

ORIGINAL ARTICLE

Non-Targeted Metabolomics Analysis of Mother and Infant in Gestational Diabetes Mellitus and Neonatal Clinical Characterization

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SUMMARY

Background: The goal was to analyze serums of GDM patients and healthy pregnant women using HPLC-MS and preliminarily screen differential metabolites by metabolomics.

Method: Sixty pregnant women who underwent elective cesarean section at term in Dongguan Dalang Hospital from January 2023 to April 2023 were selected and divided into the GDM group and healthy pregnancy group. Pre-pregnancy and pregnancy examination information, such as age, BMI, OGTT results, triglyceride, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and other clinical data were collected for statistical analysis. Non-targeted metabolomics of serum from 30 GDM patients and 30 healthy pregnant women were studied by HPLC-MS, and different ions were searched. The structures of differential metabolites were identified by HMDB database. The metabolic pathways of differential metabolites were analyzed by KEGG database.

Results: The OGTT result, pCO₂, pO₂, HCO₃, BE, Apgar score, and bilirubin levels in the GDM group were higher than those in the healthy pregnancy group ($p < 0.05$). However, there were no significant differences in age, triglyceride, total cholesterol, newborn birth weight, newborn birth blood glucose, and blood gas pH between the two groups (all $p > 0.05$). Using $p < 0.05$ as the screening standard, 55 differential metabolites were identified in serum, mainly including fatty acyl, carboxylic acids and their derivatives, steroids and their derivatives, ketoacids and their derivatives, and pyrimidine nucleosides, etc., all of which were up-regulated or down-regulated to varying degrees. The 55 metabolites were mainly involved in the metabolism of pyrimidine, pyruvate, alanine, aspartic acid, glutamic acid, and arachidonic acid, glycolysis, and biosynthesis of unsaturated fatty acids.

Conclusions: The discovery of these metabolites provides a theoretical basis for an in-depth understanding of GDM pathogenesis. Non-targeted metabolomics analysis of blood metabolomics research technology has shown great potential value in the early diagnosis of obstetric diseases and the study of disease mechanisms.

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Supplementary Data

Table S1. Differential metabolite data.

Name	Formula	Molecular weight	RT (minutes)	Class	p-value	Up/down
Prostaglandin G2	C20 H32 O6	368.22042	13.404	Fatty Acyls	1.05E-14	down
(2S)-4-Oxo-2-phenyl-3,4-dihydro-2H-chromen-7-yl beta-D-glucopyranoside	C21 H22 O8	448.14245	12.692	--	5.00E-05	up
Trichothec-9-ene-3,4,8,15-tetrol,12,13-epoxy-	C15 H22 O6	344.1477	14.306	--	0.000141496	down
Protectin D1	C22 H32 O4	360.23064	13.005	Fatty Acyls	0.000322668	down
all-cis-4,7,10,13,16-Docosapentaenoic acid	C22 H34 O2	330.25619	14.887	--	0.00034987	down
N'1-[1-(2-hydroxyphenyl)ethylidene]-3-methoxybenzene-1-carbohydrazide	C16 H16 N2 O3	284.11769	14.664	--	0.000473774	up
8Z,11Z,14Z-Eicosatrienoic acid	C20 H34 O2	306.25606	14.93	Fatty Acyls	0.000536973	down
2-[(3-methylbenzo[b]thiophen-2-yl)carbonyl]benzoic acid	C17 H12 O3 S	194.03792	16.956	--	0.000549501	down
LysoPC 12:1	C20 H36 N O7 P	433.22185	9.377	--	0.001065042	up
Methylmalonic acid	C4 H6 O4	118.02671	1.188	Carboxylic acids and derivatives	0.001173583	up
2-Hydroxy-2-methylbutanoic acid	C5 H10 O3	118.06315	1.72	Fatty Acyls	0.002054042	up
Arachidonic acid	C20 H32 O2	304.24039	14.698	Fatty Acyls	0.002469578	down
11-Deoxy prostaglandin F2	C20 H34 O4	338.24619	13.061	--	0.002743972	down
MAG (18:3)	C21 H36 O4	352.26181	13.702	--	0.002885833	down
Cholesteryl sulfate	C27 H46 O4 S	466.31216	15.725	Steroids and steroid derivatives	0.003320927	up
Lysopc 16:1	C24 H48 N O7 P	493.3181	14.632	--	0.003461239	up
Argininosuccinic acid	C10 H18 N4 O6	290.12269	1.176	Carboxylic acids and derivatives	0.003493031	up
LPC 22:2	C30 H58 N O7 P	635.41772	15.8	--	0.003984373	up
methyl 7-hydroxy-4-oxo-8-propyl-4H-1-benzothiine-2-carboxylate	C14 H14 O4 S	278.0593	16.957	--	0.005446035	down
L-Glutamic acid	C5 H9 N O4	147.05323	1.189	Carboxylic acids and derivatives	0.00546888	up
Adrenic acid	C22 H36 O2	332.27185	15.102	Fatty Acyls	0.005845082	down
Deoxycholic acid	C24 H40 O4	392.29386	12.073	Steroids and steroid derivatives	0.007821625	down
Uridine	C9 H12 N2 O6	244.0698	1.358	Pyrimidine nucleosides	0.00841696	up
1a, 1b-Dihomo prostaglandin F2 α	C22 H38 O5	364.26203	13.36	--	0.008886186	down
Prostaglandin A1 ethyl ester	C22 H36 O4	364.26203	12.579	--	0.009315185	down
2-Phenylpropionic acid	C9 H10 O2	150.06812	8.251	Phenylpropanoic acids	0.009337234	up
Oxoadipic Acid	C6 H8 O5	160.0366	1.18	Keto acids and derivatives	0.00947571	down
Nervonic acid	C24 H46 O2	366.35011	16.452	Fatty Acyls	0.009994433	up
N-Oleoyl Glycine	C20 H37 N O3	339.2778	14.648	--	0.01118667	up
ent-17-Hydroxykaur-15-en-19-oic acid	C20 H30 O3	318.21984	12.281	--	0.012448004	down
Arachidic acid	C20 H40 O2	312.30318	15.872	Fatty Acyls	0.0124856	up

