

Gut microbial richness as an earlier biomarker of Mediterranean diet intervention in type 2 diabetes metabolic control

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Mediterranean diet has been recommended for type 2 diabetes treatment⁽¹⁾. The impact of diet in shaping the gut microbiota is well known, particularly Mediterranean diet^(2–4). However, the link between Mediterranean diet and diabetes outcomes improvement is not completely clear. The aim of this clinical trial was to study the role of microbiota modulation by a Mediterranean diet intervention on the clinical outcomes in a diabetic population.

In this 12-week single-arm pilot study, nine participants received individual nutritional counselling sessions promoting Mediterranean diet. Gut microbiota was analysed by next-generation sequencing at baseline, 4 weeks, and 12 weeks after the intervention. Biochemical parameters, body composition and blood pressure were assessed at the same time-points (baseline, 4 weeks, and 12 weeks). Mediterranean diet adherence was assessed by MEDAS score at baseline and after 12 weeks. Statistical analysis was performed using One-way ANOVA followed by Bonferroni test for parametric variables and Friedman test followed by repeated Wilcoxon tests for non-parametric variables. Effect sizes (Cohen d test) are also presented to decide whether a clinically relevant effect is found ($|d| > 0.50$ indicates a medium effect size and $|d| > 0.80$ a large effect size)⁽⁵⁾. This study was approved by the Ethics Committee of Administração Regional de Saúde de Lisboa e Vale do Tejo (Ref. 016/CES/ INV/2019) and Faculdade de Ciências Médicas|NOVA Medical School, Universidade NOVA de Lisboa (Ref. 55/2018/CEFCM) and was registered at clinicaltrials.gov as NCT04403217.

Data are presented as mean \pm SD. Adherence to the Mediterranean diet (MEDAS score) increased from 8.11 \pm 2.26 at baseline to 10.8 \pm 1.25 after the intervention ($p < 0.05$; Cohen $d = 1.58$). Changes in microbial richness was observed right after 4 weeks of the intervention (73.14 \pm 39.91 to 100 \pm 41.5, $p = 0.205$; Cohen $d = 0.66$), being negatively correlated with fasting glucose levels ($r = -0.634$; $p < 0.05$) and HOMA-IR ($rs = -0.464$; $p < 0.05$). On the other hand, HbA1c decreased from 7.53 \pm 1.07% to 6.86 \pm 0.85% ($p < 0.05$; Cohen $d = -0.70$) and HOMA-IR decreased from 3.79 \pm 2.98 to 2.76 \pm 2.05 at the end of study (12 weeks) ($p < 0.05$; Cohen $d = -0.41$). Alkaline phosphatase activity was assessed in faecal samples and was negatively correlated with HbA1c ($rs = -0.584$; $p < 0.05$) and positively correlated with microbial diversity ($rs = 0.608$; $p < 0.05$).

This study reinforces that increasing adherence to the Mediterranean diet resulted in a better glycaemic control in subjects with type 2 diabetes. Gut microbial richness changes seemed relevant in mediating the metabolic impact of therapeutic interventions and may constitute new target for the treatment of type 2 diabetes. Nonetheless, the number of participants that enrolled in this pilot study was small (9 participants), thus studies with a larger sample size are needed to confirm these findings.

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