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Beyond BMI: Metabolomic Profiling of Obesity Phenotypes in Women

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Introduction:

Obesity is a heterogeneous condition where people with similar body fat can have very different cardiometabolic risk. Some women with obesity remain metabolically healthy (MHO), while others develop impaired glucose control and high blood pressure (MUO). Routine clinical measurements do not fully explain this difference. Metabolomic profiling may help identify early metabolic changes underlying these phenotypes. This study aimed to compare anthropometric, clinical, and circulating metabolite profiles between women with MHO and MUO.

Methods:

This cross-sectional study analysed baseline data from 70 women with overweight or obesity (36 MHO; 34 MUO) enrolled in a lifestyle intervention study. Anthropometry, blood pressure and biochemical parameters were measured at baseline. Serum metabolites were analysed using proton nuclear magnetic resonance spectroscopy (1H NMR). Forty metabolites were quantified and log-transformed. Groups were compared using analysis of covariance adjusting for age, BMI and baseline medication use.

Results:

Women with MUO were older and had higher systolic and diastolic blood pressure and higher HbA_{1c} than women with MHO. Body weight, BMI and waist circumference were similar between groups, although MUO showed a higher waist-to-hip ratio. Lipid levels showed no difference between groups. Eight of 40 metabolites differed significantly between groups after adjustment ($p < 0.05$), namely acetate, citrate, cystine, glucose, histidine, N-acetylglycine, valine, and τ -methylhistidine. Citrate and N-acetylglycine demonstrated significant phenotype- medication interaction effects.

Conclusion:

This study demonstrates that women with MHO and MUO possess a distinct metabolic signature characterized by alterations in eight key metabolites, despite having similar BMI. These findings highlight the potential of metabolomic profiling to identify early physiological shifts in obesity.