Table S1. The supplement to clinical characteristics of ICP/NC groups

Group	ICP (n=18)	Normal (n=6)	P value
ALT (IU/L), Mean±SD	58.41±100.33	16.13±22.81	0.071
AST (IU/L), Mean±SD	43.19±57.73	22.15±15.10	0.230
ADA (IU/L), Mean±SD	11.51±14.24	7.48±1.77	0.779
ALP (IU/L), Mean±SD	184.41±58.65	215.17±77.75	0.441
GGT (IU/L), Mean±SD	36.43±43.72	13.12±5.31	0.386
LDH (IU/L), Mean±SD	202.69±47.81	202.33±41.67	0.712
TBil (μmol/L), Mean±SD	11.47±10.92	7.13±1.27	0.109
DBil (μmol/L), Mean±SD	3.77±8.11	0.97±0.36	0.002
IBil (μmol/L), Mean±SD	7.7±3.16	6.17±1.02	0.161
TP, Mean±SD	58.32±5.35	61.85±3.50	0.133
ALB, Mean±SD	31.52±3.04	34.17±0.89	0.071
GLO, Mean±SD	26.81±2.92	27.68±2.88	0.463
A/G (%)	1.19±0.11	1.25±0.10	<0.001
BUN, Mean±SD	3.48±1.36	3.50±1.43	1.000
Crea, Mean±SD	55.33±20.87	48.83±13.20	0.385
UA, Mean±SD	346.89±131.07	319.67±68.37	0.594
CysC, Mean±SD	1.51±0.63	1.16±0.26	0.398
TC (mmol/L), Mean±SD	6.48±1.79	6.02±1.13	0.594
TG (mmol/L), Mean±SD	3.22±1.50	3.54±1.06	0.317
HDL (mmol/L), Mean±SD	1.58±0.45	1.42±0.18	0.229
LDL (mmol/L), Mean±SD	3.71±1.57	3.61±0.83	0.739
ApoA, Mean±SD	1.72±0.40	1.98±0.30	0.016
ApoB, Mean±SD	1.29±0.33	1.19±0.20	0.114
Hcy, Mean±SD	7.59±2.09	8.92±1.77	0.075
CK, Mean±SD	55.71±33.58	74.65±45.04	0.396
CK-MB, Mean±SD	8.81±5.54	10.35±7.71	0.734
P-ChE, Mean±SD	5086.56±947.60	5733.17±687.55	0.122
UIBCs, Mean±SD	64.67±17.84	72.53±9.04	0.338
TIBCs, Mean±SD	81.94±12.04	85.78±6.16	0.396
Fe, Mean±SD	17.27±9.27	13.25±4.00	0.439
K, Mean±SD	3.96±0.21	3.77±0.31	0.334
Na, Mean±SD	136.90±1.39	137.30±1.29	0.554
Cl, Mean±SD	106.56±1.80	105.10±1.33	0.150
Ca, Mean±SD	2.15±0.08	2.21±0.09	<0.001
P, Mean±SD	1.24±0.19	1.20±0.28	0.103
Mg, Mean±SD	0.78±0.07	0.80±0.07	<0.001

Abbreviations in the table: SD means standard deviation; ALT means alamine aminotransferase; AST means aspartate aminotransferase; ADA means adenosine deaminase; ALP means alkaline phosphatase; GGT means γ-glutamyltransferase; LDH means lactate dehydrogenase; TBil means total bilirubin; DBil means direct bilirubin; IBil means indirect bilirubin; TP means total protein; ALB means albumin; GLO means globulin; A/G means the value of albumin/ globulin; BUN means blood urea nitrogen; Crea means creatinine; UA means uric acid; CysC means serum cystatin C; TC means total cholesterol; TG means triacylglycerol; HDL means high density lipoprotein; LDL means low density lipoprotein; ApoA means apolipoprotein A; ApoB means apolipoprotein B; Hcy means

homocysteine; CK means creatine kinase; CK-MB means creatine kinase-MB; P-ChE means cholinesterase; UIBCs means unsaturated iron-bonding capacity; TIBCs means total iron-bonding capacity. The P value from the MannWhitney U-test to compare the clinical parameters of ICP and NC groups. P value <0.05 indicates significance for statistical analysis.

