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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 (HbA_{1c}) 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 HbA_{1c} 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 HbA_{1c} levels. A significant marginal association of insoluble dietary fibre intake with subsequent HbA_{1c} levels was observed only when the HbA_{1c} level was over 6·8 %. The associations appeared to be greater when the quantile levels of HbA_{1c} 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 HbA_{1c} levels. In conclusion, the present results indicate that the associations of insoluble dietary fibre intake and GI value with subsequent HbA_{1c} 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 (HbA_{1c}) 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 HbA_{1c} 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. In the

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Abbreviations: GI, glycaemic index; HbA_{1c}, glycosylated Hb; QR, quantile regression.

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present study, we aimed to determine the possible difference in associations of insoluble dietary fibre intake with HbA_{1c} levels across the quantile levels of HbA_{1c} using a quantile regression (QR) approach. The QR model allows us to determine how the covariates influence the location, scale and shape of the entire response distribution rather than just its conditional mean[13–15]. If insoluble dietary fibre intake had a minimal impact on the mean level of HbA_{1c} and could greatly reduce HbA_{1c} levels in the upper percentiles, the differential associations might be overlooked when using typical mean regression models such as ordinary least-squares regression, but could be captured using a QR model.

Materials and methods

Subjects and data collection

As described in our previous study[12], 979 prevalent patients with type 2 diabetes were recruited from the communities of Pudong New Area of Shanghai, China, and were interviewed from October to December 2006. They were followed up from May to July 2011 using a similar protocol. Structured questionnaires were used during baseline and follow-up surveys to collect information on age, sex, time from being diagnosed with type 2 diabetes, regular exercise (at least three times per week and at least half an hour per time), oral hypoglycaemic drug use, insulin use and family history of diabetes. The standing height and body weight of the patients were measured to calculate BMI, which was defined as weight divided by height squared (kg/m^2).

Dietary intake was assessed using an interview-administered FFQ modified based on a validated FFQ in which the correlation coefficient for validation was 0·53 for insoluble dietary fibre[16]. The modified FFQ specified 103 food items, covering 90 % of the food items commonly consumed by the residents of Shanghai. The participants were asked to report the frequency (daily, weekly, monthly, annually or never) and duration (months per year) of consumption of each food item, as well as the estimated amount that they ate each time in the unit of liang (1 liang = 50 g). The amount of intake was reported in millilitres for liquid foods such as milk, juice and beverages and was further converted into grams in the data analysis. The daily intakes of oil, salt and sugar were calculated as the average amount consumed by each member of the participant's family.

The Chinese food composition tables were used to estimate the intake of nutrients from all food items and obtain glycaemic index (GI) values for most of the food items[17], leaving the others, the values for which were obtained by referring to the report of Foster-Powell *et al.*[18]. The daily intake of each nutrient was calculated by summing up the intakes of the nutrient from each food item consumed. For calculating dietary fibre intake, the intake of only insoluble fibre was considered. Glycaemic load was calculated by multiplying a food's GI by the carbohydrate content of the food and the average amount of the food consumed per d. Average GI for each individual was obtained by dividing the total dietary glycaemic load, which was obtained by summing up the glycaemic loads from each food item consumed, by the total amount of carbohydrate consumed.

In both surveys, an overnight fasting blood sample was collected from each participant to measure fasting glucose and HbA_{1c} levels. The quality control of the assays was assessed internally and externally[2]. After excluding eight subjects with extreme values of total energy intake (<3347 or >16 736 kJ/d for men; <2092 or >14 644 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 (HbA_{1c} level ≥7·0 %) and those with a controlled glycaemic status (HbA_{1c} level <7·0 %) using the HbA_{1c} 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 HbA_{1c} 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[20] 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 HbA_{1c}[23,24], which is practically meaningful in that it can distinguish the association of insoluble dietary fibre intake with HbA_{1c} 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 χ^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 HbA_{1c} 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.

