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CLINICAL RESEARCH ARTICLE

# Abdominal obesity-related lipid metabolites may mediate the association between obesity and glucose dysregulation

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**BACKGROUND:** Children with obesity is associated with a higher risk of cardiovascular disease (CV) risk in adulthood. This study is to explore the obesity-related lipid metabolites and identify the associations of lipid metabolites with selected CV risk in children and adolescents.
**METHODS:** A case–control study was designed to include a total of 197 children (aged 9–13 years, male 56.34%, 99 children in the obesity group). The lipidomics profiling was measured by ultra-high-performance liquid tandem chromatography quadrupole time-of-flight mass spectrometry.
**RESULTS:** Four FDR-significant abdominal obesity-related lipid metabolites were identified. Compared to the lean group, decreased phosphatidylcholine O-21:2 level ($q = 0.010$) and sphingomyelins d21:1 ($q = 0.029$) were found and two lipid metabolites levels were higher in the obese group, including phosphatidylglycerol 43:6 and one did not match with any candidate compounds in databases. After adjusting for covariates, PC3 (O-21:2) and SM (d21:1) were significantly associated with blood glucose. Mediation analysis showed that all three lipid metabolites may mediate the association between abdominal obesity and glucose regulation.
**CONCLUSIONS:** This study identified several novel central obesity-related lipid metabolites, and we found that PC3 (O-21:2) and SM (d21:1) were significantly associated with blood glucose, and all these lipid metabolites can mediate the association between abdominal obesity and glucose dysregulation.

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**IMPACT:**

- Serum lipidomic profiles in children with abdominal obesity and their associations with selected CV risk factors were examined.
- Our study identified 4 lipid metabolites associated with abdominal obesity, including PC3 (O-21:2), SM (d21:1), PG (43:6), and one did not match with any candidate compounds in the databases.
- PC3 (O-21:2) and SM (d21:1) were significantly associated with blood glucose.
- Mediation analysis showed that all three lipid metabolites [PC3 (O-21:2), SM (d21:1), PG (43:6)] may mediate the association between abdominal obesity and abnormal glucose regulation.
- This study identified several novel obesity-related lipid metabolites.

## INTRODUCTION

Children with obesity have become a major public health issue worldwide.[1] In China, the prevalence of overweight and obesity has increased dramatically in the past decades, and the latest national prevalence reported a 6·8% for overweight and 3.6% for children with obesity younger than 6 years, as well as 11.1–13.36% for overweight and 7.9–8.6% for children with obesity and adolescents aged 6–17 years.[2,3] Obesity has been well recognized as a major risk factor for diabetes and cardiovascular (CV) disease,[4] which are the leading causes of death or disability globally.[5] Previous studies, including ours, have shown that children with obesity are correlated with a higher risk of CV risk in adulthood.[6–8]

One of the main causes of the increased risk of CV diseases due to obesity is dyslipidemia. It is suggested that obesity is involved in the process of altered lipid metabolism and dyslipidemia.[9] However, the underlying mechanism has still not been fully clarified. Plasma lipid metabolites have been consistently found to be associated with CV disease in adults. On the other hand, few studies have already examined obesity-associated lipid metabolites and identified several potential metabolites (including amino acids, phospholipids, acylcarnitines, etc.).[10,11] Therefore, lipid metabolites may have an important role in the relationships between obesity and CV risk factors.

We hypothesized that obesity-related lipid metabolites could explain, at least in part, the associations between obesity and CV

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risk factors, and a case–control designed study was performed to find the obesity-related lipid metabolites, then analyzed the associations of lipid metabolites with selected CV risk factors in children. The results of our study may shed some light on the early identification of a high CV risk population and novel therapeutic targets for CV diseases.

