Glycaemic and insulin responses, glycaemic index and insulinaemic index values of rice between three Asian ethnic groups

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Abstract

Asians exhibit larger glycaemic response (GR) and insulin response (IR) than Caucasians, predisposing to an increased risk of type 2 diabetes mellitus (T2DM). We aimed to determine the GR and IR as well as the glycaemic index (GI) and insulinaemic index (II) of two rice varieties among three ethnic groups in Singapore. A total of seventy-five healthy males (twenty-five Chinese, twenty-five Malay and twenty-five Asian-Indians) were served the available equivalent carbohydrate amounts (50 g) of test foods (Jasmine rice and Basmati rice) and a reference food (glucose) on separate occasions. Postprandial blood glucose and plasma insulin concentrations were measured at fasting (−5 and 0 min) and at 15, 30, 45, 60, 90 and 120 min after food consumption. Using the trapezoidal rule, GR, IR, GI and II values were determined. The GR did not differ between ethnic groups for Jasmine rice and Basmati rice. The IR was consistently higher for Jasmine rice (P=0.002) and Basmati rice (P=0.002) among Asian-Indians, probably due to compensatory hyperinsulinaemia to maintain normoglycaemia. The GI and II of both rice varieties did not differ significantly between ethnicities. The overall mean GI for Jasmine rice and Basmati rice were 91 (so 21) and 59 (so 15), respectively. The overall mean II for Jasmine rice was 76 (so 26) and for Basmati rice was 57 (so 24). We conclude that the GI values presented for Jasmine rice and Basmati rice were applicable to all three ethnic groups in Singapore. Future studies should include deriving the II for greater clinical utility in the prevention and management of T2DM.

Key words: Glycaemic response; Insulin response; Glycaemic index; Jasmine rice; Basmati rice; Ethnic groups; Asians

Numerous studies have shown that Asians, Chinese and non-Caucasians exhibit a 2–3-fold larger postprandial glycaemic response (GR) and insulin response (IR) than Caucasians1–4. In a recent study, GR following rice consumption is over 60% greater among Chinese compared with Europeans5. Higher blood glucose concentrations stimulate increased production of insulin, resulting in a state of hyperinsulinaemia. The chronically increased insulin demand may eventually result in pancreatic β-cell failure and, as a consequence, impaired glucose tolerance, leading to type 2 diabetes mellitus (T2DM)6.

Rice is a staple carbohydrate of many Asian populations, providing up to two-thirds of daily energy intake in Southeast Asian countries5, making it a major contributor to the overall glycaemic load of most Asian diets7–10. The extent to which different varieties of rice influence postprandial glycaemia has potential relevance in the prevention and treatment of obesity and T2DM in Asia, where the recent increase in prevalence outweighs other parts of the world11. In many studies, rice consumption, especially white rice, has been implicated in the deterioration of glucose metabolism, which leads to an increased risk of T2DM12–14. This is probably mediated by the glycaemic potency of rice, as measured by their dietary glycaemic index (GI), a classification of carbohydrates according to their effect on postprandial glycaemia12,14.

The question whether GI varies between ethnicities is equivocal. Some studies have shown no ethnic differences in GI values15,16; however, other studies have demonstrated significant effects of ethnicity on the GI value of white bread16 and rice. One of the major impediments in the use of GI tables worldwide has been the uncertainty of the applicability to different ethnic groups. If the standard
classifications of low, medium and high GI differ between Asians of different ethnicities, this has important implications for dietary recommendations for individuals living in a multi-ethnic Asian population, especially for those with T2DM. Insulinaemic index (II), derived similar to GI, measures the extent to which a food raises plasma insulin levels\(^{13,17,18}\). The insulinaemic effects of foods may be relevant to the prevention of T2DM as prolonged postprandial insulinaemia may play a role in the pathogenesis of T2DM\(^{19}\) and associated chronic diseases\(^{20,21}\).

The population in Singapore comprises three major ethnic groups: Chinese; Malays; Asian-Indians. Yet, there are significant differences in the prevalence of obesity and T2DM between our three ethnic groups. The Malay population has the highest prevalence of obesity (24·0 %), while our Asian-Indian population has the highest prevalence of T2DM (17·2 %)\(^{22}\). This offers us an unusual opportunity to study the effect of different Asian ethnicities on postprandial GR and IR as well as GI and II values to the same food.

