Heterogeneous associations of insoluble dietary fibre intake with subsequent glycosylated Hb levels among Chinese adults with type 2 diabetes: a quantile regression approach

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Abstract
Dietary fibre intake has been suggested to reduce blood glucose levels in diabetic patients, particularly when glycosylated Hb (HbA1c) levels are high. In the present study, we used a quantile regression (QR) approach to characterise the possible heterogeneous associations of dietary fibre intake with HbA1c levels in Chinese diabetic patients. A total of 497 diabetic patients participated in the baseline survey in 2006 and in the follow-up survey in 2011, both of which were conducted in Pudong New Area of Shanghai, China. Structured in-person interviews were conducted to collect information on demographic characteristics and lifestyle factors. Dietary intake was assessed using a validated FFQ. Blood samples were collected during the interviews for biochemical assays. QR models were used to examine the heterogeneous associations of dietary factors with HbA1c levels. A significant marginal association of insoluble dietary fibre intake with subsequent HbA1c levels was observed only when the HbA1c level was over 6.8%. The associations appeared to be greater when the quantile levels of HbA1c were higher. The coefficient estimates were \(0.174\) (95% CI \(0.433, 0.025\)) at the quantile of \(0.60\), \(0.200\) (95% CI \(0.306, 0.008\)) at \(0.70\), \(0.221\) (95% CI \(0.426, 0.117\)) at \(0.80\), and \(0.389\) (95% CI \(0.516, 0.018\)) at \(0.90\). A similar pattern was observed for the associations of dietary glycaemic index (GI) value with HbA1c levels. In conclusion, the present results indicate that the associations of insoluble dietary fibre intake and GI value with subsequent HbA1c levels depend on glycaemic control status in Chinese diabetic patients. More studies are required to confirm our findings.

Key words: Type 2 diabetes: Insoluble dietary fibre intake: Glycosylated Hb: Quantile regression

Dietary fibre intake has been reported to be associated with a lower glycosylated Hb (HbA1c) level and an improved glycaemic control status in patients with type 2 diabetes (1–4). However, this association has been suggested to vary by race (5) and severity of glucose impairment (6). In a systematic review, Livesey et al. (6) reported that higher amounts of unavailable carbohydrate in diets, e.g. dietary fibre, reduce the levels of glycated proteins, particularly in patients with a poorer glycaemic control status. Mechanisms underlying this effect are not very clear. It is plausible that dietary fibre may retard food digestion and nutrient absorption (7,8), improve insulin sensitivity (9–11) and thus play an important role in carbohydrate metabolism.

In our previous study, we observed an association of insoluble dietary fibre intake with subsequent HbA1c levels among Chinese adults with type 2 diabetes (12). However, little is known whether and how the associations would vary in patients with different glycaemic control status. More studies are required to confirm our findings.

Abbreviations: GI, glycaemic index; HbA1c, glycosylated Hb; QR, quantile regression.

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In both surveys, an overnight fasting blood sample was collected from each participant to measure fasting glucose and HbA1c levels. The quality control of the assays was assessed internally and externally\(^ {21}\). After excluding eight subjects with extreme values of total energy intake (<5347 or >16736 kJ/d for men; <2092 or >14644 kJ/d for women), a total of 497 patients who took part in both surveys and provided a blood sample were included in the present study. The patients were categorised into those with an uncontrolled glycaemic status (HbA1c level ≥7.0%) and those with a controlled glycaemic status (HbA1c level <7.0%) using the HbA1c value recorded during the second survey according to the recommendation of the American Diabetes Association\(^ {19}\).

The study was approved by the Institutional Review Board of Fudan University (IRB00002408, FWA00002399). Written informed consent was obtained from each participant before data collection.

**Statistical analyses**

We applied a QR analytical approach to evaluate the associations of insoluble dietary fibre intake with HbA1c levels at a set of quantile levels ranging from 0.05 to 0.95. The QR approach, which was introduced by Koenker & Bassett\(^ {20}\), has been used in various fields\(^ {21}\) because it assumes no parametric form of the error distribution and the QR estimates are more robust against outliers\(^ {22}\) and more accurate in the tails\(^ {13,22}\). The distinguishing feature of the QR model is that the regression coefficients of insoluble dietary fibre intake may differ across the quantile levels of HbA1c\(^ {23,24}\), which is practically meaningful in that it can distinguish the association of insoluble dietary fibre intake with HbA1c levels between the upper/lower tails and the central trends.

