J Obes Weight Loss Ther 2019, Volume 9
DOI: 10.4172/2165-7904-C1-091

Bile Acid metabolism is altered in those with Insulin Resistance after Gestational Diabetes Mellitus

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Background: Bile acids (BAs) are known mediators of glucose metabolism that are altered in type 2 diabetes mellitus (T2DM) and gestational diabetes mellitus (GDM). We hypothesised that post-prandial BA fractions are changed in women with Insulin resistance (IR) after recovery from GDM using homeostatic model assessment (HOMA-IR).

Methods: 45 women median age 44(31-47) with previous GDM, including 20 with HOMA-IR >2.8 and 25 age-matched controls with HOMA-IR ≤ 2.8 were studied. After an overnight fast, all underwent an oral glucose tolerance test. Blood samples were collected at baseline and every 30min for 120min and analysed for glucose on automated platform and for total BAs, their conjugates and fractions using liquid-chromatography tandem mass-spectrometry. Baseline samples were analysed for insulin on automated platform. Delta (Δ) change (difference between baseline and maximal post-prandial response) were calculated. Data is presented as median (IQR).

Results: Fasting primary and unconjugated BAs were higher in women with HOMA-IR >2.8 vs. those with HOMA-IR ≤ 2.8 [0.24 (0.16-0.33) vs 0.06(0.04-0.22) μmol/L and 0.91(0.56-1.84) μmol/L vs. 0.69(0.32-0.89) μmol/L respectively. Δ taurine-conjugated BAs was higher in women with HOMA-IR ≤ 2.8 than those with HOMA-IR>2.8 [0.33(0.20-0.54) vs 0.23(0.13-0.34) μmol/L]. Fasting glucose and non-12α-hydroxylated BAs were negatively correlated in women with HOMA-IR >2.8 (all $p<0.05$).

Conclusions: Following GDM, individuals with HOMA-IR >2.8 have altered conjugated and non-12α-hydroxylated fractions of BAs. It remains to be elucidated if the altered BA metabolism is a contributing factor to the pathogenesis or a consequence of GDM.