The aims of the present study were to examine GR and IR as well as to determine the GI and II of two varieties of commonly consumed rice among the ethnic groups in Singapore. This is the first study known to the authors to examine the role of three ethnic groups residing in a shared and common multi-ethnic Asian environment. The results obtained will provide insights into the metabolic effects of consuming the same food among the different ethnic groups.

**Methods**

**Subjects**

A total of seventy-five healthy male participants, consisting of twenty-five Chinese, twenty-five Malays and twenty-five Asian-Indians, were recruited for the present study. The participants initially underwent a screening visit to assess eligibility, which comprised of a health assessment, where anthropometric measurements (Table 1) were taken and a health questionnaire (relating to medical history, smoking habits, history of any illness and use of any medications) was administered. All anthropometric measurements were made at least 2 h after food consumption. Height and weight were measured without shoes by using a digital scale cum stadiometer (SECA 763). A digital blood pressure monitor (Omron HEM-907) was used to obtain blood pressure readings. Waist circumference was measured using a standard measuring tape (SECA tape measure) at the midpoint between the coastal margins of the ribs and the upper margin of iliac crest and the hip circumference at the widest level of the greater trochanters on both sides. Percentage of body fat was measured by air displacement plethysmography method (Bod Pod; Cosmed).

Those who fulfilled all acceptable criteria (BMI 18·5 to <25 kg/m\(^2\), age 18–45 years, both parents and grandparents were of the same ethnicity, blood pressure 110–120/70–90 mmHg, fasting blood glucose 4–6 mmol/l, not on prescription medication, non-smoking, and no genetic or metabolic diseases) were included in the present study. On the day before the test visit, participants were asked to avoid intake of alcohol, restrict caffeine-containing drinks, refrain from intense strenuous physical activity and to consume their usual meals. Participants were also requested to fast overnight for 10–12 h before each test visit.

The present study was conducted according to the guidelines laid down in the Declaration of Helsinki, and all procedures involving human subjects were approved by the National Healthcare Group Domain Specific Review Board, Singapore. All the participants provided written informed consent before their participation in the study. This was registered at clinicaltrials.gov as NCT01804738.

**Study procedures**

A randomised, cross-over, within-subject, repeated-measure non-blind design was adopted. Participants arrived at the research centre between 08.00 and 09.00 hours after 10–12 h

### Table 1. Anthropometric characteristics by ethnicity

<table>
<thead>
<tr>
<th></th>
<th>Chinese (n 25)</th>
<th>Malay (n 25)</th>
<th>Asian-Indians (n 25)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>23·0 ± 1·3</td>
<td>23·0 ± 2·3</td>
<td>24·1 ± 2·0</td>
<td>0·072</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>63·8 ± 6·9</td>
<td>65·8 ± 7·1</td>
<td>68·7 ± 8·5</td>
<td>0·073</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>172·6 ± 6·0</td>
<td>170·8² ± 6·0</td>
<td>176·2 ± 7·0</td>
<td>0·012</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>21·4 ± 1·8</td>
<td>22·5 ± 1·7</td>
<td>22·1 ± 1·9</td>
<td>0·085</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>125 ± 11</td>
<td>127 ± 8</td>
<td>124 ± 7</td>
<td>0·528</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>76 ± 9</td>
<td>73 ± 8</td>
<td>72 ± 10</td>
<td>0·247</td>
</tr>
<tr>
<td>Mean fasting glucose (mmol/l)</td>
<td>4·55 ± 0·31</td>
<td>4·46 ± 0·25</td>
<td>4·54 ± 0·32</td>
<td>0·484</td>
</tr>
<tr>
<td>Mean fasting insulin (mU/l)</td>
<td>7·43 ± 2·85</td>
<td>9·10 ± 3·38</td>
<td>8·10 ± 3·93</td>
<td>0·225</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>75·5 ± 5·4</td>
<td>72·7² ± 4·4</td>
<td>77·7² ± 6·9</td>
<td>0·010</td>
</tr>
<tr>
<td>Body fat (%)</td>
<td>16·0³ ± 5·9</td>
<td>17·8 ± 5·2</td>
<td>20·5 ± 6·8</td>
<td>0·035</td>
</tr>
<tr>
<td>Mean HOMA-IR</td>
<td>1·45³ ± 0·53</td>
<td>1·43³ ± 0·51</td>
<td>2·16³ ± 0·89</td>
<td>&lt;0·001</td>
</tr>
<tr>
<td>Mean HOMA-B</td>
<td>165·7² ± 86·1</td>
<td>172·6 ± 76·8</td>
<td>229·2² ± 93·3</td>
<td>0·020</td>
</tr>
</tbody>
</table>

