton pregnancy (P > 0.05). For the twin pregnancy, 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 first, second and third trimester of twin pregnancy combined with PIH group was higher than that in the non-hypertensive group (P < 0.05), while there was no difference in the TC level between the hypertensive group and the non-hypertensive group (P > 0.05).

Conclusions

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 with GDM or PIH, indicating that the blood lipid metabolism was related to the occurrence of GDM and PIH in twin pregnancy to some extent.
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 the singleton pregnancy under normal pregnancy conditions increases, but the abnormally elevated blood lipids is closely related to the adverse pregnancy outcome [5–7]. Similarly, the increased blood lipid level in the twin pregnancy also increase the adverse pregnancy outcome [8, 9]. Our study aimed to explore the changing characteristics of blood lipid level in different gestational weeks of the twin pregnancy and the 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. This study was conducted with approval from the Ethic committee of The No. 1 Hospital of Wuhan. Written informed consent was obtained from the participants.

1.1 General information:

96 pregnant women with twins who were led in our hospital, undergone antenatal examination and gave birth from March 2016 to March 2021 were selected. Among them, 62 cases experienced naturally conceived twins, and 34 cases experienced twin pregnancy by assisted reproductive technology.

Exclusion criteria:1) Cases suffered from hypertension, diabetes, thyroid function or other metabolic diseases before pregnancy, primary aldosteronism or pheochromocytoma; 2) Monochorionic twin pregnancy; 3) No serious organic diseases such as liver or kidney disease.

After those who had hypertension, diabetes, liver disease, or kidney disease before pregnancy were excluded, 232 women with full-term singleton pregnancy who were led in our hospital and gave birth during the same period were enrolled into this study. Among them, 151 cases experienced naturally conceived singletons, and 81 cases experienced twin pregnancy by assisted reproductive technology.

1.2 Diagnosis of gestational diabetes mellitus and hypertension

Diagnostic criteria for gestational diabetes mellitus (GDM): a 75g oral glucose tolerance test (OGTT) was performed. The critical values of fasting blood glucose, 1-hour and 2-hour OGTT were 5.1mmol/L, 10.0mmol/L and 8.5mmol/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.

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 height and weight of each case were recorded at the first obstetric examination, and the body mass index (BMI) of each case was calculated as the pre-pregnancy body mass index (BMI, kg/m2). A fully automated immunoassay analyzer and kit were used to detect TC and TG. All pregnant women fasted and did not drink water the night before visiting the hospital, and 6ml 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.

1.3 Statistical analysis

SPSS19.0 was used for statistical analysis of the data. The enumeration data were analyzed by chi-square $\chi^2$ test, and the measurement data were expressed by ± standard deviation (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 (SNK)-q test. $p < 0.05$ was considered a statistically significant difference.

**Results**

2.1 General data

As shown in the Table 1, the age and BMI (kg/m2) 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 them with gestational diabetes mellitus ($23.56 \pm 1.91$) was higher than that of them without gestational diabetes mellitus ($22.97 \pm 2.83$), the BMI of them with gestational hypertension ($23.49 \pm 2.05$) was higher than that of them without gestational hypertension ($22.86 \pm 1.83$), and the differences were statistically significant ($P < 0.05$).
2.2 The increase of triglyceride (TG) and total cholesterol (TC) in twin pregnancy gradually 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.

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

<table>
<thead>
<tr>
<th>Groups</th>
<th>Cases</th>
<th>Age (years old $\bar{x} \pm s$)</th>
<th>Gravidity ($\bar{x} \pm s$)</th>
<th>Parity ($\bar{x} \pm s$)</th>
<th>BMI (kg/m²)</th>
<th>Conception method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Singleton pregnancy</td>
<td>232</td>
<td>28.62 ± 3.41</td>
<td>3.15 ± 0.62</td>
<td>0.82 ± 0.56</td>
<td>21.54 ± 2.76</td>
<td>151</td>
</tr>
<tr>
<td>Twin pregnancy</td>
<td>96</td>
<td>30.83 ± 4.10</td>
<td>3.21 ± 0.64</td>
<td>0.81 ± 0.63</td>
<td>23.12 ± 3.05</td>
<td>62</td>
</tr>
<tr>
<td>t/χ²</td>
<td></td>
<td>4.927</td>
<td>1.847</td>
<td>1.050</td>
<td>4.750</td>
<td>0.008</td>
</tr>
<tr>
<td>p</td>
<td></td>
<td>0.000</td>
<td>0.066</td>
<td>0.295</td>
<td>0.000</td>
<td>0.931</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th></th>
<th>TG</th>
<th>TC</th>
</tr>
</thead>
<tbody>
<tr>
<td>The first trimester</td>
<td>1.46 ± 0.30</td>
<td>4.29 ± 0.07</td>
</tr>
<tr>
<td>The second trimester</td>
<td>3.19 ± 1.11</td>
<td>6.31 ± 1.32</td>
</tr>
<tr>
<td>The third trimester</td>
<td>3.58 ± 1.10</td>
<td>6.47 ± 1.30</td>
</tr>
<tr>
<td>F</td>
<td>146.287</td>
<td>109.410</td>
</tr>
<tr>
<td>p1</td>
<td>0.000</td>
<td>0.000</td>
</tr>
<tr>
<td>p2</td>
<td>0.004</td>
<td>0.347</td>
</tr>
<tr>
<td>p3</td>
<td>0.000</td>
<td>0.000</td>
</tr>
</tbody>
</table>

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

The TG level of twin pregnancy was significantly higher than that of singleton pregnancy in the first, second, and third trimesters, and the differences were statistically significant (p < 0.05), while there was no significantly statistical difference in the TC level between twin pregnancy and singleton pregnancy in the first, second, and third trimesters (p > 0.05). See Table 3.