## METHODS

### Study population and sample size

The abnormal lipid metabolism in children with central obesity was analyzed by a case–control study from the Health Cohort Study of Children and Adolescents in Chongqing. A formula of $n_A = \kappa n_B$ and $n_B = \left(1+\frac{1}{\kappa}\right)\left(\sigma\frac{z_{1-\alpha/2}+z_{1-\beta}}{\mu_A-\mu_B}\right)^2$ was used to calculate the sample size, with the parameters of achieving 95% power to detect a difference of lipid metabolism of 2 between the obesity and control groups at a significance level of 0.05 and a standard deviation of 3. A sample of 59 from the obese group and 59 from the control group were needed for this study. In this study, 99 children in the obese group and 99 children in the control group were included; finally, 1 subject was excluded from the control group after quality control. All children were selected from an established cohort that includes 4536 children aged 9–13 years from 6 elementary schools in 1 urban and 1 rural area of Chongqing, which was introduced in our previous publications.[2,12–14]

The inclusion criteria were as follows: age 9–13 years, not received obesity control treatment, diagnosed with central obesity in the obese group, waist–height ratio (WHtR) was lower than the sex of central obesity diagnostic criteria[15] in the control group, children and parents or guardians have signed informed consent forms. The exclusion criteria were as follows: hormone treatment-induced obesity; children with obvious clinical symptoms; children with diseases (e.g., diabetes, CV disease, or cancer), taking medications, which affect lipid metabolism disorders. This study was conducted under the ethical guidelines of the 1964 Declaration of Helsinki and those later revisions that were agreed upon by the Institutional Review Board of Chongqing Medical University and parents and children signed informed consent before their recruitment to the study.[12]

### Demographic variables

Demographic information was investigated by study coordinators through a comprehensive questionnaire.[16] Height and weight were measured by a mobile medical ultrasonic machine (Ws-h300d), and body mass index (BMI) was calculated by the formula of BMI = weight/ (height × height) ($kg/m^2$).[14,16] The waist circumference (WC) was measured when the children were fasting, wearing close-fitting clothes, standing upright, and with their abdomen relaxing. WC was measured twice at the center of the umbilicus over one T-shirt at the end of exhalation and without inspiration and the averaged values of two times measure were used.[17] Parental education degree was considered as three levels (1 = ~ 9, 2 = ~12, 3 = >12 years)

### Biochemical index

The venous blood (3 mL) was drawn at 8:00–10:00 in the morning at least 12 h after fasting and 24 h after withholding from a high-fat and spicy diet.[12] Blood lipid and fasting blood glucose (FBG) were measured by the automatic biochemical analyzer (Mindray BS-800).

### Metabolomic profiling

The absolute quantitation of lipids profiling was measured by ultra-high-performance liquid tandem chromatography quadrupole time-of-flight mass spectrometry (UPLC–QTOF-MS) in 198 serum samples in total by Shanghai Biotree Biomedical Technology Co., Ltd. The metabolites extraction is as follows steps: first, 60 µL of the serum was put in an EP tube and added up to 400 µL with water. Second, 960 µL extract solution (MTBE:methanol = 5:1) containing internal standard was added. Third, after a 30 s vortex, the samples were sonicated for 10 min in an ice-water bath. Fourth, the samples were centrifuged at 3000 rpm for 15 min at 4 °C. In all, 400 µL of supernatant was transferred to a fresh tube. Fifth, the rest of the sample was added with 400 µL of MTBE, followed by vortex, sonication, and centrifugation, and another 400 µL of supernatant was taken out. This step was repeated once. Sixth, the supernatants were combined and dried in a concentrator with a vacuum at 37 °C, then the dried samples were reconstituted in 100 µL of 50% methanol in dichloromethane. Seventh, after the constitution was centrifuged at 13,000 rpm for 15 min at 4 °C, LC/MS analysis was made with 75 µL of supernatant in a fresh glass vial. In addition, the quality-control sample was made by mixing an equal aliquot of the supernatants from every sample.