Statistical analyses were conducted using R for Windows version 3.0.1 (R Foundation for Statistical Computing). The characteristics of patients with uncontrolled and controlled glycaemic status were compared at the 0.05 α-level of significance for two sides, using the \( \chi^2 \) test for categorical variables and the Wilcoxon test for continuous variables. A QR analysis was carried out using R package ‘quantreg’ (R Foundation for Statistical Computing). Ordinary least-squares estimations were also performed using R function ‘lm’ (R Foundation for Statistical Computing) as a reference.

**Results**

The descriptive statistics of important covariates according to the glycaemic control status of patients are summarised in Table 1. Patients with a controlled glycaemic status were older \((P=0.0304)\), had lower BMI \((P=0.0156)\), lower baseline HbA1c levels \((P<0.0001)\), higher insoluble fibre intake \((P=0.0046)\) and lower GI value \((P=0.0066)\), on average, and were less likely to use hypoglycaemic drugs \((P=0.0007)\) compared with those with an uncontrolled glycaemic status. Patients with a controlled glycaemic status tended to have diabetes for a shorter duration and were more likely to be female, to have a family history of diabetes, to exercise, to use insulin, and to have lower energy and carbohydrate intake; however, the differences did not reach statistical significance.
The coefficient estimates and 95% CI for the associations of GI value with HbA1c levels when the quantile level was 0.52 (HbA1c level = 6.8%) or higher and became stronger afterwards. Similarly, in the sensitivity analysis, the associations of GI value with HbA1c levels

Table 2. Marginal associations of glycosylated Hb (HbA1c) levels with insoluble dietary fibre intake at the mean and selected quantile levels of HbA1c

<table>
<thead>
<tr>
<th>Variables</th>
<th>Uncontrolled, HbA1c level ≥ 7% (n 227)</th>
<th>Controlled, HbA1c level &lt; 7% (n 270)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Median: 62, 25th–75th percentile: 56–71</td>
<td>Median: 66, 58–72</td>
<td>0.0304</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>Median: 26.0, 24.0–28.5</td>
<td>Median: 25.2, 22.9–27.9</td>
<td>0.0156</td>
</tr>
<tr>
<td>Time from being diagnosed with diabetes (years)</td>
<td>8, 5–12</td>
<td>8, 4–12</td>
<td>0.1413</td>
</tr>
<tr>
<td>Regular exercise (yes)</td>
<td>n = 108</td>
<td>n = 133</td>
<td>0.7086</td>
</tr>
<tr>
<td>Hypoglycaemic drug use (yes)</td>
<td>n = 207</td>
<td>n = 217</td>
<td>0.0007</td>
</tr>
<tr>
<td>Insulin use (yes)</td>
<td>n = 91.2</td>
<td>n = 80.4</td>
<td>0.7286</td>
</tr>
<tr>
<td>Family history of diabetes (yes)</td>
<td>n = 15</td>
<td>n = 20</td>
<td>0.1590</td>
</tr>
<tr>
<td>Energy intake (kJ/d)</td>
<td>Median: 6292, 5236–7617</td>
<td>Median: 6350, 5119–7690</td>
<td>0.9503</td>
</tr>
<tr>
<td>Carbohydrate intake (g/1000 kJ per d)</td>
<td>39.1, 35.7–43.3</td>
<td>38.6, 35.3–42.2</td>
<td>0.2518</td>
</tr>
<tr>
<td>Insoluble fibre intake (g/1000 kJ per d)</td>
<td>1.3, 1.0–1.7</td>
<td>1.5, 1.1–2.0</td>
<td>0.0046</td>
</tr>
<tr>
<td>Glycaemic index</td>
<td>61.1, 54.5–68.8</td>
<td>59.2, 53.7–64.5</td>
<td>0.0066</td>
</tr>
<tr>
<td>Baseline HbA1c level (%)</td>
<td>7.9, 7.0–9.0</td>
<td>6.7, 6.1–7.5</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

HbA1c, glycosylated Hb.
*χ² test (for categorical variables) or Wilcoxon test (for continuous variables).