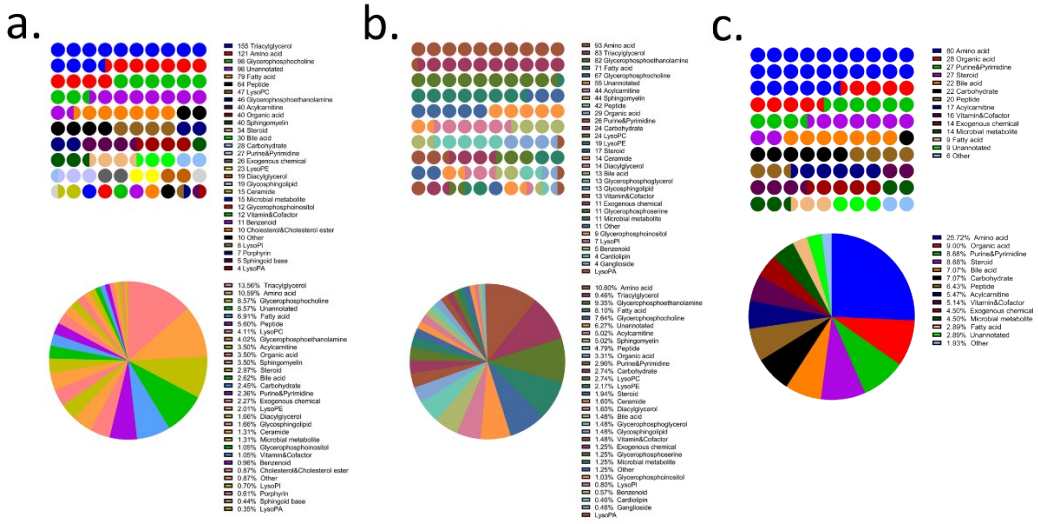

Figure S1. The pie charts of chemical classes detected from (a) serum samples, (b) placenta tissue samples and (c) urine samples in this study.

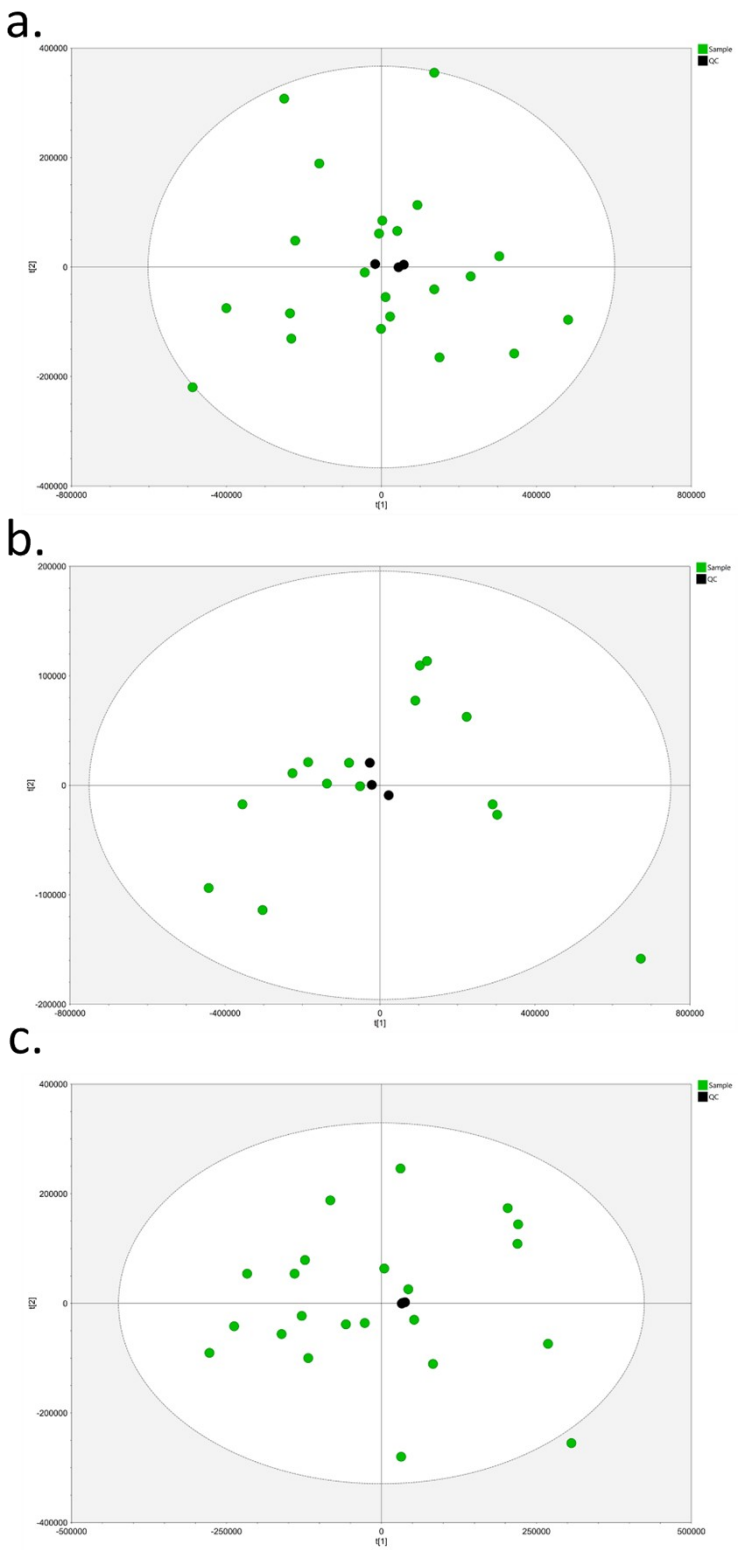

Figure S2. The score plots in the PCA analysis of metabolites from (a) serum samples, (b) placenta tissue samples and (c) urine samples in this study. Quality control samples scattering tightly in the unsupervised PCA score plot indicated analytical performance maintained stable during analytical batch and untargeted metabolomics data is of high quality. Black dots: QC samples.

