Plasma Carnitine, Choline, γ-Butyrobetaine, and Trimethylamine N-oxide, but not Zonulin, are reduced in overweight/obese Patients with Pre/diabetes or Impaired Glycemia

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ABSTRACT

Background and Aims: Zonulin**,** carnitine, choline, γ-butyrobetaine (γ-BB), and trimethylamine N-oxide (TMAO) are intricately involved in metabolic anomalies and type 2 diabetes mellitus (T2D). This study aimed to compare and correlate the plasma levels of zonulin**,** carnitine, choline, γ-butyrobetaine, and TMAO, along with the adiposity, atherogenicity, surrogate insulin resistance (sIR), and proinflammatory hematological indices of newly diagnosed drug-naive pre-diabetic and diabetic patients vs. apparently healthy normoglycemic controls.

Methods: In a cross-sectional study, 30 normoglycemic subjects (controls) and 16 pre-diabetic (PreDM) and 14 type 2 diabetes (T2D) cases, that were gender and age-matched, were enrolled. Zonulin**,** carnitine, choline, γ-BB, and TMAO plasma levels were appraised using colorimetric assays. A comparison between the study groups was conducted by ANOVA while Spearman rank correlations between the metabolic risk biomarkers and between the risk markers and adiposity, sIR, atherogenicity, and proinflammatory hematological indices were also examined.

Results: Significant intergroup discrepancies in plasma carnitine, choline, γ-BB, and TMAO (but not zonulin) could be recognized in the cases vs. controls. Fasting blood glucose (FPG), glycated hemoglobin (A1C), triglycerides (TG), body mass index (BMI), lipid accumulation product (LAP), visceral adiposity index (VAI), atherogenic index of plasma (AIP), and all sIR were outstandingly higher in the cases vs. controls. Blood indices lacked a scoring value to discriminate cases from controls. Inadvertently, no relation was found between plasma carnitine, choline, γ-BB, TMAO, or zonulin in cases. Among the rest of the markers and sIR indices; The triglyceride-glucose-body mass index (TyG*BMI) related reciprocally to zonulin. Noticeably, among adiposity indices, TyG*BMI, triglyceride glucose-waist circumference (TyG*WC), and metabolic score for insulin resistance (MetS-IR) positively associated with waist circumference (WC), hip circumference (HC), BMI, body adiposity index (BAI), and waist-to-height ratio (WHtR). Exceptionally LAP proportionally correlated with all sIR. TyG*WC and MetS-IR correlated directly with the conicity index (CI). WHR directly associated with triglyceride-glucose (TyG) index and TyG*WC. Remarkably, the TyG index (but not TyG*BMI, TyG*WC, or MetS-IR) positively associated with all atherogenicity indices and RDW (but none of other blood indices). TMAO correlated inversely ($P < 0.05$) and moderately with choline. Distinctively, carnitine associated negatively with TC ($P < 0.05$). Both choline and carnitine related similarly and directly with PLR but inversely with lymphocytes ($p < 0.05$). Effectively, γButyrobetaine associated with both WC and the TyG-WC index equally negatively ($P < 0.05$). Substantially, γButyrobetaine correlated inversely with both atherogenic LDL-C/HDL-C ratio and MPV ($P < 0.05$). No pronounced relations were detected between the five microbiome signature determinants and glycemic control parameters (FBG and A1C %), sIR (TyG, TyG-BMI or MetS-IR), adiposity (WHR, WHtR, CI, BAI, LAP, or VAI), atherogenicity indices (TC/HDL-C ratio, non-HDL-C/HDL-C ratio, or AIP), or blood indices (NLR or MLR).**Conclusion:** Given the intergroup discrepancies in sIR, plasma zonulin, carnitine, choline, γ-BB, and TMAO along with their elective correlations with indices and clinical parameters of metabolic dysregulations, our study cannot rule out any possible molecular crosstalk and interplay of the biomarkers studied with the pathophysiology of prediabetes/diabetes. All in all, plasma zonulin, carnitine, choline, γ-BB, and TMAO with sIR can be putative surrogates for molecular cardiometabolic risk biomarkers to use as prognostic/predictive tools for the diagnosis/prevention and potential targets for prediabetes/diabetes management modalities.

Keywords: Zonulin trimethylamine-N-oxide, choline, carnitine, γ-butyrobetaine (γ-BB), trimethylamine-N-oxide (TMAO), flavin monooxygenase 3, atherogenic index of plasma, intestinal barrier integrity, metabolomics.