Table S1. Differential metabolite data (continued).

Name	Formula	Molecular weight	RT (minutes)	Class	p-value	Up/down
2-Hydroxymyristic acid	C14 H28 O3	244.20406	13.207	Fatty Acyls	0.013159822	down
cis-5, 8, 11, 14, 17-Eicosapentaenoic acid	C20 H30 O2	302.22481	14.413	Fatty Acyls	0.013303065	down
GM3 d34:1; [M-H]-	C57 H104 N2 O21	1152.71468	16.538	--	0.013867249	up
Phe-Phe	C18 H20 N2 O3	312.14785	10.224	Carboxylic acids and derivatives	0.014025377	up
2'-Deoxycytidine	C9 H13 N3 O4	227.09188	9.851	Pyrimidine nucleosides	0.0142609	down
Lysopc 17:0	C25 H52 N O7 P	509.3488	15.534	--	0.014334142	up
N1-(3-pyridyl)-2, 3, 4, 5, 6-pentamethylbenzene-1-sulfonamide	C16 H20 N2 O2 S	608.25083	9.055	--	0.014713397	up
Fumaric acid	C4 H4 O4	116.01115	1.137	Carboxylic acids and derivatives	0.015997939	up
D-Sedoheptulose 7-phosphate	C7 H15 O10 P	290.03589	1.358	Organooxygen compounds	0.016838649	up
Glucuronic acid-3, 6-lactone	C6 H8 O6	176.02907	1.138	--	0.017780645	up
1-Palmitoyl-Sn-Glycero-3-Phosphocholine	C24 H50 N O7 P	495.33328	15.279	Glycerophospholipids	0.019926088	up
L-Malate	C4 H6 O5	134.02171	1.185	Hydroxy acids and derivatives	0.025724953	up
Cholic acid	C24 H40 O5	408.28827	12.417	Steroids and steroid derivatives	0.026359534	down
PC (2:0/18:2)	C28 H52 N O8 P	621.36565	13.833	--	0.02653468	up
L-Ascorbate	C6 H8 O6	176.03213	9.579	Dihydrofurans	0.027483694	up
1,5-Anhydro-D-glucitol	C6 H12 O5	164.06879	1.353	Organooxygen compounds	0.027724124	down
trans-2-Butene-1,4-dicarboxylic Acid	C6 H8 O4	144.04227	1.299	Fatty Acyls	0.028754748	down
D-(+)-Mannose	C6 H12 O6	180.06363	1.294	--	0.030291863	down
PA (16:0/17:1)	C36 H69 O8 P	660.46168	16.088	--	0.030547679	up
Aldosterone	C21 H28 O5	360.19429	11.286	Steroids and steroid derivatives	0.031891137	down
6-methyl-2-oxo-4,6-diphenyl-1,2,5,6-tetrahydropyridine-3-carbonitrile	C19 H16 N2 O	288.13133	11.763	--	0.036306474	up
Cinnamoylglycine	C11 H11 N O3	205.07406	8.66	Carboxylic acids and derivatives	0.036902407	up
PC (18:0/22:5)	C48 H86 N O8 P	895.63219	15.826	--	0.038099459	up
2-Ketohexanoic acid	C6 H10 O3	130.06307	5.543	Keto acids and derivatives	0.042818587	up