SHORT COMMUNICATION

The influence of fasting insulin level in post-gestational diabetes mellitus women receiving low-glycaemic-index diets

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Post-gestational diabetes mellitus (GDM) women are recommended weight loss to manage increased cardio-metabolic risks. We investigated the effects of lowering diet glycaemic index (GI) on fasting blood glucose (FBG), serum lipids, body weight and composition of post-GDM women with varying fasting insulin levels (INS). Seventy-seven Asian, non-diabetic women with previous GDM (aged 20–40 years, mean BMI: $26.4 \pm 4.6 \text{ kg m}^{-2}$) were recruited. At baseline, 20 subjects with $\text{INS} < 2 \mu\text{IU ml}^{-1}$ and 18 with $\text{INS} \geq 2 \mu\text{IU ml}^{-1}$ received conventional dietary recommendations (CHDR) only. CHDR emphasised energy and fat intake restriction and encouraged increase in dietary fibre intakes. Twenty-four subjects with $\text{INS} < 2 \mu\text{IU ml}^{-1}$ and 15 with $\text{INS} \geq 2 \mu\text{IU ml}^{-1}$, in addition to CHDR, received low-GI education (LGI). Changes in FBG, serum lipids, body weight and body composition were evaluated. Subjects with $\text{INS} < 2 \mu\text{IU ml}^{-1}$ had similar outcomes with both diets. After 1 year, subjects with $\text{INS} \geq 2 \mu\text{IU ml}^{-1}$ who received LGI education had reductions in FBG and triglycerides. Subjects who received CHDR observed increase in both FBG and triglycerides ($P < 0.05$). Among all subjects, diet GI was lower and dietary fibre intakes were higher in LGI compared with CHDR subjects (all $P < 0.05$). Thus, in Asian post-GDM women with normal/higher INS, adding low-GI education to CHDR improved management of FBG and triglycerides.

Nutrition & Diabetes (2014) 4, e107; doi:10.1038/nutd.2014.5; published online 17 February 2013

Keywords: gestational diabetes mellitus; glycaemic index; type 2 diabetes mellitus; prevention; fasting insulin; diet

INTRODUCTION

Gestational diabetes mellitus (GDM) increases the risk for metabolic syndrome and type 2 diabetes mellitus.¹ To attenuate these risks, lifestyle intervention including components of diet, exercise and behavioural changes is recommended to post-GDM women to enable a moderate body weight loss of 7–10%.¹ However, when compared with subjects with similar metabolic risks and glucose tolerance states, women with previous GDM achieve lower weight loss in response to standard recommendations and regain the weight lost rapidly.² Subjects with hyperinsulinaemia, a condition commonly accompanying GDM, have a greater weight loss when on low-glycaemic-index (GI) diets.^{3,4} Therefore, we analysed the effect of dietary GI on fasting blood glucose (FBG), serum lipids, body weight and body fat of post-GDM subjects with varying fasting serum insulin levels (INS) during weight loss.

MATERIALS AND METHODS

Seventy-seven post-GDM subjects, aged 20–40 years (mean $\pm$ s.d. = 30.5 ± 9 years), without a current diagnosis of diabetes were recruited. The mean body mass index of the subjects at baseline was $26.4 \pm 4.6 \text{ kg m}^{-2}$. Subjects were screened at a minimum of 2 months postpartum and the median duration since the last GDM delivery to the time of screening was 4 months (interquartile range 2). Mean parity among subjects was 2.0 ± 1.1 . Forty-four of the subjects had $\text{INS} < 2 \mu\text{IU ml}^{-1}$, which was below the detectable limits of the automated IMMULITE 2000

Systems, which was used for INS assay. The rest of the subjects had $\text{INS} \geq 2 \mu\text{IU ml}^{-1}$ (range 2.43 – $28.6 \mu\text{IU ml}^{-1}$, with a median of $5.7 \mu\text{IU ml}^{-1}$). A fasting insulin value of $2 \mu\text{IU ml}^{-1}$ was chosen to be the cutoff to analyse the differential dietary effects, as it was approximately the natural median INS value for our subjects.