Fig. 2(a) shows the associations between dietary GI value and HbA1c levels, which reached statistical significance when the quantile level was 0.52 (HbA1c level = 6.8%) or higher and became stronger afterwards. Similarly, in the sensitivity analysis, the associations of GI value with HbA1c levels

Table 2. Marginal associations of glycosylated Hb (HbA1c) levels with insoluble dietary fibre intake at the mean and selected quantile levels of HbA1c

<table>
<thead>
<tr>
<th>Coefficients*</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>OLS†</td>
<td>−0.258</td>
</tr>
<tr>
<td>QR‡</td>
<td>−0.249</td>
</tr>
<tr>
<td>0.1</td>
<td>−0.173</td>
</tr>
<tr>
<td>0.2</td>
<td>−0.264</td>
</tr>
<tr>
<td>0.3</td>
<td>−0.194</td>
</tr>
<tr>
<td>0.4</td>
<td>−0.239</td>
</tr>
<tr>
<td>0.5</td>
<td>−0.174</td>
</tr>
<tr>
<td>0.6</td>
<td>−0.200</td>
</tr>
<tr>
<td>0.7</td>
<td>−0.221</td>
</tr>
<tr>
<td>0.8</td>
<td>−0.389</td>
</tr>
</tbody>
</table>

OLS, ordinary least squares; QR, quantile regression.
†The corresponding values of HbA1c at the quantile levels ranging from 0.1 to 0.9 were 5.1, 5.6, 6.0, 6.4, 6.7, 7.2, 7.7, 8.4 and 9.3%, respectively.
were more evident after the quantile of 0.56 (HbA1c level = 7.0%; Fig. 2(b)).

**Discussion**

In the present study, using QR models, we were able to evaluate whether and how the associations of insoluble dietary fibre intake with HbA1c levels changed across the selected quantile levels of HbA1c among Chinese adults with type 2 diabetes. We found that both insoluble dietary fibre intake and GI value were significantly associated with subsequent HbA1c levels among diabetic patients, especially among those with high HbA1c levels. Our findings indicate the importance of insoluble dietary fibre intake in Chinese diabetic patients with uncontrolled glycaemia. So far, no other study has been carried out to evaluate the associations of dietary factors with HbA1c levels by applying a QR model.

The role of dietary fibre intake in glycaemic control has long been controversial, and its close correlation with dietary GI value may be one of the reasons. Fibre-rich foods usually have a low GI value\(^{10,25}\), making it difficult to distinguish their independent effects. In recent years, attempts have been made to determine the individual and joint effects of dietary fibre intake and GI value on glucose control. In a randomised trial, patients consuming low-GI diets were found to have lower HbA1c levels than those consuming high-cereal fibre diets during a 6-month treatment period\(^{26}\). In a meta-analysis, unavailable carbohydrate (e.g. dietary fibre) was found to have at least as much effect on health outcome as GI itself, which was independent of GI value\(^{6}\). In our prior analysis of observational data, we observed a significant association of glycaemic control status with insoluble dietary fibre intake, but not with GI value\(^{12}\), which, however, was probably because it was not taken into account whether the absolute size of the association was conditional on the level

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**Fig. 1.** Coefficients (β) for the associations of glycosylated Hb (HbA\(_{1c}\)) levels with insoluble dietary fibre intake across the quantile levels of HbA\(_{1c}\). The coefficients indicate the change in HbA\(_{1c}\) levels (%) with one unit (g/1000 kJ per d) increase in insoluble fibre. The black solid horizontal line represents β = 0, black dots represent the estimated coefficients and the grey area represents 95% CI of the corresponding parameters. The mean values of insoluble dietary fibre intake at the quantile levels of HbA\(_{1c}\) ranging from 0.1 to 0.9 were 1.5, 1.4, 1.4, 1.5, 1.7, 1.6, 1.4, 1.5 and 1.0, respectively. All coefficients and 95% CI were adjusted for age (continuous variable), sex (male/female), BMI (continuous variable), time from being diagnosed with diabetes (continuous variable), regular exercise (ever/never), family history of diabetes (ever/never), carbohydrate intake per 1000 kJ/d (continuous variable), energy intake (continuous variable) and HbA1c level at baseline (continuous variable) in both (a) and (b) and additionally baseline hypoglycaemic drug use (ever/never) and insulin use (ever/never) in (a) and additionally hypoglycaemic drug use (ever/never) and insulin use (ever/never) during the follow-up survey in (b).