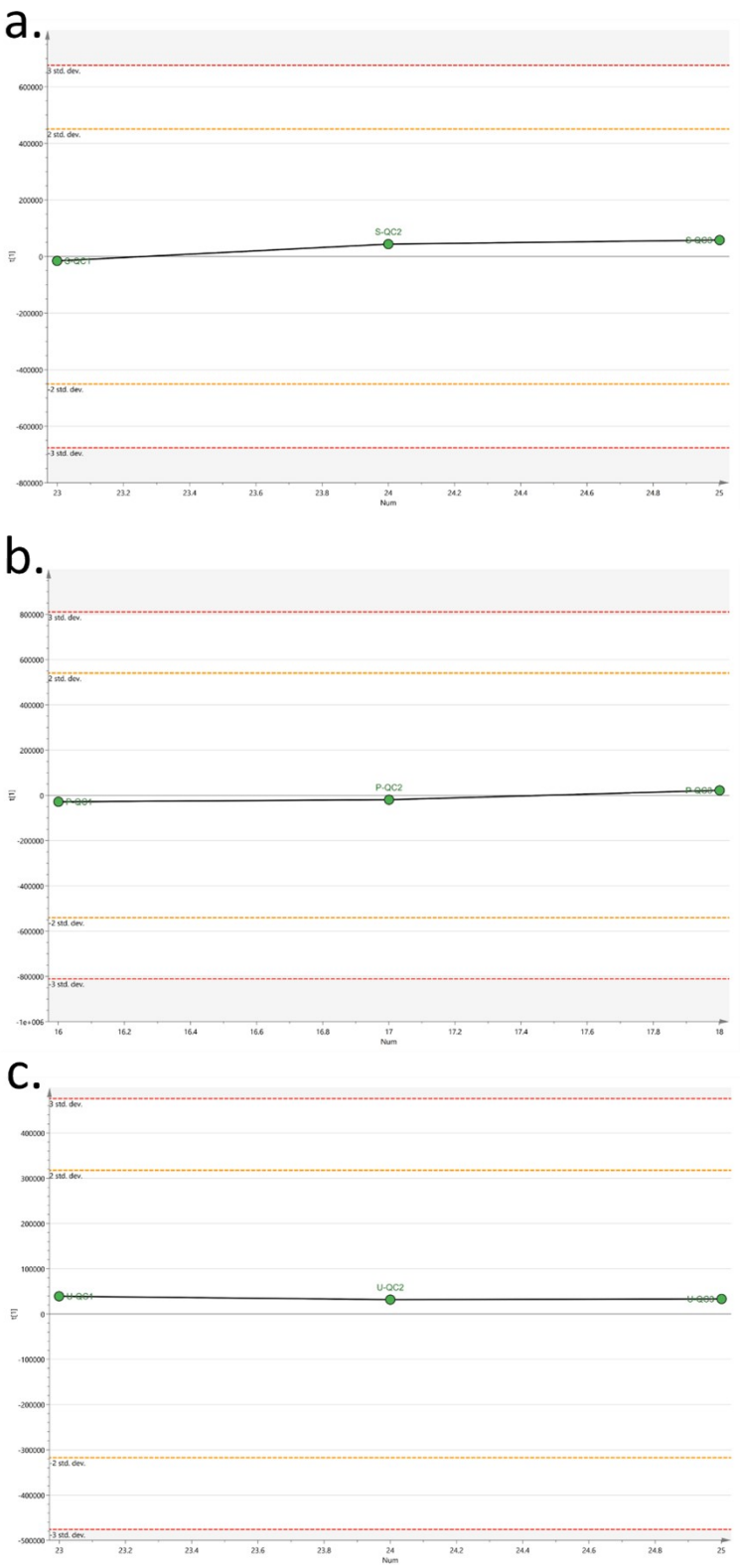

Figure S3. The characteristic of score plots in the PCA analysis of metabolites from (a) serum samples, (b) placenta tissue samples and (c) urine samples in this study. Time series plot of principal component 1 in Fig. S2 during analytical batch.