LC-MS/MS were analyzed by a UHPLC system (1290, Agilent Technologies) with a Phenomen Kinetex C18 column (2.1 × 100 mm, 1.7 µm) coupled to TripleTOF 6600 mass spectrometry (AB Sciex). The raw data were preprocessed and annotated. The "msconvert" program from ProteoWizard was used to convert the raw data files to files in mzXML format. The CentWave algorithm in XCMS was used for peak detection with the MS/MS spectrum; lipid metabolites identification was achieved through a spectral match using LipidBlast library. The absolute quantitation of lipids was achieved using the peak area, SIL-IS, and RF information.

### Diagnostic criteria

The diagnostic criteria of central obesity of children and adolescents from China in this study were used,[15] which is suitable for the growth and development characteristics of Chinese children. Obesity was defined as the WHtR cut-off value was 0.481 for boys and 0.456 for girls.

### Statistical analysis

This study detected 822 peaks, 709 metabolites, and 197 samples (99 in the central-obesity group and 98 in the lean group) were kept after quality control. Half of the minimum value was used to fill up the missing values. And log transformation of data was used to normalize variables and minimize the impact of noise and high variance. The final dataset was imported to SIMCA16.0.2 software package (Sartorius Stedim Data Analytics AB, Umea, Sweden) for multivariate analysis, which contained peak number, sample name, and normalized peak area. Principal component analysis (PCA) was performed to display the distribution of the samples (eFig. 1). Potential outliers were identified by a 95% confidence interval in the PCA score plot. Significantly changed metabolites were calculated by supervised orthogonal projections to latent structures-discriminate analysis (OPLS-DA). Then sevenfold cross-validation was performed to calculate the value of $R^2$ (the explained variable variation) and $Q^2$ (means the power a variable could be predicted), which was a default setting of Simca software. Metabolites with variable importance in projection (VIP) value >1 in OPLS-DA analysis and $P < 0.05$ in univariate analysis (Student's $t$ test) were considered altered metabolites. The predictive ability and robustness of the OPLS-DA model were checked by 200 times permutations.

Means were calculated to present continuous variables and were compared by $t$ tests. Categorical variables were represented as a percentage and were tested by Chi-square tests. Linear regression was used to examine the associations between lipid metabolites and selected CV risk factors with the adjustment of age, sex, height, father's education, and abdominal obesity. The $\beta$ and 95% confidence interval (CI) were calculated. In addition, mediation models (medeff package) were performed to investigate the mediation role of lipid metabolites in the associations between obesity and CV risk factors, in which age, sex, height, and father's education were adjusted for. All analyses were performed using the Stata software version 15.0 (STATA Corp., TX, US). A two-sided $P < 0.05$ was considered statistically significant.

## RESULTS

Descriptive characteristics of the participants are summarized in Table 1. The abdominal obese group had more boys than the lean group ($P < 0.001$). Most selected CV risk factors showed significant associations between abdominal obesity and the lean group ($P < 0.05$) except for triglyceride (TG), insulin, and creatinine.

The relationship of the plasma lipid profiles with abdominal obesity was calculated by performing OPLS-DA analyses; OPLS-DA score plots are shown in Fig. 1. We observed a distinct separation of the abdominal obese and lean groups. The $R^2$ and $Q^2$ values of the OPLS-DA models are shown in eTable 1.

We identified four False Discovery Rate (FDR)-significant abdominal obesity-related lipid metabolites (Table 2 and eFig. 2), and the significance was displayed in Fig. 2 and eFig. 3. In Fig. 2, each dot in the lipid group bubble chart indicates a metabolite,