Twenty subjects with $\text{INS} < 2 \mu\text{IU ml}^{-1}$ (low INS) and 18 with $\text{INS} \geq 2 \mu\text{IU ml}^{-1}$ (normal/high INS) were randomized to a group that only received conventional dietary recommendations (CHDR). CHDR education emphasised restriction of energy and fat intake and encouraged increase in dietary fibre intakes. Twenty-four subjects with $\text{INS} < 2 \mu\text{IU ml}^{-1}$ (low INS) and 15 with $\text{INS} \geq 2 \mu\text{IU ml}^{-1}$ (normal/high INS) received low-GI education in addition to CHDR (LGI). A detailed account of the educational intervention used in this study has been published earlier.⁵ In brief, nutrition education was provided once at the baseline and take-home reference booklets were provided. Quarterly follow-up visits were scheduled. Fortnightly reminders reinforcing concepts of healthy living and motivating subjects to comply with the intervention were sent using email or short messaging services. Compliance was monitored through assessments of dietary intake, physical activity and nutrition knowledge assessment pertaining to the group-specific concepts. Frequency of subject contact was kept similar between groups. Subjects' self-reported and calculated adherence to dietary prescription was monitored. Low-GI education taught subjects to choose low-GI options for high-GI staples like bread, rice and so on. A 1500-kcal sample menu used in the two diet groups is presented in Table 1. The differences in FBG, serum lipids, body weight and body fat changes between the two dietary intervention groups among subjects differing in baseline INS were studied.

The study was approved by the Ethics and Review Committees of the institutions involved. Baseline INS was analysed using IMMULITE 2000

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Received 12 March 2013; revised 23 December 2013; accepted 18 January 2014

Table 1. Sample menu for the diet groups (~1500 kcal)

Meal	Timing (hours)	Sample menu low GI	Sample menu high GI ^a
Breakfast	0700	Whole-grain bread—3 slices with baked beans Coffee/tea with 1/2 cup low-fat milk + 1 tsp sugar	Tuna whole-meal bread sandwiches—3 slices of bread Tea (1 tsp sugar)
Morning snack	1000	1 apple (medium size)	1 slice watermelon (portion size to fit a small cup)
Lunch	1230	Noodles 1and1/2 cup with chicken or fish (1 match box size) (or) chappati (6' dia, 2 nos)/ + 1/2 cup dhal Egg—1 medium Green vegetables salad—1 cup Orange—1	White rice—1and1/2 cup Egg—1 medium Baked/steamed fish—1 piece Green vegetables salad—1 cup Banana—1 small
Afternoon snack	1600	3 oatmeal biscuits/high calcium cream crackers Low-fat yoghurt—1 small tub	3 Marie biscuits Tea (with 1 tsp sugar)
Dinner	2000	Parboiled/basmati rice—1 cup baked chicken/fish 1 piece (matchbox size) (or) spaghetti with meat sauce (1 cup) Salad—1 cup (use lettuce, cucumber, tomato, chick peas, peas, beans and lemon juice)	White rice—1 cup Baked chicken/fish—1 piece (matchbox size) Egg 1 medium Vegetable/salad—1cup (lettuce, cucumber, carrot, potato)

^aUsed for the conventional dietary recommendations (CHDR) group.

System (Siemens, Healthcare Diagnostics, Deerfield, IL, USA). This insulin-automated assay had a coefficient of variation of 3%. Low INS samples were placed in the same category when the test results were duplicated. Blood glucose was measured using Cobas Integra 700 model (Roche Diagnostics, Indianapolis, IN, USA) using the enzymatic reference Hexokinase/G6PD method. Serum lipids were measured using standard enzymatic colorimetric method and low-density lipoprotein was calculated. Body weight was measured in light clothing without footwear using digital weighing scales (Model: BWB-800A, Tanita Corporation, Tokyo, Japan). Body fat was measured using the dual-emission X-ray absorptiometry (DEXA, Model: Delphi, Hologic Systems; Bedford, MA, USA). Dietary analysis was performed using a Malaysian diet intake calculator.⁶

Statistical analyses were performed using IBM SPSS (version 19, Somers, NY, USA). The statistical significance standard was set at 5%. Data normality was tested using the Shapiro–Wilks test. If data points were not normally distributed, statistical analysis was attempted on the natural logarithm of the values to improve the symmetry and homoscedasticity of the distribution. If the transformation was not successful, statistical analysis was carried out using non-parametric tests.