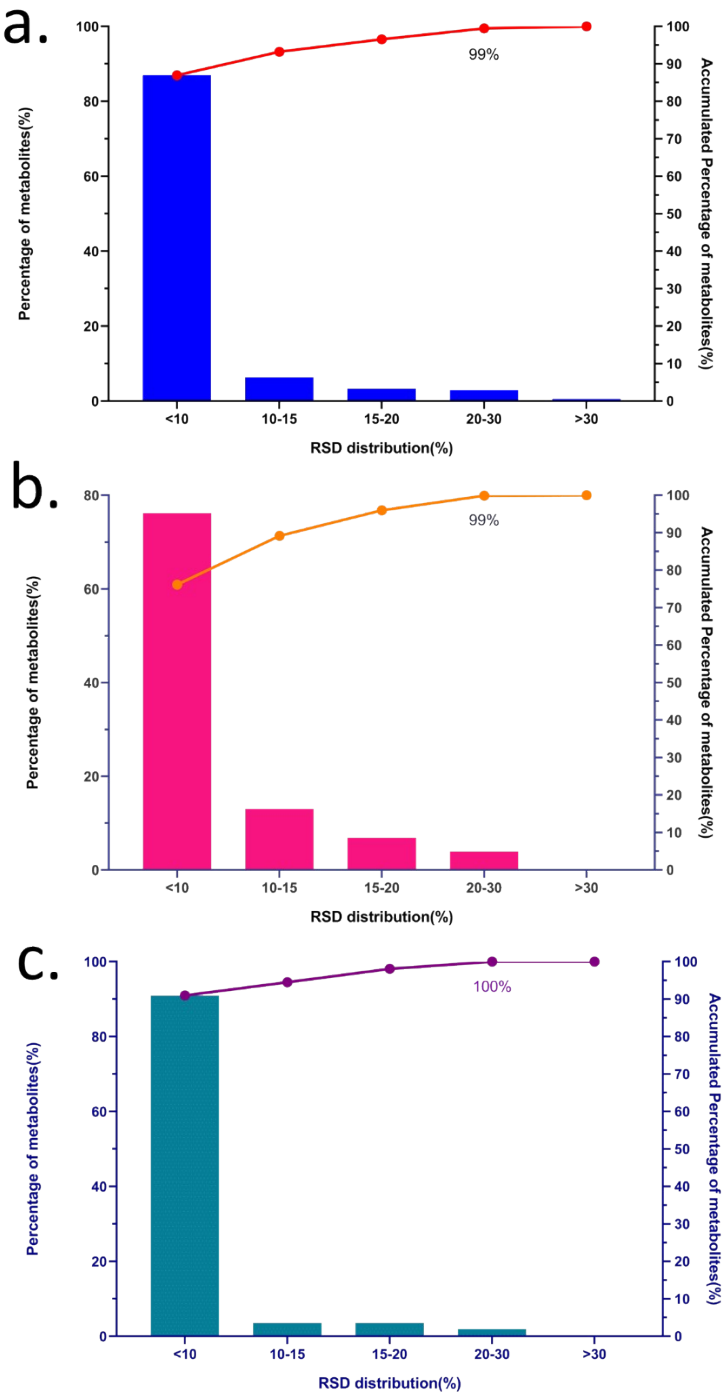

Figure S4. The characteristic of metabolite intensity RSD% distribution in QCs samples from (a) serum samples, (b) placenta tissue samples and (c) urine samples in this study.