**Table 1.** Characteristics of the participants.

| Variables | Lean group | Abdominal obesity group | *P* |
|---|---|---|---|
| Sample size | 98 | 99 | |
| Age, years | 11.9 ± 0.1 | 11.7 ± 0.1 | 0.089 |
| Sex, male (%) | 38 (38.8) | 63 (63.6) | <0.001 |
| Height, cm | 152.8 ± 0.8 | 153.8 ± 1.0 | 0.442 |
| Weight, Kg | 43.6 ± 1.0 | 59.6 ± 1.2 | <0.001 |
| WHtR | 0.40 ± 0.04 | 0.53 ± 0.05 | <0.001 |
| BMI, Kg/m$^2$ | 18.6 ± 0.3 | 25.2 ± 0.4 | <0.001 |
| Father's education, level, year (%)[a] | | | 0.026 |
| ~9 | 43 (43.8) | 34 (34.7) | |
| ~12 | 36 (36.7) | 28 (28.6) | |
| >12 | 19 (19.4) | 36 (36.7) | |
| TC, mmol/L | 3.4 ± 0.1 | 3.6 ± 0.1 | 0.003 |
| TG, mmol/L | 1.1 ± 0.1 | 1.2 ± 0.1 | 0.070 |
| HDL-C, mmol/L | 1.4 ± 0.3 | 1.3 ± 0.3 | 0.023 |
| LDL-C, mmol/L | 1.7 ± 0.5 | 2.0 ± 0.4 | <0.001 |
| FBG, mmol/L | 4.3 ± 0.4 | 4.5 ± 0.4 | 0.008 |
| HbA1c, mean, % | 5.4 ± 0.2 | 5.4 ± 0.2 | 0.547 |
| IR | 2.0 ± 0.2 | 3.4 ± 0.4 | <0.001 |
| Insulin, pmol/L | 70.5 ± 5.2 | 115.9 ± 10.6 | <0.001 |
| Creatinine, μmol/L | 54.0 ± 2.1 | 55.9 ± 3.5 | 0.639 |
| UA, μmol/L | 299.9 ± 7.8 | 357.5 ± 8.4 | <0.001 |

*WHtR* waist–height ratio, *BMI* body mass index, *TC* total cholesterol, *TG* triglyceride, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol, *FBG* fasting blood glucose, *HbA1c* glycated hemoglobin, *IR* insulin resistance index, *UA* uric acid.
[a]One participant was excluded due to missing data for father's education.

and the size of the dot indicates the *P* value of the Student's *t* test, the larger the dot, the smaller the value of the *P* value, with colored dots indicating significant difference ($P < 0.05$). Compared to the lean group, decreased phosphatidylcholine O-21:2 [PC3 (O-21:2)] level ($q = 0.010$) and sphingomyelins d21:1 [SM (d21:1)] ($q = 0.029$) were observed in the abdominal obese group. Two lipid metabolite levels were higher in the abdominal obese group, including phosphatidylglycerol 43:6 [PG (43:6)] and one did not match with any candidate compounds in the databases.

After adjusting for age, sex, height, father's education, and abdominal obesity, PC3 (O-21:2) and SM (d21:1) were significantly associated with blood glucose, while PG (43:6) was significantly associated with high-density lipoprotein cholesterol (HDL-C; Table 3). Also, all three lipid metabolites were significantly associated with blood pressure.

Mediation analysis showed that all three lipid metabolites may mediate the association between abdominal obesity and abnormal glucose regulation. PC3 (O-21:2) and SM (d21:1) may mediate the association between abdominal obesity and uric acid, while PG (43:6) may mediate the association between abdominal obesity and LDL-C (Table 4).

## DISCUSSION

We examined serum lipidomic profiles in children with abdominal obesity using a case–control study and their associations with selected CV risk factors. Four lipid metabolites were associated with abdominal obesity in our study, which included PC3 (O-21:2, SM (d21:1), PG (43:6), but one did not match with any candidate compounds of the databases. PC3 (O-21:2) and SM (d21:1) were significantly associated with blood glucose. Further, mediation analysis showed that all three lipid metabolites may mediate the association between abdominal obesity and abnormal glucose regulation.