HOMA-IR, homeostatic model assessment-insulin resistance; HOMA-B, homeostatic model assessment-β cell function.  
²Mean values within each row with unlike superscript letters were significantly different (P<0·05).  
*P values represent comparison between the ethnic groups.  
†To convert insulin from mU/l to pmol/l, multiply by 6·945.
of overnight fast. Following a 10 min rest, two fasting blood samples were obtained 5 min apart for determining baseline blood glucose and insulin levels. After that, participants were given either a reference food or a test food with water to consume at a comfortable pace within 15 min. The reference food consisted of 50 g of glucose anhydrous powder dissolved in 250 ml water, while the test food was Jasmine rice (Double FP Thai Hom Mali premium quality fragrant rice, Thailand) or Basmati rice (Dreamrice™, Singapore). These two rice varieties were chosen as they were commonly consumed by the local population. Jasmine rice was tested locally to be classified as high GI (23), while Basmati rice was tested in a local laboratory and certified as low GI on its product packaging. Both rice samples were served in portions containing 50 g of available carbohydrates (difference between total carbohydrates and dietary fibre). This amounted to 63.6 g (with 130 ml water) and 66.5 g (with 170 ml water) of uncooked Jasmine rice and Basmati rice, respectively, cooked in individual portions in a rice cooker (Iona GL12 rice cooker, Singapore) and served with 250 ml water. In total, the reference food was tested thrice, and the test food was tested once by each participant in a randomised order. This is in accordance with FAO/WHO recommendations (24) for the determination of GI value that each subject will test each test food once and the reference food thrice in a random order on separate days, with at least 2 d gap between measurements to minimise carry-over effects.

After the commencement of eating, further blood samples were taken at 15, 30, 45, 60, 90 and 120 min. The protocol used to measure blood glucose response was adopted from that described by Brouns et al. (25) and is in line with the FAO/WHO recommendations (24). Blood sample was obtained by finger prick using sterile, single-use lancing device (Accu-check Safe-T-Pro Plus; Roche Diagnostics). Before a finger prick, participants were encouraged to warm their hand to increase blood flow. To minimise plasma dilution, fingertips were not squeezed to extract blood but were gently massaged starting from the base of the hand moving towards the tips. The first two drops of expressed blood were discarded, and the next drop was used for testing. Blood glucose was measured using the HemoCue 201+ Glucose analyzer (HemoCue 201 RT).

For the measurement of blood insulin levels at each time point, after blood glucose measurement, 300 µl of capillary blood (obtained from finger pricks) was collected into Microvette® capillary blood collection tubes treated with di-potassium EDTA (CB 300 K2E; Sarstedt) and stored in crushed ice immediately until the end of the study visit. The Microvette® tubes were centrifuged at 4500 rpm for 12 min (Rotina 420R; Hettich), and the supernatant plasma was transferred into individually labelled 1.5 ml microtubes (Axygen Scientific, Inc.), which were immediately transferred to a freezer held at −80°C until analysis of insulin. Plasma insulin concentrations were determined by electrochemiluminescence immunoassay using an automated analyzer (Cobas E411; Roche Diagnostics). The Cobas system is a reliable method of blood insulin determination (26).