Effect size (ES) statistics were computed to study the magnitude of changes. ES values are typically computed to compare the effects of different treatments.⁷ ES provides a measure to assess the magnitude of difference between groups that cannot be obtained solely by focusing on *P*-values.⁸ *P*-values are dependent on both the magnitude of difference between groups and the sample size. Therefore, with other factors held constant, increasing the sample size increases the probability of finding a statistically significant difference.⁸ ES reported in this study was calculated as the 'standardized' mean difference: that is, as a ratio between the mean change and s.d. of change.⁸ Individual ES values were calculated for changes in outcomes for each of the two diet groups and compared. ES values between 0.2–0.5, 0.5–0.8 and >0.8 were taken to denote 'small', 'moderate' and 'large' changes in outcomes.⁷

RESULTS AND DISCUSSION

The baseline characteristics of subjects randomized to the two diet groups in each INS stratum were comparable (see Table 2). A comparison of the outcome changes in the diet groups among subjects with low and normal/high INS levels is shown in Table 2. Among subjects with low INS, there were no significant differences in outcomes between the diet groups. After 1 year, normal/high INS subjects in the LGI group had a 2.2% reduction from baseline in FBG (-0.12 ± 0.27 mmol l⁻¹), whereas CHDR subjects had a 3.8% (0.17 ± 0.32 mmol l⁻¹) increase ($P = 0.025$, see Table 2). In addition, normal/high INS subjects in the LGI group had a 12% reduction in triglycerides, whereas, in contrast, a 20% increase in triglycerides was noted in the CHDR group (-0.26 ± 0.55 vs 0.19 ± 0.54 mmol l⁻¹, $P = 0.041$, see Table 2). Changes in other serum lipids were not significantly different between the diet groups (see Table 2).

Among subjects with baseline INS $\geq 2 \mu\text{U ml}^{-1}$, weight loss (LGI vs CHDR: -1.7 ± 3.8 vs -0.16 ± 2.9 kg, ES = 0.47 vs 0.08, $P = 0.361$) and changes in total body fat (g) (LGI vs CHDR: 0.37 ± 2.7 kg, ES = 0.14 vs 1.5 ± 2.8 kg, ES = 0.53; $P = 0.37$) were not significantly different. These observations suggest beneficial effects of low-GI diets in the management of body weight and composition among normal/high INS subjects, although it is emphasised that the study is not statistically powered to evaluate these outcomes. However, these observations are consistent with the 6 months finding from the CALERIE study, which reported that women with postprandial hyperinsulinaemia lost more weight on low-GI diets after 6 months on intervention.⁴ The observations from this study are also in agreement with the findings of Ebbeling *et al.*,⁹ who showed that subjects with higher insulin levels ($\geq 57.5 \mu\text{U ml}^{-1}$ at 30 min after a 75-g dose of oral glucose) lost significantly higher amounts of body weight and body fat loss when on low-glycaemic-load diets as compared with conventional low-fat diets. Also, weight regain that is commonly observed after weight loss in trials of duration >6 months was absent among these normal/high-INS Asian subjects in the LGI arm of the current study (see Figure 1). A similar observation was noted among hyperinsulinaemic obese young adults (aged 18–35 years) studied in Boston.⁹

Baseline dietary intakes were similar between groups among all subjects. Among subjects with both INS levels, reported dietary intakes varied significantly only in terms of diet GI and dietary fibre content after intervention (see Table 3). In all subjects, estimated diet GI was lower and reported dietary fibre intakes were higher in LGI as compared with CHDR subjects (all $P < 0.05$). In subjects with low INS, calculated diet GI means $\pm$ s.d. in the LGI and CHDR groups were 59 ± 4 and 65 ± 4 , respectively ($P < 0.001$). Their estimated dietary fibre intakes were 12 ± 3 vs 16 ± 4 g, respectively ($P = 0.004$). Among subjects with normal/high INS mean (s.d.) calculated diet GI means (s.d.) in the LGI and CHDR groups were 56 ± 4 and 62 ± 6 , respectively ($P < 0.021$). Their estimated dietary fibre intakes were 13 ± 5 vs 17 ± 4 g, respectively ($P = 0.045$).

