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MATERNAL GESTATIONAL PROTEIN RESTRICTION AFFECTS PLACENTAL AND FETAL HEPATIC AMMONIA METABOLISM IN INTRAUTERINE GROWTH RESTRICTED RATS

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Objectives: Clinical metabolomics enables the characterization of diseases beyond genomic and proteomic levels, thus enhancing the etiopathological comprehension. Human pregnancies afflicted with intrauterine growth restriction (IUGR) exhibit a distinct metabolic profile. In this study, we investigated the similarity of these metabolic changes in a rat model of IUGR.

Methods: Pregnant Wistar dams were fed a low protein (8%, LP; IUGR) or an isocaloric normal protein diet (17%, NP; controls). Maternal serum, placenta and fetal liver was subjected to reverse-phase liquid chromatography mass spectrometry (LC-MS) (Agilent Eclipse XDB-C18 column) coupled with an ESI-MS/MS-system (API6500+, Sciex; Agilent HPLC1260 series) using the AbsoluteIDQ p180 kit (Biocrates). Data analysis was performed using MetaboAnalyst v5.0.

Results: Pathway enrichment analysis revealed changes in hepatoplacental ammonia metabolism in LP rats, along with the engagement of maternal metabolic pathways associated with epigenetic programming and energy regulation. Logistic regression, combined with receiver-operating characteristic (ROC) curve analysis, pinpointed the tryptophan/kynurenine ratio in fetal liver and the phenylalanine/tryptophan ratio in the placenta as significant discriminators between groups.

Conclusion: LC-MS/MS fingerprinting has emerged as a promising method for probing metabolic shifts. In our rat model of intrauterine growth restriction (IUGR) induced by low protein intake, we noted metabolic changes in multiple fetal compartments and maternal blood. These changes closely mirror metabolic alterations seen in human pregnancies affected by this condition. Our results emphasize the need for additional investigation into the underlying mechanisms and potential interventions.