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

<table>
<thead>
<tr>
<th></th>
<th>TG</th>
<th>TC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Singleton pregnancy</td>
<td>Twin pregnancy</td>
</tr>
<tr>
<td>The first trimester</td>
<td>1.18 ± 0.47</td>
<td>1.46 ± 0.29</td>
</tr>
<tr>
<td>The second trimester</td>
<td>2.27 ± 0.89</td>
<td>3.19 ± 1.11</td>
</tr>
<tr>
<td>The third trimester</td>
<td>3.02 ± 1.01</td>
<td>3.57 ± 1.09</td>
</tr>
</tbody>
</table>

2.4 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.
Table 4
Comparison of the TG level and the TC level between the GDM group and the non-GDM group in twin pregnancy

<table>
<thead>
<tr>
<th>Groups</th>
<th>Cases</th>
<th>The first trimester</th>
<th>The second trimester</th>
<th>The third trimester</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>TG</td>
<td>TC</td>
<td>TG</td>
</tr>
<tr>
<td>The GDM group</td>
<td>22</td>
<td>1.58 ± 0.39</td>
<td>4.37 ± 0.67</td>
<td>3.85 ± 1.13</td>
</tr>
<tr>
<td>The non-GDM group</td>
<td>74</td>
<td>1.42 ± 0.28</td>
<td>4.27 ± 0.67</td>
<td>2.99 ± 1.03</td>
</tr>
<tr>
<td>t</td>
<td></td>
<td>2.323</td>
<td>0.621</td>
<td>3.324</td>
</tr>
<tr>
<td>p</td>
<td></td>
<td>0.020</td>
<td>0.523</td>
<td>0.001</td>
</tr>
</tbody>
</table>

2.5 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 TCG 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 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.

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, $\bar{x}±s$)

<table>
<thead>
<tr>
<th>Groups</th>
<th>Cases</th>
<th>The first trimester</th>
<th>The second trimester</th>
<th>The third trimester</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>TG</td>
<td>TC</td>
<td>TG</td>
</tr>
<tr>
<td>The PIH group</td>
<td>18</td>
<td>1.62 ± 0.35</td>
<td>4.34 ± 0.85</td>
<td>3.92 ± 1.09</td>
</tr>
<tr>
<td>The non-PIH group</td>
<td>78</td>
<td>1.45 ± 0.34</td>
<td>4.33 ± 0.79</td>
<td>2.95 ± 1.05</td>
</tr>
<tr>
<td>t</td>
<td></td>
<td>2.465</td>
<td>0.637</td>
<td>3.453</td>
</tr>
<tr>
<td>p</td>
<td></td>
<td>0.002</td>
<td>0.496</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Discussion

During the normal pregnancy, in order to meet the needs of fetal growth and development, childbirth preparation and postpartum breastfeeding, 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 of triglycerides and cholesterol in blood lipids during
pregnancy are the most obvious [13]. Under normal circumstances, from the 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 the twin pregnancy was higher than that of the singleton pregnancy, while there was no significant difference in the TC level between singleton pregnancy and twin pregnancy, which is consistent with the research by Wei Jianxia 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 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 in them with hypertension during pregnancy were higher than that in them 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 addition, there are some limitations in our present study. Firstly, 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. Secondly, 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. Thirdly, we also did not investigate the low-density lipoprotein cholesterol 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.

In summary, we found that the TG level of twin pregnancy was higher than that of 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, regular 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.

**Declarations**

**Ethics approval and consent to participate:** This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethic committee of Wangjing Hospital of China Academy of Chinese Medical Sciences. The written informed consent was obtained from the participants.

**Consent for publication:** written informed consent to publish the clinical details and images of the patient was obtained.

**Availability of data and materials:** The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

**Funding:** This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

**Conflict of interests:** all authors declare that they have no conflict of interests

**Authors' Contributions:** 1) Yanqin Lou, Pei He, Substantial contributions to the conception and design of the work; And 2) Yanqin Lou, Pei He, Huijun Jiang, Li Xiang, the acquisition, analysis, and interpretation of data for the work; And 3) Yanqin Lou, Pei He, drafting the work; AND 4) Xuemei Gao, revising it critically for important intellectual content; AND 5) Yanqin Lou, Pei He, Huijun Jiang, Li Xiang, Xuemei Gao, final approval of the version to be published; AND 6) Yanqin Lou, Pei He, Huijun Jiang, Li Xiang, Xuemei Gao,
agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

**Acknowledgements:** N/A

**References**