We acknowledge that $2 \mu\text{U ml}^{-1}$ is very low as a cutoff to suggest fasting hyperinsulinaemia. As published earlier by this research group, data on the normal fasting insulin range for young healthy Malaysian women are currently unavailable.¹⁰ A small Malaysian study found a median fasting insulin level of $4.7 \mu\text{U ml}^{-1}$ with a central 95% range of 2.1 – $12.1 \mu\text{U ml}^{-1}$ among 30 healthy volunteers (including 12 females).¹¹ This preliminary study also observed that the range for fasting insulin in their group of Malaysian subjects was lower than the 95% CI of 6 – $29 \mu\text{U ml}^{-1}$ typically reported.¹¹ Our study did

Table 2. Baseline characteristics and outcome changes in diet groups among subjects differing in fasting insulin levels (mean $\pm$ s.d.)

Outcome	INS < 2 $\mu\text{IU ml}^{-1}$			INS $\geq$ 2 $\mu\text{IU ml}^{-1}$		
	LGI (n = 24)	CHDR (n = 20)	P-value	LGI (n = 15)	CHDR (n = 18)	P-value
<i>Baseline characteristics</i>						
Age (years)	31.2 $\pm$ 4.2	31.0 $\pm$ 3.8	0.892	31.5 $\pm$ 5.2	31.8 $\pm$ 5.1	0.863
Parity	2.1 $\pm$ 1.1	2.0 $\pm$ 1.2	0.721	2.1 $\pm$ 1.2	2.2 $\pm$ 1.21.0	0.801
Duration postpartum (months)	4.3 $\pm$ 1.3	7.2 $\pm$ 10.1	0.170	4.5 $\pm$ 1.8	4.4 $\pm$ 1.4	0.801
<i>Weight (kg)</i>						
Baseline	61.7 $\pm$ 10.2	57.9 $\pm$ 10.1	0.221	71.1 $\pm$ 11.3	72.1 $\pm$ 10.6	0.807
Change	-0.6 $\pm$ 4.3	-0.2 $\pm$ 2.7	0.673	-1.7 $\pm$ 3.8	-0.2 $\pm$ 2.9	0.361
<i>Total body fat (kg)</i>						
Baseline	23.2 $\pm$ 6.8	22.3 $\pm$ 6.7	0.673	28.6 $\pm$ 7.2	29.8 $\pm$ 7.1	0.643
Change	1.2 $\pm$ 2.7	1.2 $\pm$ 2.6	0.692	0.4 $\pm$ 2.7	1.3 $\pm$ 2.4	0.368
<i>Trunk fat (kg)</i>						
Baseline	10.0 $\pm$ 3.4	9.7 $\pm$ 3.5	0.777	13.1 $\pm$ 3.9	14.3 $\pm$ 4.3	0.433
Change	0.75 $\pm$ 2.1	0.6 $\pm$ 1.5	0.798	0.2 $\pm$ 1.5	0.7 $\pm$ 1.4	0.252
<i>FBG (mmol l⁻¹)</i>						
Baseline	4.5 $\pm$ 0.4	4.7 $\pm$ 0.5	0.151	5.0 $\pm$ 0.5	4.9 $\pm$ 0.6	0.553
Change	0.48 $\pm$ 1.2	0.18 $\pm$ 0.32	0.155	-0.12 $\pm$ 0.27	0.17 $\pm$ 0.32	0.025
<i>Total-cholesterol (mmol l⁻¹)</i>						
Baseline	5.0 $\pm$ 0.98	5.3 $\pm$ 0.81	0.366	5.2 $\pm$ 0.7	5.2 $\pm$ 0.77	0.808
Change	-0.09 $\pm$ 0.85	-0.18 $\pm$ 0.58	0.704	-0.11 $\pm$ 0.73	-0.11 $\pm$ 0.76	0.536
<i>Triglyceride (mmol l⁻¹)</i>						
Baseline	0.7 $\pm$ 0.2	0.93 $\pm$ 2.8	0.121	1.3 $\pm$ 0.5	1.1 $\pm$ 0.5	0.180
Change	0.16 $\pm$ 0.43	-0.08 $\pm$ 0.34	0.075	-0.26 $\pm$ 0.55	0.19 $\pm$ 0.54	0.041
<i>HDL cholesterol (mmol l⁻¹)</i>						
Baseline	1.5 $\pm$ 0.4	1.5 $\pm$ 0.5	0.744	1.2 $\pm$ 0.3	1.3 $\pm$ 0.2	0.206
Change	0.04 $\pm$ 0.3	0.04 $\pm$ 0.2	0.978	0.1 $\pm$ 0.18	0.01 $\pm$ 0.31	0.283
<i>LDL cholesterol (mmol l⁻¹)</i>						
Baseline	3.2 $\pm$ 1.0	3.3 $\pm$ 0.7	0.496	3.4 $\pm$ 0.8	3.3 $\pm$ 0.7	0.726
Change	-0.23 $\pm$ 0.66	-0.18 $\pm$ 0.41	0.796	-0.1 $\pm$ 0.54	-0.21 $\pm$ 0.57	0.573
<i>TC:HDL cholesterol</i>						
Baseline	3.4 $\pm$ 0.8	3.8 $\pm$ 1.2	0.185	4.5 $\pm$ 1.3	4.0 $\pm$ 1.0	0.186
Change	-0.14 $\pm$ 0.43	-0.26 $\pm$ 0.37	0.360	-0.52 $\pm$ 0.87	-0.1 $\pm$ 0.60	0.113
<i>LDL:HDL cholesterol</i>						
Baseline	2.2 $\pm$ 0.75	2.4 $\pm$ 0.96	0.279	3.0 $\pm$ 1.1	2.6 $\pm$ 0.79	0.241
Change	-0.2 $\pm$ 0.38	-0.22 $\pm$ 0.3	0.929	-0.38 $\pm$ 0.71	-0.16 $\pm$ 0.55	0.326