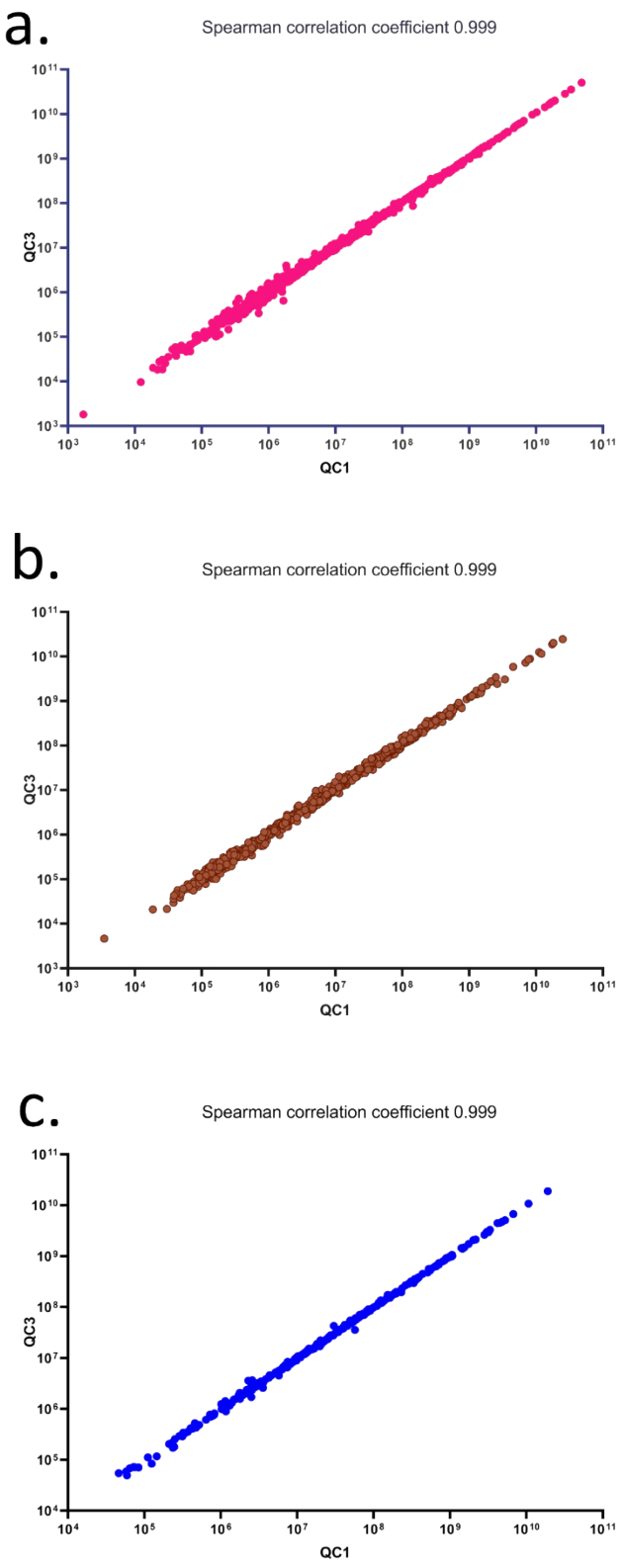

Figure S5. The characteristic of Spearman correlation analysis of the first and last QC samples in the analysis batch from (a) serum samples, (b) placenta tissue samples and (c) urine samples in this study. High correlation indicated high data quality of acquired untargeted metabolomic data.

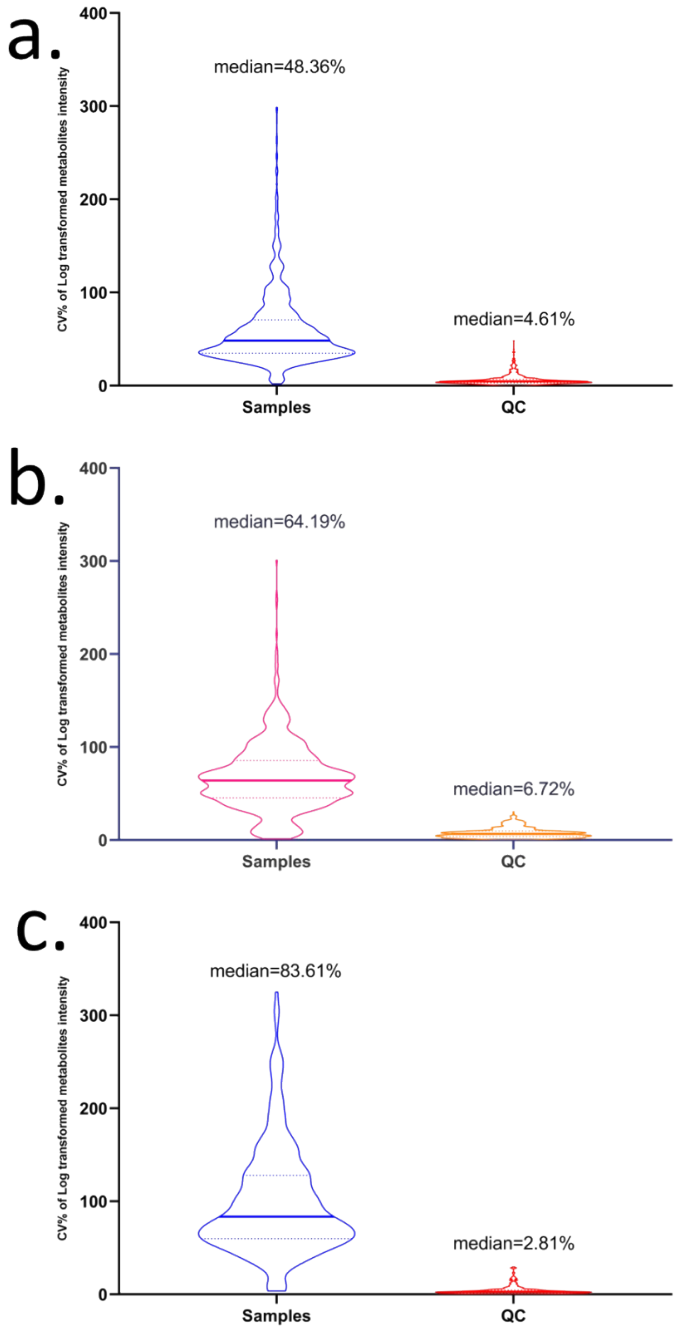

Figure S6. The characteristic of boxplot of CV% for all quantified metabolites from (a) serum samples, (b) placenta tissue samples and (c) urine samples in this study (Median value shown).

