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Early pregnancy probiotic supplementation with *Lactobacillus rhamnosus* HN001 may reduce the prevalence of gestational diabetes mellitus: a randomised controlled trial

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Abstract

The study aims to assess whether supplementation with the probiotic *Lactobacillus rhamnosus* HN001 (HN001) can reduce the prevalence of gestational diabetes mellitus (GDM). A double-blind, randomised, placebo-controlled parallel trial was conducted in New Zealand (NZ) (Wellington and Auckland). Pregnant women with a personal or partner history of atopic disease were randomised at 14–16 weeks' gestation to receive HN001 (6×10^9 colony-forming units) (*n* 212) or placebo (*n* 211) daily. GDM at 24–30 weeks was assessed using the definition of the International Association of Diabetes and Pregnancy Study Groups (IADPSG) (fasting plasma glucose ≥5·1 mmol/l, or 1 h post 75 g glucose level at ≥10 mmol/l or at 2 h ≥8·5 mmol/l) and NZ definition (fasting plasma glucose ≥5·5 mmol/l or 2 h post 75 g glucose at ≥9 mmol/l). All analyses were intention-to-treat. A total of 184 (87 %) women took HN001 and 189 (90 %) women took placebo. There was a trend towards lower relative rates (RR) of GDM (IADPSG definition) in the HN001 group, 0·59 (95 % CI 0·32, 1·08) ($P = 0·08$). HN001 was associated with lower rates of GDM in women aged ≥35 years (RR 0·31; 95 % CI 0·12, 0·81, $P = 0·009$) and women with a history of GDM (RR 0·00; 95 % CI 0·00, 0·66, $P = 0·004$). These rates did not differ significantly from those of women without these characteristics. Using the NZ definition, GDM prevalence was significantly lower in the HN001 group, 2·1 % (95 % CI 0·6, 5·2), *v.* 6·5 % (95 % CI 3·5, 10·9) in the placebo group ($P = 0·03$). HN001 supplementation from 14 to 16 weeks' gestation may reduce GDM prevalence, particularly among older women and those with previous GDM.

Key words: Randomised controlled trials: Probiotics: *Lactobacillus rhamnosus* HN001: Gestational diabetes mellitus

Lifestyle factors such as changes in patterns of food consumption with economic development have led to the well-recognised and increasing problems of obesity and associated diseases, including gestational diabetes mellitus (GDM), both in New Zealand (NZ)[1] and other developed countries[2]. Pre-pregnancy overweight and obesity have been shown to account for 46 % of GDM[3], with excess weight gain during pregnancy, previous GDM or a family history of diabetes, polycystic ovary syndrome (PCOS), older age and higher parity also identified as risk factors[4]. GDM itself increases the risk for preeclampsia, miscarriage, preterm birth, macrosomia, induction of labour and caesarean section[2,3]. GDM also increases the risk for later maternal and child obesity and subsequent type 2 diabetes mellitus[5].

GDM definitions are variable, and establishing an international consensus on diagnostic criteria that predict adverse pregnancy outcomes has been challenging. In 2008, the International Association of Diabetes and Pregnancy Study Group (IADPSG)[6] used data from the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study[7] to develop recommendations for oral glucose tolerance test (GTT) threshold glucose concentrations for the diagnosis of GDM (fasting plasma glucose ≥5·1 mmol/l or 1 h post 75 g glucose level ≥10 mmol/l or at 2 h ≥8·5 mmol/l). This was based on the findings of the HAPO study[7] of a curvilinear dose–response relationship between fasting, 1 and 2 h glucose concentrations and adverse pregnancy outcomes, including macrosomia and caesarean

Abbreviations: Fonterra, Fonterra Co-operative Group Ltd; GDM, gestational diabetes mellitus; GTT, glucose tolerance test; HN001, *Lactobacillus rhamnosus* HN001; IADPSG, International Association of Diabetes and Pregnancy Study Group; NZ, New Zealand; RR, relative rate.

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