Few studies have reported obesity-related changes in plasma lipidomics profiling in adults[18,19] or children.[10,11] For example, the study in adults showed that 39 lipids and 8 lipids were associated with obesity and dysglycemia, respectively. This study identified 9 PCs correlated to central obesity in children, and 5 PCs were replicated. SM (d18:0/24:0) and SM 36:0 were positively associated with obesity. This study also reported that lysophosphatidylcholines (LPC) 18:1 and PC 36:2 were negatively correlated to glucose level, while both SM 36:0 and SM (d18:0/24:0) were positively correlated to glucose value.[18] Wang et al. found that the values of 5 LPCs were lower in adolescents with obesity than those with normal BMI.[11] Therefore, our study added more evidence about the lipid disorder in children with obesity.

Previous studies reported that certain species of PC (PC (22:6, 20:4) and LPC (C18:2)) were significantly negatively associated with the risk of diabetes, which suggested that PC could play a role in regulating insulin metabolism.[11,20] Similar to our results, a study with 30 samples of men found that LPC levels decreased in participants with only obesity or with both obesity and type 2 diabetes (T2DM) compared with lean subjects, but the difference was not found between adults with obesity and adults with both obesity and T2DM,[21] which suggested that LPC was only associated with obesity, not with T2DM. However, the conclusion about the relationship between LPC and glycometabolism needs more studies with a well-designed large sample size to confirm. In addition, a previous study found that diet-induced obesity control could relieve insulin resistance (IR), and induced lower fasting plasma insulin levels was associated with the composition and fluidity of membrane phospholipid.[22] Besides, other evidence from adults found that differential expression of some species of lipid metabolites was negatively associated with IR.[23,24]

In in vitro experiments, the transfer of PCs was catalyzed only by PC-TP.[25] Therefore, PCs may influence the three-dimensional structure of PC-TP. Scapa et al. found that the levels of fasting glucose and free fatty acids were lower in PC-TP-deficient mice than those of wild type, while insulin concentration was unchanged, which indicated that PC-TP had a regulation effect on insulin sensitivity and the utilization of energy and metabolic substrate.[26]

Sphingomyelin, as one kind of sphingolipid also important for obesity and insulin resistance,[27,28] and ceramide, as a precursor of sphingolipids, after the reduction of it in muscle tissues, will impact the metabolism and the levels of sphingolipids.[29] Evidence from both humans and animals found that ceramide concentration in skeletal muscles was inversely associated with insulin sensitivity.[30–32] In addition, PC metabolites have a vital impact on modifying the functions of membranes, such as the formation of lipid microdomain.[33] All these results, along with ours, suggest that lipid metabolites may mediate the association between obesity and glucose metabolism.

In this study, we found that PG (43:6) was positively associated with HDL-C. Minor HDL phospholipids (<1 wt% of total HDL lipids) are represented by phosphatidylglycerol (PG).[34] However, the role of PG (43:6) in HDL-C metabolism still needs to be further studied.

We have several limitations. First, we may not have enough statistical power to detect more important lipid metabolites due to the relatively small sample size. Second, we did not have an independent cohort to replicate our results. Third, one FDR-significant lipid metabolite that did not match with any candidate compounds in the databases merits further study.

We identified several novel obesity-related lipid metabolites. Furthermore, our study found that PC3 (O-21:2 and SM (d21:1) were remarkably correlated with FBG, and the mediation analysis showed that all these lipid metabolites can mediate the