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<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Glucose reference</th>
<th>Jasmine rice</th>
<th>Basmati rice</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IAUC glucose</td>
<td>IAUC insulin</td>
<td>IAUC glucose</td>
</tr>
<tr>
<td></td>
<td>(mmol L⁻¹ min⁻¹)</td>
<td>(mU L⁻¹ min⁻¹)</td>
<td>(mmol L⁻¹ min⁻¹)</td>
</tr>
<tr>
<td>Chinese</td>
<td>237 ± 68.2</td>
<td>4350 ± 313.7</td>
<td>1763 ± 213.8</td>
</tr>
<tr>
<td>Malay</td>
<td>224 ± 60.3</td>
<td>4500 ± 313.7</td>
<td>2010 ± 213.8</td>
</tr>
<tr>
<td>Asian Indians</td>
<td>240 ± 60.3</td>
<td>4500 ± 313.7</td>
<td>2010 ± 213.8</td>
</tr>
</tbody>
</table>

GI, glycaemic index; II, insulinogenic index.

- Mean values within a column with unlike superscript letters are significantly different (P < 0.05).

* To convert IAUC insulin from mU L⁻¹ min⁻¹ to pmol L⁻¹ min⁻¹, multiply by 6.945.
We computed homeostatic model assessment-insulin resistance (HOMA-IR) as follows:

\[ \text{fasting insulin (mU/l)} \times \text{fasting glucose (mmol/l)} / 22.5 \]

Homeostatic model assessment-\( \beta \) cell function (HOMA-\( \beta \)) was calculated using the following formula:

\[ 20 \times \text{fasting insulin (mU/l)} / (\text{fasting glucose (mmol/l)} - 3.5) \]

(To convert insulin in mU/l to pmol/l, multiply by 6.945).

Statistical analyses

One study on ethnic differences in postprandial glycaemia\(^{(3)}\) between UK Caucasians and Asian Indians has observed at least a 59 mmol/min per litre difference in GR between the two groups with standard deviations of 79 and 47 mmol/min per litre, respectively. At the 5% level of significance with power of 80%, a minimum sample size of twenty-one subjects for each group would be required. Studies on in vivo assessment of GI have been based on ten subjects, to take into account inter-individual variations\(^{(24,25)}\). As we were investigating ethnic differences, a sample size of twenty-five from each ethnic group (total sample size of seventy-five) was considered adequate for the present study.

The GR data was analysed using ‘change in GR’, which was calculated by taking the difference between the blood glucose reading at each time point and mean baseline blood glucose value (based on two baseline values taken at 5 min apart). This represented the relative increment in GR at any time point compared with the baseline value. The total GR over 120 min was expressed as the incremental AUC (IAUC) ignoring the area under the baseline using the trapezoidal rule\(^{(24,25)}\). The IR data was analysed in the same manner as the GR data, using ‘change in IR’. These data were then used to construct IR curves and calculate the IAUC (using the trapezoidal rule).

The intention-to-treat analysis included data from all the participants. All physiologically valid data were included in the computation of GI and II. In the calculation of GI, the absolute IAUC glucose values for each rice variety was expressed as a percentage of the mean IAUC glucose values of the reference food, and the resulting values were averaged to obtain the GI value for each rice variety. The II, which measures the IR of food, was calculated similar to GI, where the absolute IAUC insulin values for each rice variety were expressed as a percentage of the mean IAUC glucose values of the reference food.

Results were expressed as means with standard deviations where appropriate. Differences in GR and IR and GI values were analysed using one-way ANOVA with post hoc Bonferroni correction for multiple comparisons. The temporal GR and IR over 120 min were analysed using repeated-measures ANOVA with post hoc Bonferroni correction. Paired \( t \) tests were used to compare the IAUC and rates of decline from 45 to 60 min, 60 to 90 min and 90 to 120 min for Jasmine rice and Basmati rice. Correlation analyses were conducted to determine the relationships between GI, II with body composition (waist circumference and percentage of body fat) and metabolic indices (HOMA-IR and HOMA-B). Statistical analyses were conducted using the SPSS version 19 (SPSS, Inc.). A \( P \) value \(< 0.05\) was considered statistically significant.