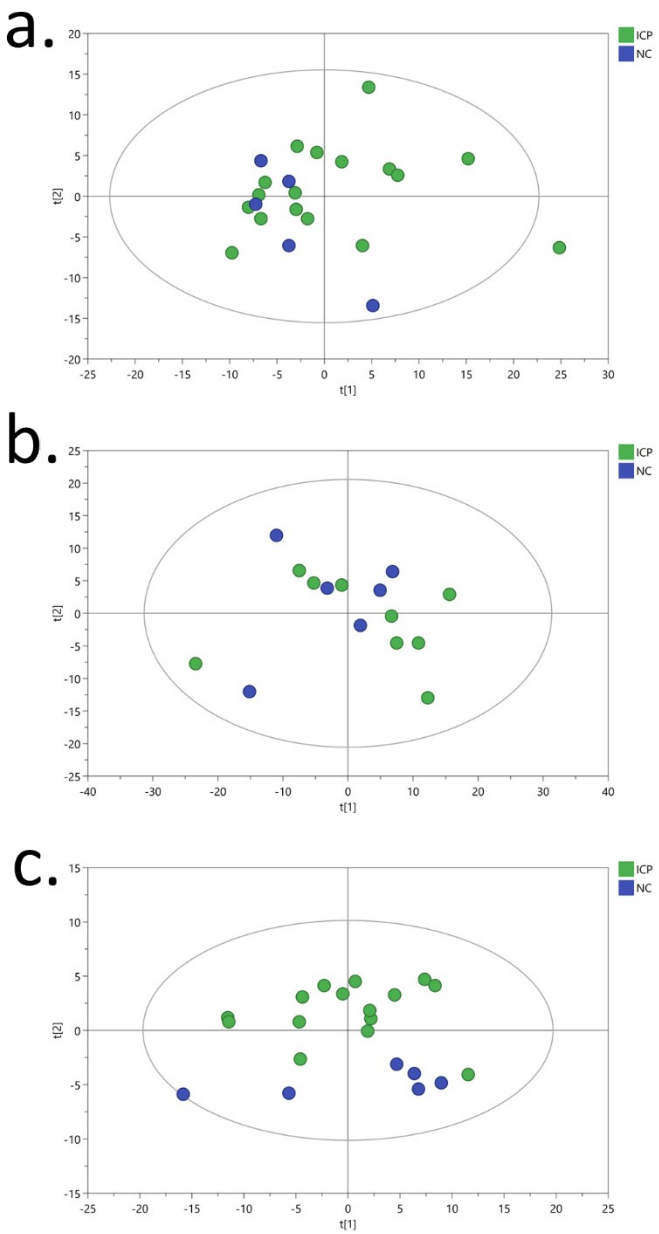

Figure S7. The unsupervised PCA score plots of metabolic phenotypes between ICP/NC groups from (a) serum samples, (b) placenta tissue samples and (c) urine samples in this study. Metabolomics data was pareto scaled to for modeling. Model parameters from serum samples, placenta tissue samples and urine samples are R^2X=0.367, R^2X=0.61 and R^2X=0.51, respectively (cumulative variance proportion of 2 principal components).

