Recent developments in omics technologies enable physicians to examine the metabolic and epigenetic rationales behind various medical disorders whose etiological backgrounds are not clear. Metabolomics data with genomic information helps understanding the interaction between phenotypes (or diseases) and genes, transcripts, proteins, metabolites, and the environment; thus, it may be possible to predict the occurrence of certain disorders. Metabolomics analysis includes identification and quantification of small molecules (molecular weight < 1000 Da) with different physical properties in tissues, cells, or physiological fluids in a specific period.

This study involved 21 and 32 pregnant women carrying nondisjunction DS and euploid fetuses, respectively, determined as a result of prenatal screening and diagnosis within the framework of an antenatal care program. In this study, metabolomics analyses were performed on maternal plasma using gas chromatography-mass spectrometry (GC-MS) and liquid chromatography-quadrupole time-of-flight mass spectrometry (LC-qTOF-MS) to determine the appropriate metabolites to be used in the evaluation of pregnant women carrying Down Syndrome (DS) fetuses.

After deconvolution and alignment of GC-MS data, 95 metabolites were identified in plasma samples. Forty-six of these metabolites were significantly altered between the control and DS groups (p < 0.05). GC-MS analysis indicated that levels of 2-hydroxybutyric acid, benzoic acid, nonanoic acid, 3-hydroxybutyric acid, and 2-ketoisocaproic acid were increased in the DS group, whereas beta-alanine, threonic acid, oxalic acid, alpha-Tocopherol, uracil, 2-piperidone, and creatinine were decreased. These identified metabolites belong to Krebs cycle, amino acid and fatty acid metabolism. The multivariate analysis shows clear separation between DS and control groups. LC-qTOF-MS based metabolomic analyses were carried out in positive and negative ionization mode and allowed identification of 296 metabolites. In LC-qTOF-MS metabolomic profiling, the control and DS groups showed perfectly different metabolomic profiles. Lipid-related metabolites were decreased in the DS group, whereas creatine, N4-phosphoagmatine, citrate, 2, 5-dioxopentanoate, 2-furoate, pyruvate, and fructose were increased. The significantly altered metabolites were presented in heat color graphics.

Pathway analysis was also performed using metabolites that were significantly altered (p < 0.05) between the groups. Pathway analysis results showed that the biosynthesis of aminoacyl-t RNA and valine-leucine-iso leucine, and metabolism of nitrogen, alanine-aspartate-glutamate, glycine-serine-threonine, cysteine, methionine, arginine, proline, phenylalanine, glyoxylate, and dicarboxylate, as well as the pentose phosphate pathway and citrate cycle (TCA cycle) seem to be influenced/impaired in DS pregnancies.

Our findings indicate a special type of metabolic status/syndrome in pregnant women carrying DS fetuses. It could be speculated that altered metabolic status might influence both gametogenesis and embryogenesis at various levels because the DS phenotype shows variations in terms of structural malformations.