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Relationships between the gut microbiota, dietary intake and metabolic disease manifested as non-alcoholic fatty liver disease

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Non-alcoholic fatty liver disease (NAFLD) is of growing concern with approximately 25% of the global population affected.[1,2] Clinical therapies for NAFLD focus on dietary changes related to weight management, with weight loss associated with reduced pathology.[3] Specific dietary profiles have been associated with NAFLD improvements however consensus regarding optimal intake, beyond simply reducing energy intake, remains elusive. Exact diet-disease mechanisms are not confirmed, however the role of the gut microbiota in mediating this relationship is of interest, with distinct microbiota profiles evident in individuals with NAFLD. Current literature addresses the relationship between diet and NAFLD, or microbiota and NAFLD, however detail is lacking regarding a potential relationship between all three. This research employed a retrospective case control design to observe relationships between diet, microbiota and NAFLD with an aim to direct future intervention-based research. Adults with NAFLD were recruited via public hospital clinics. Control participants without NAFLD were recruited to enable comparison. Outcome measures included dietary data, anthropometry, clinical markers of NAFLD and inflammation, demographic information, mental health and gastrointestinal symptom surveys and metagenomic sequencing of microbiota taxonomy and functional pathways. In total, 31 individuals with NAFLD and eight healthy controls were recruited. Significant differences between groups were evident for markers of metabolic disease and inflammation including BMI ($p = 0.001$), HbA1c ($p < 0.001$), hs-CRP ($p = 0.03$) and TNF-*a* ($p = 0.04$). No significant differences were evident regarding energy or macronutrient intake however the control group consumed significantly more dietary fibre ($p = 0.014$). Food group intake between groups indicated significant differences only in intake of whole grains ($p = 0.001$), specifically from whole grain or higher fibre oats ($p = 0.03$) and cereals ($p = 0.02$). Significant differences in microbial abundance were evident across all taxonomic levels and Spearman's correlation indicated significant associations between these and dietary intake and markers of metabolic disease and inflammation. Beta diversity, but not alpha diversity, was significantly different between groups ($p = 0.046$). There were 358 significantly different microbiota functional pathways between groups, including those involved in nutrient metabolism. Gastrointestinal symptom scores were significantly less burdensome in the control group across all domains ($p < 0.05$). The current research provides evidence for differences in the microbiota of individuals with NAFLD compared to controls and demonstrates that these differences are associated with dietary choices as well as clinical outcomes. In particular, this research highlighted a role for diet quality considerations in NAFLD management given evidence of potential advantages of dietary fibre, particularly from whole grains, in benefitting both microbiota and clinical outcomes. This study also indicates a potential focus area for future interventions that are powered to detect associations between diet and the microbiota in NAFLD and related metabolic conditions.

References

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