Abbreviations: CHDR, conventional healthy dietary recommendation group; FBG, fasting blood glucose; HDL, high-density lipoprotein; INS, fasting insulin; LGI, low glycaemic index group; LDL, low-density lipoprotein. Baseline variables were not significantly different between the diet groups among subjects in both insulin strata. P-values shown are calculated from independent tests for difference between the diet groups, within individual insulin groupings.

demonstrate similarly low fasting INS levels as reported in a small pilot study among Austrian GDM women ($n=10$), at 3 months postpartum.¹² This study reported a median fasting insulin level of 1.63 $\mu\text{IU ml}^{-1}$.¹² Furthermore, lactation is associated with lower levels of INS at 6–9 weeks postpartum.¹³ However, in this study, only 12 out of 77 subjects (<16%), recruited at a median of 4 months postpartum, were reportedly breastfeeding.

This study demonstrated significant lowering of FBG and TG in post-GDM women with baseline fasting insulin $>2 \mu\text{IU ml}^{-1}$ who received iso-caloric LGI diets in comparison with those on conventional low-fat diets. These observations are corroborated by earlier findings that suggest that dietary GI may have varying effects depending on individual metabolic phenotypes.¹⁴ As FBG is considered to be the strongest predictor of development of type 2 diabetes mellitus in women with previous GDM,¹⁵ a reduction in FBG by lowering dietary GI may translate to

added clinical benefits of lowering diabetes risk among these women with normal or higher insulin levels. Moreover, triglycerides increase cardiovascular disease risk to a higher extent in women than in men.^{16,17} Therefore, LGI diets may also be considered cardio-protective to post-GDM women with normal to higher insulin levels.

The favourable anthropometric and glycaemic responses to low GI intervention seen in those with higher insulin levels, in comparison with subjects with low baseline insulin levels, could possibly be explained by the exaggerated glycaemic responses to increase in diet GI among high/normal INS subjects as compared with the low INS subjects. Asian subjects known to demonstrate insulin resistance at much lower body weight and waist circumference¹⁸ could have exaggerated postprandial glycaemic response to carbohydrate foods even while presenting fasting insulin levels that are typically considered as being 'normal'.

Table 3. Dietary intake among subjects after the intervention (mean $\pm$ s.d.)^a

Dietary intake	$INS < 2 \mu\text{U ml}^{-1}$			$INS \geq 2 \mu\text{U ml}^{-1}$		
	LGI	CHDR	P-value	LGI	CHDR	P-value
Energy (kcal)	1706 $\pm$ 351	1595 $\pm$ 298	0.298	1554 $\pm$ 292	1595 $\pm$ 442	0.927
Carbohydrate (g)	221 $\pm$ 46	221 $\pm$ 55	0.975	186 $\pm$ 62	208 $\pm$ 48	0.331
Protein (g)	68 $\pm$ 15	60 $\pm$ 13	0.086	70 $\pm$ 11	67 $\pm$ 28	0.259
Fat (g)	59 $\pm$ 17	51 $\pm$ 11	0.093	50 $\pm$ 10	55 $\pm$ 20	0.977
Dietary fibre (g)	17 $\pm$ 4	13 $\pm$ 3	0.004	17 $\pm$ 4	13 $\pm$ 5	0.048
Glycaemic index	59 $\pm$ 4	65 $\pm$ 4	<0.001	56 $\pm$ 4	62 $\pm$ 6	0.021
Glycaemic load	130 $\pm$ 29	145 $\pm$ 41	0.195	113 $\pm$ 38	128 $\pm$ 28	0.244

