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GUT HORMONE, ANTI-INFLAMMATORY, ANTI-OXIDATIVE AND QUALITY OF LIFE OUTCOMES OF PROBIOTICS MEDIATED GLYCAEMIC CONTROL

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PhD

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AUTHOR'S DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Teknologi MARA. It is original and is the results of my own work, unless otherwise indicated or acknowledged as referenced work. This thesis has not been submitted to any other academic institution or non-academic institution for any degree or qualification.

I, hereby, acknowledge that I have been supplied with the Academic Rules and Regulations for Post Graduate, Universiti Teknologi MARA, regulating the conduct of my study and research.

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ABSTRACT

The rising prevalence of type 2 diabetes mellitus (T2DM) has called for alternatives and probiotics have been seen as viable option in managing T2DM effectively. The general aim of this thesis was to investigate the effects of probiotics on glycaemic control and QoL among T2DM patients. A systematic review and meta-analysis was first performed to identify the research gaps and to strengthen the experimental design for investigation of probiotic effects on glycaemic control and QoL amongst T2DM patients. A 15-item Diabetes Quality of Life Brief Inventory (DQoL-BCI) was then translated into Malay language and validated under Malaysian setting. A randomised controlled trial with 100 T2DM patients who were randomly assigned to receive either probiotics mixtures [Probio-Tec® 10^9 Colony Forming Unit (CFU), Chr Hansen Holding A/S, Denmark] or placebo daily for 24 weeks was conducted. Blood sample were analyse to evaluate the hypoglycaemic, anti-inflammatory, anti-oxidative and gut hormone regulation effects of probiotics. The meta-analysis revealed a moderate beneficial hypoglycaemic effect of probiotics, with significant reduction in fasting blood glucose (FBG) (MD = -0.98 mmol/L; 95% CI: -1.17, 0.78, $p < 0.00001$). Probiotic effects on glycosylated haemoglobin (HbA_{1c}), anti-inflammatory and anti-oxidative markers remained inconsistent. Systematic review found existing clinical trials to be limited by variations in intervention duration, quality and depth of study design. For QoL validation study, exploratory factor analysis indicated that the 4-factor structure of the translated DQoL-BCI was optimal. Confirmatory factor analysis confirmed the 4-factor model fit. Cronbach's alpha coefficient and intraclass coefficient correlations (range) obtained were 0.703 and 0.86 (0.734 to 0.934), indicating good reliability and stability of the translated DQoL-BCI. There was negative, moderate correlation between the scores of DQoL-BCI (Malaysian version) and EQ-5D-3L utility score ($r = -0.329$, $p = 0.003$). The RCT revealed that glycaemic markers [i.e. HbA_{1c}, FBG, fasting insulin and Homeostatic Model Assessment-Insulin Resistance (HOMA-IR)] did not differ significantly between the groups. Insignificant findings were also observed in the inflammatory and oxidative stress markers except for significant increases in IL-10 ($\beta = 0.054$, 95%CI: 0.008 to 0.100, $p = 0.020$) and malondialdehyde (MDA) ($\beta = 0.064$, 95%CI: 0.006 to 0.121, $p = 0.031$) among patients receiving probiotics at week 24 for per-protocol (PP) population that completed the three time-points. GEE analyses showed that the increased levels of total cholesterol (TC) ($\beta = 0.234$, 95%CI: 0.029 to 0.439, $p = 0.025$) and LDL ($\beta = 0.178$, 95%CI: 0.002 to 0.354, $p = 0.047$) among patients receiving probiotics at week 24 was significant for PP population that completed the three time-points. Similar observations were also noted in the intention-to-treat (ITT). However, in the population that further excluded patients who were initiated with insulin, the changes in the abovementioned parameters became insignificant [i.e. MDA ($\beta = 0.049$, 95%CI: 0.004 to 0.103, p=0.070), TC ($\beta = 0.140$, 95%CI: 0.075 to 0.356, p=0.201) and LDL ($\beta = 0.103$, 95%CI: 0.080 to 0.285, p=0.272)] except for IL-10 ($\beta = 0.066$, 95%CI: 0.018 to 0.114, $p = 0.007$). DQoL score showed no significant changes across all time-points within or between the two groups. In summary, the findings from the present trial revealed that probiotics supplementation does not enhance glycaemic control (i.e. HbA1c) and other parameters except for IL-10.The significant increase in IL-10 among intervention group provides fundamental data for future investigation on probiotics as alternative treatment in managing and preventing T2DM.

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