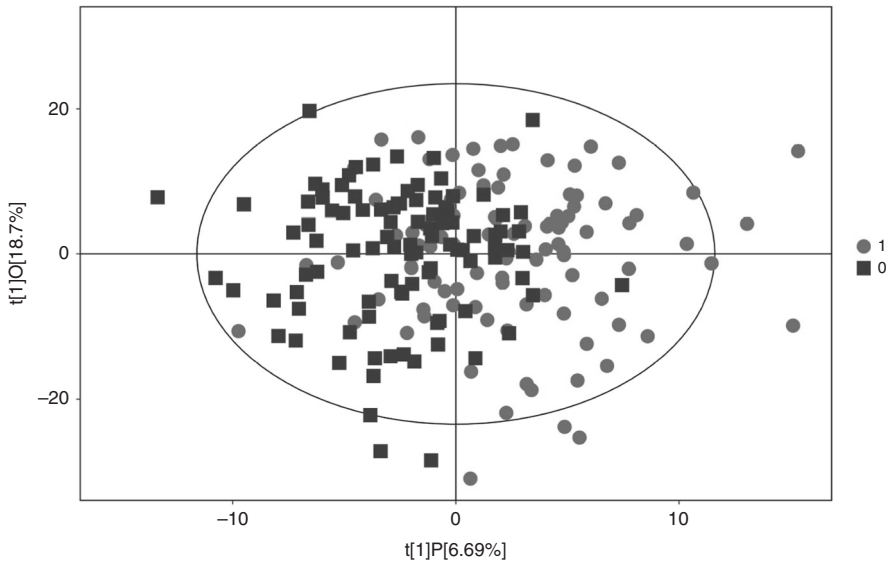


**Fig. 1** Principal component analysis (PCA) to visualize the distribution and the grouping of the samples.

**Table 2.** The top seven ranked metabolites.

| Lipidomics | Obesity group | Lean group | VIP | *P* | FDR | FC |
|---|---|---|---|---|---|---|
| PC (O-21:2) | 3.83 ± 4.39 | 6.84 ± 5.07 | 1.75 | 1.17E−05 | 0.010 | 0.56 |
| SM (d21:1) | 11.64 ± 13.52 | 19.17 ± 13.63 | 1.68 | 0.000116 | 0.029 | 0.61 |
| PG (43:6) | 34.04 ± 10.59 | 27.92 ± 12.21 | 2.67 | 0.00014 | 0.029 | 1.22 |
| NA[a] | 78.37 ± 36.36 | 58.68 ± 35.60 | 2.14 | 9.23E−05 | 0.029 | 1.34 |
| PG (41:4) | 182.32 ± 55.65 | 150.29 ± 72.91 | 2.94 | 0.000466 | 0.077 | 1.21 |
| LPC (19:0) | 128.53 ± 46.05 | 105.83 ± 48.03 | 1.45 | 0.000596 | 0.082 | 1.21 |
| LacCer (d45:1) | 20.59 ± 7.53 | 16.26 ± 10.52 | 2.53 | 0.000832 | 0.098 | 1.27 |

*VIP* variable importance in the projection, *FDR* False Discovery Rate, *FC* fold change, *PC* phosphatidylcholine, *SM* sphingomyelins, *PG* phosphatidylglycerol, *LPC* lysophosphatidylcholines, *LacCer* lactosylceramides.
[a]Not matched with any candidate compounds in the databases.