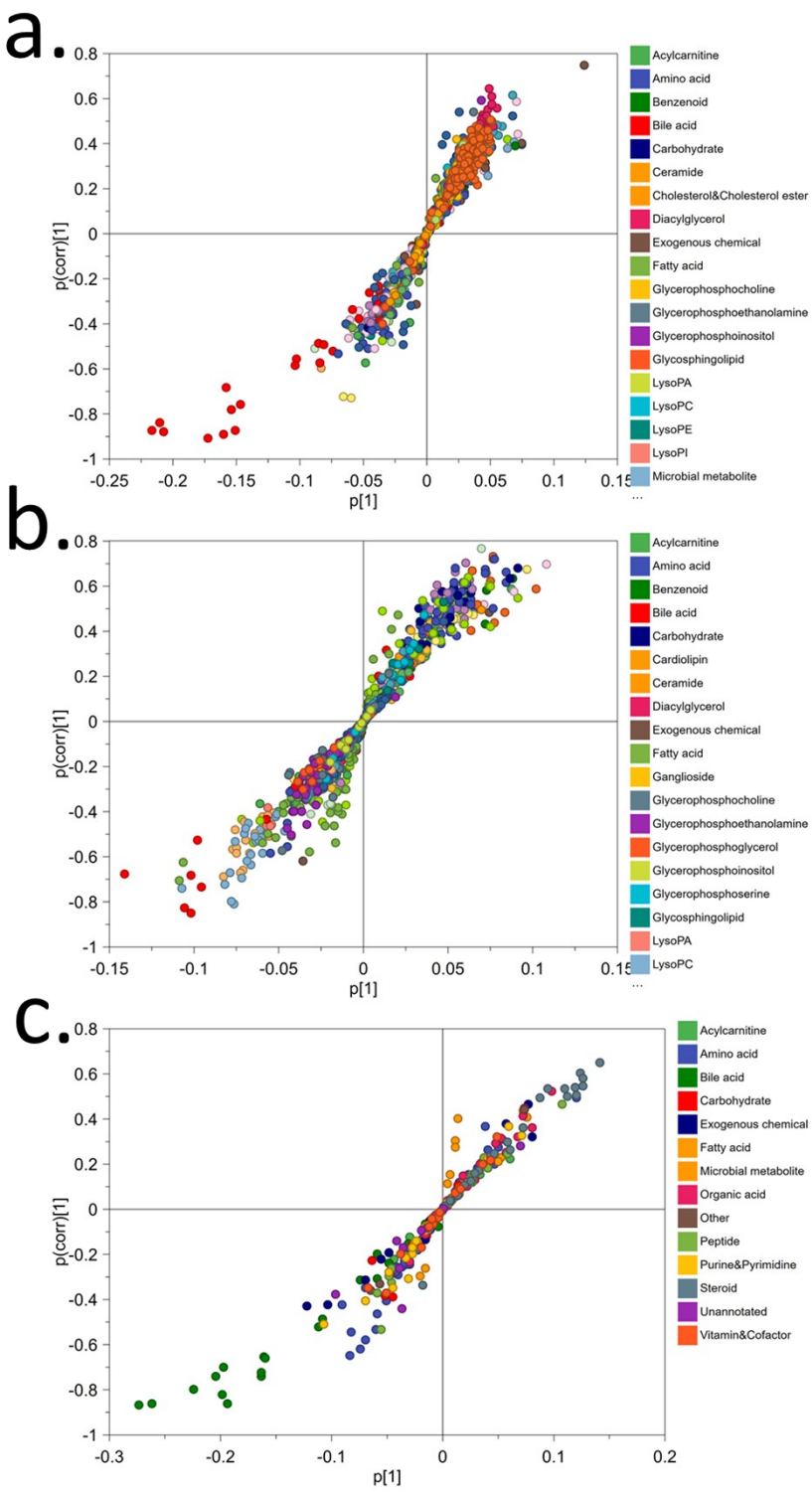

Figure S8. The S-plots of OPLS-DA model differentiating ICP/NC groups from (a) serum samples, (b) placenta tissue samples and (c) urine samples in this study. Metabolites were colored by its chemical classes.