Abbreviations: CHDR, conventional healthy dietary recommendation group; LGI, low glycaemic index group. Baseline dietary intakes were not significantly different between the diet groups for subjects in both insulin strata. P-values shown are calculated from independent tests for difference between the diet groups, within individual insulin groupings. ^aThe values shown are an average of the dietary data obtained using 3-day food records, during the quarterly visits during the 1-year trial period.

Figure 1. Changes in body weight among subjects with varying baseline fasting insulin levels (estimated marginal means, kg). Legend: panel on the left plots weight changes in subjects with baseline fasting insulin $< 2 \mu\text{U ml}^{-1}$. Panel on the right plots weight changes in subjects with baseline fasting insulin $\geq 2 \mu\text{U ml}^{-1}$. Dotted line shows weight changes in LGI. Smooth line shows weight changes in CHDR. Time points 1, 2, 3, 4 and 5 refer to body weight at baseline, 3, 6, 9 and 12 months after intervention.

Hence, even though a 15% difference in dietary GI between the groups (about 9 units based on baseline GI), thought to have clinical significance,¹⁹ could not be achieved after 12 months of intervention, significant differences in FBG and TG were seen among subjects with high/normal INS levels. Nevertheless, it is also interesting to observe that much smaller differences in the GI (among the quintiles compared in observational studies), than the 10 GI unit difference thought to be of clinical significance,^{19,20} show significant reductions in cardio-metabolic risks.^{21–24} Differences in dietary GI as low as five units have shown significant trends for improvements in high-density lipoprotein and hs-CRP.^{23,25} Lower trends for fasting insulin are seen at around seven units,²² and lower insulin resistance at three unit differences in GI²⁴ in a few of these observational studies. Furthermore, shorter Asian trials of 6 months duration, achieving a difference in GI of ≈ 6 units between groups, have also documented significant beneficial effects in terms of reductions in waist circumference, FBG and glycaemic control in diabetic subjects or those with impaired fasting glucose.^{26,27} Longer trials lasting until a year have found favourable changes in cardio-metabolic risks in the low GI/GL groups when the difference in GI established between the groups was comparable to the six-unit difference documented in the current study.^{28,29} A decrease in triglycerides was documented when a seven-unit difference in GI was established among obese young adults.²⁸ Similarly, improvements in insulin sensitivity have been documented when a six-unit GI difference was established between two groups of PCOS women.²⁹ The findings from this

study therefore extend the application of an existing body of evidence that indicates that low-GI diets may have added benefits in cardio-metabolic risk management in hyperinsulinaemic subjects^{4,9,30} among normal and hyperinsulinaemic Asian subjects.

These findings lend credence to translational research with practical approaches to lowering dietary GI, when the 'free-living conditions' of the subjects may hamper the achievement of marked diet GI reduction seen in controlled clinical trials. Further investigation of the interaction between insulin levels and response to diet GI is necessary. Such an effort may also help clarify the inconclusive associations reported between GI and risk for chronic diseases.

The small sample size limits generalisation of the results to other populations. Furthermore, $INS < 2 \mu\text{U ml}^{-1}$ was not quantifiable by the assay used. Hence, caution is needed while interpreting these data. Also, the current trial monitored fasting insulin levels and not postprandial insulin, which could have demonstrated more apparently the exaggerated insulin response typical in early pathogenesis of type 2 diabetes mellitus. Nevertheless, an increase in fasting insulin concentration is also associated with hyperinsulinaemia.³¹

CONCLUSION

Thus, in Asian women with a history of GDM, having normal or higher fasting INS, adding low-GI education to conventional dietary guidelines improved management of FBG and triglycerides. More research on the interaction between insulin levels and response to diet GI is necessary.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGEMENTS

This project was funded by an internal research grant (IMU199/2009) from International Medical University, Kuala Lumpur, Malaysia.

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