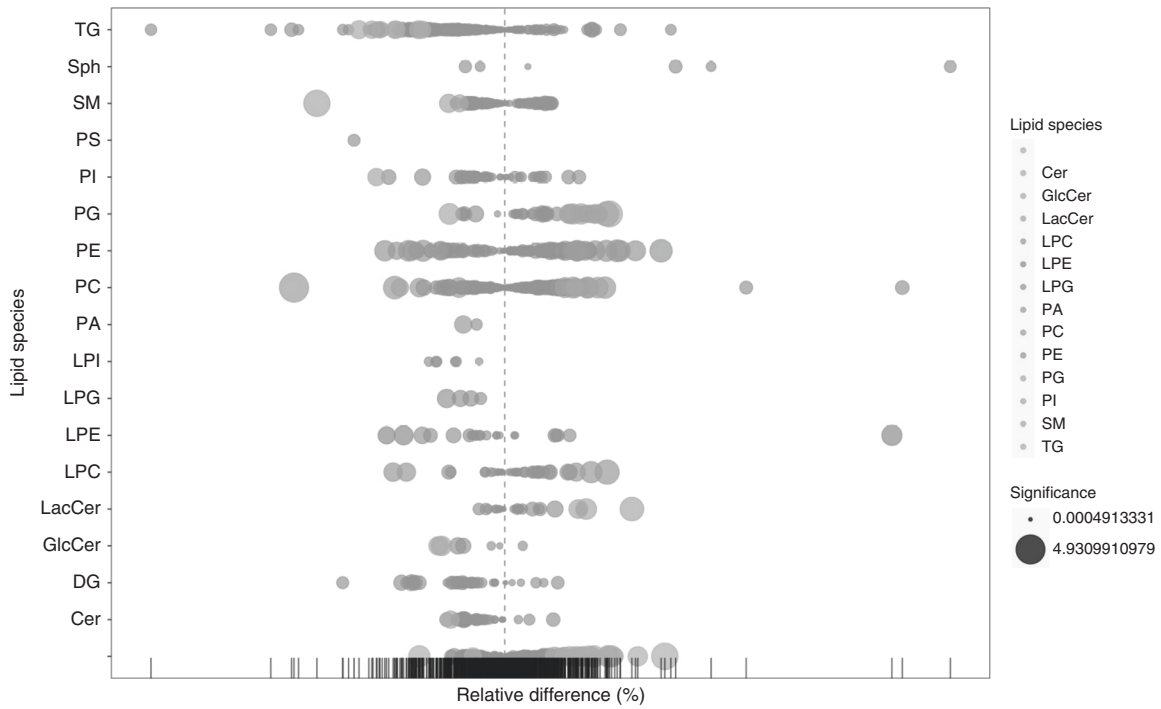


**Fig. 2** Bubble plot for the abdominal obesity group vs. lean group.

**Table 3.** Associations between FDR-significant metabolites and selected cardiovascular risk factors.

| Variables | PC (O-21:2) | | SM (d21:1) | | PG (43:6) | |
|---|---|---|---|---|---|---|
| | β (95% CI)[a] | P | β (95% CI)[a] | P | β (95% CI)[a] | P |
| TC, mmol/L | 0.26 (−0.97, 1.48) | 0.681 | 0.16 (−3.27, 3.59) | 0.928 | 1.75 (−1.27, 4.78) | 0.254 |
| TG, mmol/L | 0.14 (−0.95, 1.23) | 0.802 | −0.16 (−3.22, 2.89) | 0.915 | −0.91 (−3.61, 1.79) | 0.507 |
| HDL-C, mmol/L | 1.11 (−1.28, 3.51) | 0.361 | 3.05 (−3.67, 9.77) | 0.371 | **10.22 (4.45, 15.98)** | **0.001** |
| LDL-C, mmol/L | 0.98 (−0.52, 2.48) | 0.199 | 2.44 (−1.77, 6.66) | 0.254 | −1.63 (−5.36, 2.11) | 0.391 |
| SBP, mmHg | **0.09 (0.05, 0.14)** | **<0.001** | **0.23 (0.10, 0.37)** | **0.001** | **−0.21 (−0.33, −0.09)** | **0.001** |
| DBP, mmHg | **0.13 (0.07, 0.20)** | **<0.001** | **0.36 (0.17, 0.54)** | **<0.001** | **−0.24 (−0.41, −0.08)** | **0.005** |
| FBG, mmol/L | **−3.98 (−5.49, −2.48)** | **<0.001** | **−12.14 (−16.31, −7.97)** | **<0.001** | 2.30 (−1.70, 6.31) | 0.258 |
| Insulin, pmol/L | 2.93 (−0.46, 6.33) | 0.09 | 8.18 (−1.21, 17.57) | 0.087 | 4.36 (−3.29, 12.01) | 0.262 |
| HbA1c,% | −0.16 (−0.43, 0.11) | 0.245 | −0.43 (−1.19, 0.32) | 0.260 | −0.30 (−0.97, 0.37) | 0.378 |
| IR | 0.00 (−0.01, 0.01) | 0.544 | −0.01 (−0.03, 0.02) | 0.614 | −0.01 (−0.03, 0.01) | 0.447 |
| Creatinine, μmol/L | 0.02 (−0.01, 0.04) | 0.158 | 0.05 (−0.02, 0.12) | 0.191 | −0.01 (−0.07, 0.05) | 0.744 |
| UA, μmol/L | −0.01 (−0.02, 0.00) | 0.151 | −0.02 (−0.04, 0.01) | 0.229 | 0.00 (−0.02, 0.02) | 0.918 |