**Fig. 2.** Coefficients (β) for the associations of glycosylated Hb (HbA\(_{1c}\)) levels with dietary glycaemic index (GI) value across the quantile levels of HbA\(_{1c}\). The coefficients indicate the change in HbA\(_{1c}\) levels (%) with one unit increase in dietary GI. The black solid horizontal line represents β = 0, black dots represent the estimated coefficients and the grey area represents 95% CI of the corresponding parameters. The mean values of dietary GI at the quantile levels of HbA\(_{1c}\) ranging from 0.1 to 0.9 were 1.5, 1.4, 1.4, 1.5, 1.7, 1.6, 1.4, 1.5 and 1.0, respectively. All coefficients and 95% CI were adjusted for age (continuous variable), sex (male/female), BMI (continuous variable), time from being diagnosed with diabetes (continuous variable), regular exercise (ever/never), family history of diabetes (ever/never), carbohydrate intake per 1000 kJ/d (continuous variable), energy intake (continuous variable) and HbA1c level at baseline (continuous variable) in both (a) and (b) and additionally baseline hypoglycaemic drug use (ever/never) and insulin use (ever/never) in (a) and additionally hypoglycaemic drug use (ever/never) and insulin use (ever/never) during the follow-up survey in (b).
of glycaemic control, but which was taken into account in the QR analysis carried out in the present study.

In the present study using the QR method, we observed significant associations of both insoluble dietary fibre intake and GI value with HbA1c levels, especially among patients who did not have their blood glucose under control. Unlike the parametric logistic regression method used in our previous study\textsuperscript{(12)} in which an average association was estimated among all participants without considering whether the size of the association was dependent on the level of blood glucose control, the non-parametric QR approach adopted in the present study allowed us to identify differing regression coefficients across the conditional distribution of HbA1c and provided a more complete picture of how the dietary factors and HbA1c levels are associated\textsuperscript{(14)}.

The results of the present study are somewhat consistent with those reported by Livesey et al.\textsuperscript{(6)} who demonstrated that both dietary GI value and fibre intake have significant effects, and the strength of their effects on absolute changes was dependent on the severity of diabetes. Such results indicate that the dietary fibre may act independently of its effect on the rate of digestion. However, the mechanism for the conditionality remains to be investigated. Nevertheless, the results of the present study implicate some clinical and public health significance. In our diabetic patient setting, one unit increase in insoluble fibre intake (i.e. 1·0 g/1000kJ per d) was found to be associated with a 0·174% decrease in HbA1c content at a HbA1c level of 7·2% and with a 0·221% decrease at a HbA1c level of 8·4%.

The present study has several limitations. First, the sample size was relatively small and the follow-up rate was not very high. Possible selection biases could not be overlooked. Second, insoluble dietary fibre intake in the study population was much lower than that reported previously\textsuperscript{(27,28)} and so extreme caution should be exercised when generalising these results to a broad range of populations. The 5-year time frame was also a potential problem. The patients could have made many changes to their physical activities or diets during the study period and these could affect HbA1c levels within a few months. The possible differentiated changes in patients with low or high HbA1c levels could bias the results of the study in both directions. In the present study population, the \( \kappa \) coefficient for regular exercise between the two surveys was 0·22 (\( P<0·001 \)) for patients with low HbA1c levels, but was 0·01 (\( P>0·05 \)) for patients with high HbA1c levels, indicating more evident changes in regular exercise among patients with high HbA1c levels. Unfortunately, physical activity was poorly measured in the present study, which limited our ability to assess the confounding effect of this important factor.

In conclusion, our findings indicate that insoluble dietary fibre intake and GI value are significantly associated with HbA1c levels in Chinese diabetic patients, particularly among those with a poor glycaemic control status. Further studies are required to confirm our findings.

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The authors’ contributions are as follows: W. H. X., X. R. and G. Q. designed the study; Z. T. conducted the data analysis and wrote the manuscript; J. J., Y. Z. and H. Q. collected the data; G. Q. provided statistical support; W. H. X. and Y. C. revised the article. All the authors read and approved the final manuscript.

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

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