Serum proteome signatures associated with liver steatosis in adolescents with obesity.

P. J. Giraudi, D. Pascut, C. Banfi, S. Ghilardi, C. Tiribelli, A. Bondesan, D. Caroli, A. Minocci, A. Sartorio

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Purpose: childhood obesity, a pressing global health issue, significantly increases the risk of metabolic complications, including metabolic dysfunction associated with steatotic liver disease (MASLD). Accurate non-invasive tests for early detection and screening of steatosis are crucial. In this study, we explored the serum proteome, identifying proteins as potential biomarkers for inclusion in non-invasive steatosis diagnosis tests.

Methods: fifty-nine obese adolescents underwent ultrasonography to assess steatosis. Serum samples were collected and analyzed by targeted proteomics with the Proximity Extension Assay technology. Clinical and biochemical parameters were evaluated, and correlations among them, the individuated markers, and steatosis were performed. Receiver operating characteristic (ROC) curves were used to determine the steatosis diagnostic performance of the identified candidates, the fatty liver index (FLI), and their combination in a logistic regression model.

Results: significant differences were observed between subjects with and without steatosis in various clinical and biochemical parameters. Gender-related differences in the serum proteome were also noted. Five circulating proteins, including Cathepsin O (CTSO), Cadherin 2 (CDH2), and Prolyl endopeptidase (FAP), were identified as biomarkers for steatosis. CDH2, CTSO, Leukocyte Immunoglobulin Like Receptor A5 (LILRA5), BMI, waist circumference, HOMA-IR, and FLI, among others, significantly correlated with the steatosis degree. CDH2, FAP, and LDL combined in a logit model achieved a diagnostic performance with an AUC of 0.91 (95% CI 0.75-0.97, 100% sensitivity, 84% specificity).

Conclusions: CDH2 and FAP combined with other clinical parameters, represent useful tools for accurate diagnosis of fatty liver, emphasizing the importance of integrating novel markers into diagnostic algorithms for MASLD.