Results

Table 1 compares the characteristics of the study participants by ethnicity. There were no differences in age, BMI, blood pressure, fasting glucose level and fasting insulin level between the three groups. However, waist circumference (\( P\) = 0.010) and percentage of body fat (\( P\) = 0.035) were significantly higher among the Asian-Indians compared with Chinese and Malays. The HOMA-IR, a marker of insulin resistance, was highest for Asian-Indians (\( P\) < 0.001) compared with Chinese and Malays. In parallel with HOMA-IR, Asian-Indians showed a significantly higher HOMA-B (\( P\) = 0.020) compared with Chinese and Malays. This indicated a compensatory hyperinsulinaemia in the presence of greater insulin resistance among Asian-Indians to maintain fasting normoglycaemia.

![Fig. 1. Temporal blood glucose response curves for Jasmine rice among Chinese ( ), Malays ( ) and Asian-Indians ( ). Data are represented as change in glucose response from baseline over 120 min following the consumption of Jasmine rice. Values are means, with their standard errors represented by vertical bars. Repeated-measures ANOVA with post hoc Bonferroni multiple-comparison tests revealed an overall difference between ethnic groups (\( P\) = 0.757).](https://www.cambridge.org/core/terms. html)
The GI values for both rice varieties were not significantly different between the ethnic groups. The overall mean II for Jasmine rice was 75.8 (SD 25.9) and Basmati rice was 56.7 (SD 23.8). Adjustment for body composition (body fat or waist circumference) made no difference to the II values between the ethnic groups.

Correlation analyses indicated that GI and II for Jasmine rice and Basmati rice were not related to any of the body composition measurements (waist circumference and percentage of body fat) or metabolic indices (HOMA-IR and HOMA-B) \((P > 0.05)\). These results demonstrate that GI and II were independent of individuals’ body composition and metabolic status, making them valid properties of food.

Between rice varieties, we observed that Jasmine rice showed consistently higher GR and IR as well as significantly higher GI \((P = 0.001)\) and II \((P < 0.001)\) values (Table 2) compared with Basmati rice for each ethnic group (Figs. 5 and 6).

**Discussion**

The present study was the first to examine the role of three ethnicities in a multi-ethnic Asian environment on postprandial GR and IR as well as GI and II values to two commonly consumed rice varieties. We observed no ethnic variations in GR to Jasmine rice and Basmati rice; yet, there were considerable differences in IR.

Even though there were no differences in fasting glucose and fasting insulin levels, Asian-Indians mounted significantly higher insulin excursions for both Jasmine rice and Basmati rice compared with Chinese and Malays, even after adjustment for percentage of body fat or waist circumference. These differences in IR were probably due to a compensatory hyperinsulinaemia in the presence of greater insulin resistance among the Asian-Indians to maintain fasting normoglycaemia. Genetically, Asian-Indians have a high prevalence of insulin resistance, making them valid properties of food.
need to uncover rice varieties that are truly low GI since rice in the major carbohydrate staple in this country(7).

In the present study, we observed no differences in II values of both rice varieties despite ethnic differences in IR. The IR is a biological response to fluctuations in blood glucose levels. The II, however, is an index of the insulinaemic effects of food. The computation of II normalises an individual’s IR to a test food against a reference food, similar to the computation of the GI. Therefore, while IR may differ, II, in contrast, remained consistent between individuals. The present study showed that both GI and II are properties of food, not influenced by the anthropometric measures and metabolic status of the participants. We showed that both GI and II were similar between ethnic groups regardless of their degree of insulin sensitivity and adiposity. Recent evidence has also shown that II values of rice were not different between healthy, hyper-insulinaemic and T2DM individuals, although the II was correlated with metabolic status(41).

Our findings and existing evidence have shown that consumption of a high-GI food such as Jasmine rice leads to higher postprandial GR, more rapid decline in glucose levels from 60 min onwards and a correspondingly augmented IR compared with a lower-GI food(42). A recent study has demonstrated that consumption of a high-GI meal led to a rapid decline in blood glucose levels(43,44). In addition, brain activity is increased in regions related to food intake, reward and craving in the late postprandial phase(45). This triggered excessive hunger and a preference for foods, such as high-GI foods that rapidly restored blood glucose to normal(46,47). This could lead to overeating and contribute to problems such as overweight and obesity. These findings have considerable potential clinical significance given the global epidemic of obesity and T2DM and the especially high rates in Asian countries(9,10,12). There was growing evidence that higher white rice consumption (300–420 g/d) had been associated with a significantly increased risk of T2DM, especially in Asian populations(9,10,12).