*TC* total cholesterol, *TG* triglyceride, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *FBG* fasting blood glucose, *HbA1c* glycated hemoglobin, *IR* insulin resistance index, *UA* uric acid.
Bold values showed statistcally significant in the level of 0.05.
[a]Adjusting for age, sex, height, father's education, and abdominal obesity.

**Table 4.** Mediation effect of FDR-significant metabolites on abdominal obesity and selected cardiovascular risk factors.

| Variables | PC (O-21:2)[a] | | SM (d21:1)[a] | | PG (43:6)[a] | |
|---|---|---|---|---|---|---|
| | % of mediated | 95% CI | % of mediated | 95% CI | % of mediated | 95% CI |
| TC, mmol/L | −0.03 | −0.10, −0.02 | −0.01 | −0.02, −0.01 | −0.05 | −0.15, −0.03 |
| TG, mmol/L | 0.04 | −0.34, 0.23 | 0.01 | −0.05, 0.08 | 0.04 | −0.23, 0.44 |
| HDL-C, mmol/L | 0.12 | −0.70, 1.01 | 0.09 | −0.60, 0.82 | 0.22 | −1.95, 1.70 |
| LDL-C, mmol/L | −0.07 | −0.12, −0.05 | −0.05 | −0.09, −0.03 | **0.02** | **0.02, 0.04** |
| SBP, mmHg | −0.58 | −7.20, 7.27 | −0.41 | −4.92, 6.49 | 0.27 | −2.81, 3.16 |
| DBP, mmHg | −0.54 | −11.96, 18.96 | −0.43 | −10.02, 12.57 | 0.22 | −6.22, 4.78 |
| FBG, mmol/L | **0.50** | **0.24, 2.49** | **0.43** | **0.21, 2.05** | −0.06 | −0.29, −0.03 |
| Insulin, pmol/L | **0.04** | **0.03, 0.10** | **0.03** | **0.02, 0.07** | **0.03** | **0.02, 0.07** |
| HbA1c,% | 0.20 | −3.71, 5.86 | −0.13 | −2.74, 3.63 | −0.10 | −2.18, 2.27 |
| IR | **0.09** | **0.05, 0.22** | **0.06** | **0.04, 0.17** | **0.03** | **0.02, 0.08** |
| Creatinine, μmol/L | −0.23 | −4.12, 2.55 | −0.17 | −3.00, 2.11 | 0.02 | −0.46, 0.40 |
| UA, μmol/L | **0.09** | **0.05, 0.17** | **0.06** | **0.04, 0.12** | −0.01 | −0.01, −0.01 |

*TC* total cholesterol, *TG* triglyceride, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *FBG* fasting blood glucose, *HbA1c* glycated hemoglobin, *IR* insulin resistance index, *UA* uric acid.
Bold values showed statistcally significant in the level of 0.05.
[a]Adjusting for age, sex, height, and father's education.

association between abdominal obesity and abnormal glucose regulation. The results suggest that these lipid metabolites may mediate the association between obesity and glucose metabolism. Further studies are needed to confirm our results.

## DATA AVAILABILITY

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request. Data are available from the corresponding author X.L.

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## AUTHOR CONTRIBUTIONS

X.L. conceived and designed the experiments. G.H. wrote the paper. P.Q., X.T., and B.X. performed the experiments. P.Q., X.T., and Y.R. participated in the physical measurements. All the authors critically reviewed and approved the final paper.

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## COMPETING INTERESTS

The authors declare no competing interests.

## ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was approved by the Institutional Review Board of Chongqing Medical University and written informed consent was obtained from parents or guardians and each child before their recruitments.

## ADDITIONAL INFORMATION

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