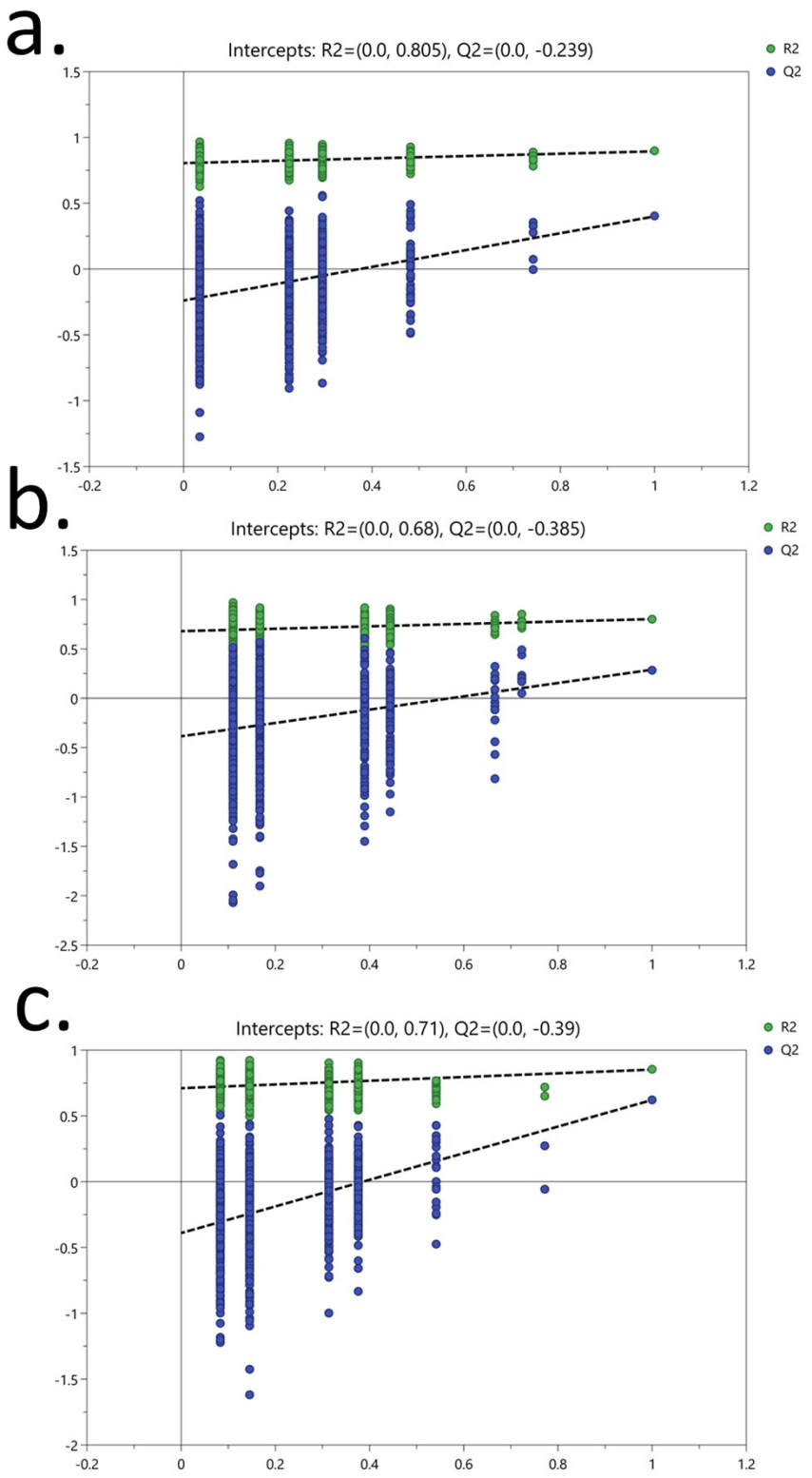

Figure S9. The 999 times permutation to test robustness of OPLS-DA modeling from (a) serum samples, (b) placenta tissue samples and (c) urine samples in this study.

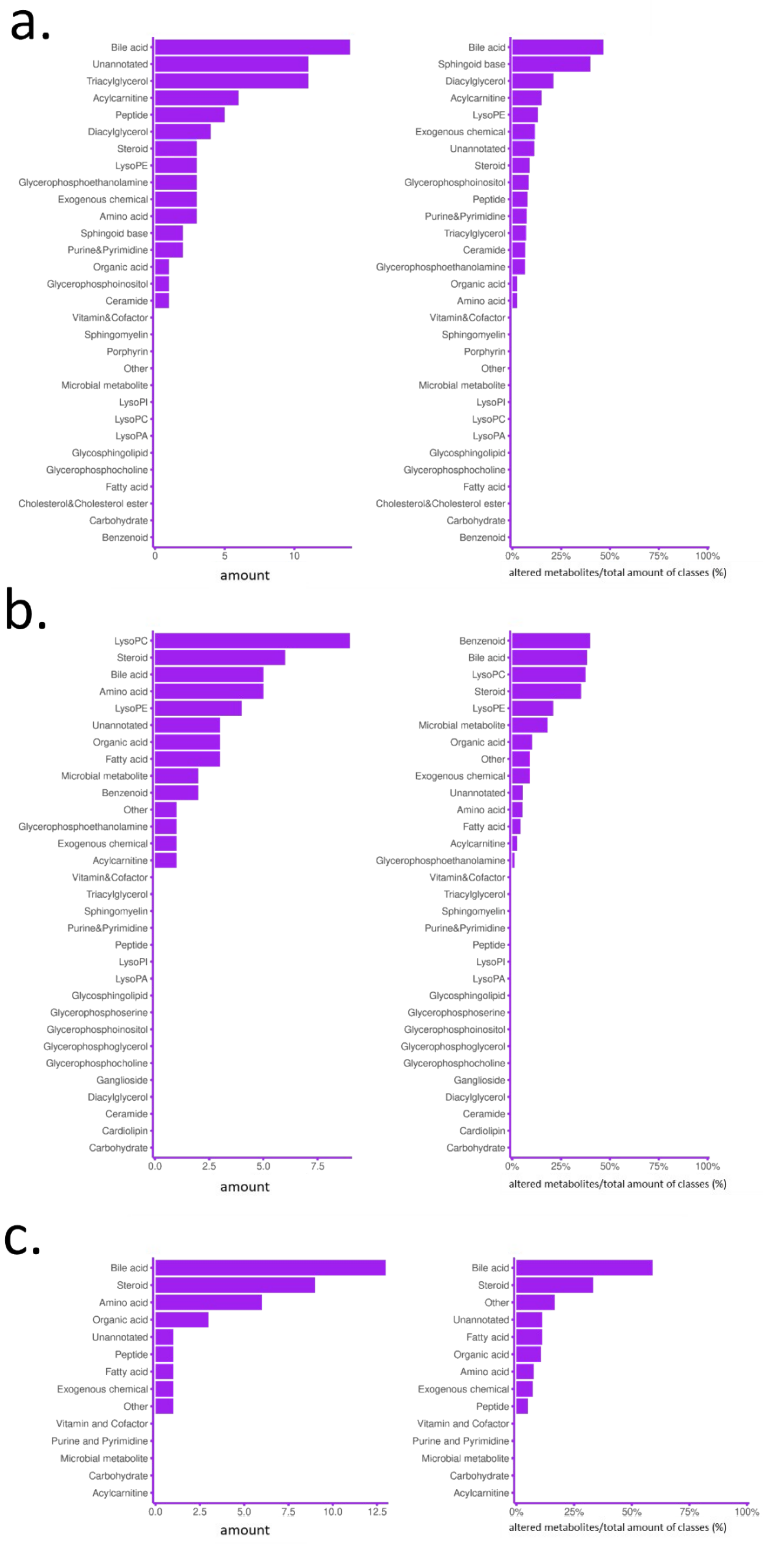

Figure S10. The chemical structure classification of differential metabolites between ICP/NC groups ($p<0.05$) from (a) serum samples, (b) placenta tissue samples and (c) urine samples in this study.