Despite the positive findings of rice consumption and increased
risk of T2DM, rice intake was not associated with diabetes in a Chinese population \cite{48} and added no additional risk of CVD in Japanese men and women \cite{49}. Therefore, evidence is still equivocal on rice intake and risk of T2DM in Asian populations.

Nonetheless, rice is a major dietary staple in Asian populations, and it appeared that Asian populations were more susceptible to the adverse effects of high intakes of white rice compared with the Western populations \cite{40}. In Singapore, the mean rice intake among the population was 361.8 (SD 5.7) g/d, with Chinese, Malay and Asian-Indians consuming 364.9 (SD 6.5), 348.1 (SD 15.5) and 352.7 (SD 19.2) g, respectively \cite{7}. This puts the population as being high consumers of white rice. It is, therefore, prudent to advice on consumption of rice with a lower GI that may reduce the glycaemic load of the diet. Additionally, a lower IR can help to improve long-term metabolic control in individuals who are insulin resistant and thereby reducing the future risk of T2DM.

The International Tables of the Glycaemic Index \cite{50} reported a wide range of GI values for different rice varieties, due to differences in the ratio of amylose to amylpectin, physical and chemical characteristics, other botanical structures and processing methods \cite{51–55}. GI values vary even when considering the same variety of rice. For example, the GI values for Jasmine rice range from 48 to 109 and for Basmati rice from 43 to 69 \cite{50,56}. As the composition of rice and other carbohydrate-containing foods may vary according to where they are grown, the recommendation that the GI of such foods are best tested locally \cite{50}. In the present study, we have used two locally available and commonly consumed rice varieties among the ethnic groups. The cooking method used was as per the manufacturers’ instructions and represented how the population would cook these two rice varieties. There is currently no cut-offs nor classification for II values to food. Future studies can thus focus on establishing the corresponding II values when determining the GI of foods for greater clinical utility.

The strengths of the present study are that it measured the GR of the three ethnic groups fed identical foods within a common environmental milieu. We standardised the cooking method by using the exact amount of water to cook each rice variety in the same rice cooker to ensure consistency in rice texture. Using a standardised cooking method also allows a valid and unbiased comparison to be made between ethnic groups by removing the confounding effects of cooking rice texture. Using a standardised cooking method also allows a valid and unbiased comparison to be made between ethnic groups by removing the confounding effects of cooking method by using the exact amount of water to cook each rice variety in the same rice cooker to ensure consistency in rice texture. Using a standardised cooking method also allows a valid and unbiased comparison to be made between ethnic groups by removing the confounding effects of cooking

methods. Using a standardised cooking method also allows a valid and unbiased comparison to be made between ethnic groups by removing the confounding effects of cooking. Moreover, we simultaneously measured the corresponding IR to gain a better understanding of the interplay between postprandial GR and IR as well as to determine both the GI and II values. However, we recognised that the limitation of the present study was that we have only tested two rice varieties and it may not be feasible to extrapolate these findings to all carbohydrate foods. However, these rice varieties were the most commonly consumed among the ethnic groups in Asia and are the major contributors to the overall glycaemic load of the Asian diet.

In summary, the present study has shown that there were no significant differences in the GI and II values to two commonly eaten rice varieties between the three ethnic groups. This suggests that GI values of Jasmine rice and Basmati rice determined in the present study are applicable to all the three ethnic groups in Singapore. Although there are currently no cut-offs for II values, the present results showed that II is a property of food, independent of the metabolic status of the individuals. Future studies testing the GI of foods may include testing the concurrent IR to derive the II for greater clinical utility in the prevention and management of T2DM. Despite similar GI values between the ethnic groups, the same rice presented greater pancreatic β-cell stress to Asian-Indians, resulting in higher compensatory IR, and possibly conferring a higher risk of T2DM in this ethnic group. Preserving β-cell function in at-risk populations is a critical factor in the prevention of T2DM onset \cite{57}. Therefore, therapeutic prevention strategies should focus on encouraging the consumption of rice varieties with lower GI especially among the high-risk groups to maintain glucose homeostasis.

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None of the authors has any conflict of interest to declare.

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