Table 1. Comparison of selected covariates at the baseline survey between patients with uncontrolled glycaemic status and those with controlled glycaemic status during the second survey

(Medians and 25th–75th percentiles for continuous variables; number of patients and percentages for categorical variables)

	Uncontrolled, HbA_{1c} level ≥7 % (*n* 227)		Controlled, HbA_{1c} level <7 % (*n* 270)		
Variables	Median	25th–75th percentile	Median	25th–75th percentile	*P**
Age (years)	62	56–71	66	58–72	0·0304
Sex (male)					0·1961
n		97		100	
%		42·7		37·0	
BMI (kg/m^2)	26·0	24·0–28·5	25·2	22·9–27·9	0·0156
Time from being diagnosed with diabetes (years)	8	5–12	8	4–12	0·1413
Regular exercise (yes)					0·7086
n		108		133	
%		47·6		49·3	
Hypoglycaemic drug use (yes)					0·0007
n		207		217	
%		91·2		80·4	
Insulin use (yes)					0·7286
n		15		20	
%		6·6		7·4	
Family history of diabetes (yes)					0·1590
n		86		86	
%		37·9		31·9	
Energy intake (kJ/d)	6292	5236–7617	6350	5119–7690	0·9503
Carbohydrate intake (g/1000 kJ per d)	39·1	35·7–43·3	38·6	35·3–42·2	0·2518
Insoluble fibre intake (g/1000 kJ per d)	1·3	1·0–1·7	1·5	1·1–2·0	0·0046
Glycaemic index	61·1	54·5–68·8	59·2	53·7–64·5	0·0066
Baseline HbA_{1c} level (%)	7·9	7·0–9·0	6·7	6·1–7·5	<0·0001

HbA_{1c}, glycosylated Hb.
* χ^2 test (for categorical variables) or Wilcoxon test (for continuous variables).

The coefficient estimates and 95 % CI for the associations of HbA_{1c} levels with insoluble dietary fibre intake across the quantile levels of HbA_{1c} are given in Table 2. According to the ordinary least-squares estimations, a significant inverse association was observed between insoluble dietary fibre intake at baseline and HbA_{1c} levels during the follow-up survey ($\beta = -0{\cdot}258$; 95 % CI −0·450, −0·065). In the QR analysis, however, the association was found to be not significant until after the quantile level of 0·52 (i.e. the HbA_{1c} level of 6·8 %). The 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. Further adjustment for other dietary factors such as protein and fat intake did not alter the results substantially.

The plot in Fig. 1(a), with the quantile levels of HbA_{1c} ranging from 0·05 to 0·95 on the *x*-axis and regression coefficients for the associations of HbA_{1c} levels with insoluble dietary fibre intake (β) derived from QR models on the *y*-axis, shows the changes in HbA_{1c} levels with one unit (g/1000 kJ per d) intake of insoluble dietary fibre across the quantile levels of HbA_{1c}. The association of insoluble dietary fibre intake with subsequent HbA_{1c} levels was found to be significant at and after the quantile of 0·52 (HbA_{1c} level = 6·8 %). Considering the significant influence of drug use on HbA_{1c} levels, we conducted a sensitivity analysis by including hypoglycaemic drug use and insulin use during the follow-up survey into the QR models. As shown in Fig. 1(b), the inverse associations of insoluble dietary fibre intake with HbA_{1c} levels were more pronounced after the quantile of 0·56, where the HbA_{1c} level was 7·0 %.

Fig. 2(a) shows the associations between dietary GI value and HbA_{1c} levels, which reached statistical significance when the quantile level was 0·52 (HbA_{1c} level = 6·8 %) or higher and became stronger afterwards. Similarly, in the sensitivity analysis, the associations of GI value with HbA_{1c} levels

Table 2. Marginal associations of glycosylated Hb (HbA_{1c}) levels with insoluble dietary fibre intake at the mean and selected quantile levels of HbA_{1c}

(Coefficients and 95 % confidence intervals)

	Coefficients*	95% CI
OLS†	−0·258	−0·450, −0·065
QR‡		
0·1	−0·249	−0·453, 0·047
0·2	−0·173	−0·364, −0·052
0·3	−0·264	−0·477, 0·162
0·4	−0·194	−0·405, 0·045
0·5	−0·239	−0·465, 0·017
0·6	−0·174	−0·433, −0·025
0·7	−0·200	−0·306, −0·008
0·8	−0·221	−0·426, −0·117
0·9	−0·389	−0·516, −0·018

OLS, ordinary least squares; QR, quantile regression.
* Refers to the change in HbA_{1c} levels (%) with one unit (g/1000 kJ per d) intake of insoluble fibre; all estimations were adjusted for age (continuous variable), sex (male/female), BMI (continuous variable), time from being diagnosed with diabetes (continuous variable), regular exercise (ever/never), hypoglycaemic drug use (ever/never), insulin use (ever/never), family history of diabetes (ever/never), carbohydrate intake per 1000 kJ/d (continuous variable), energy intake (continuous variable) and HbA_{1c} level during the baseline survey (continuous variable).
† The mean value of HbA_{1c} was 7·0 %.
‡ The corresponding values of HbA_{1c} 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.

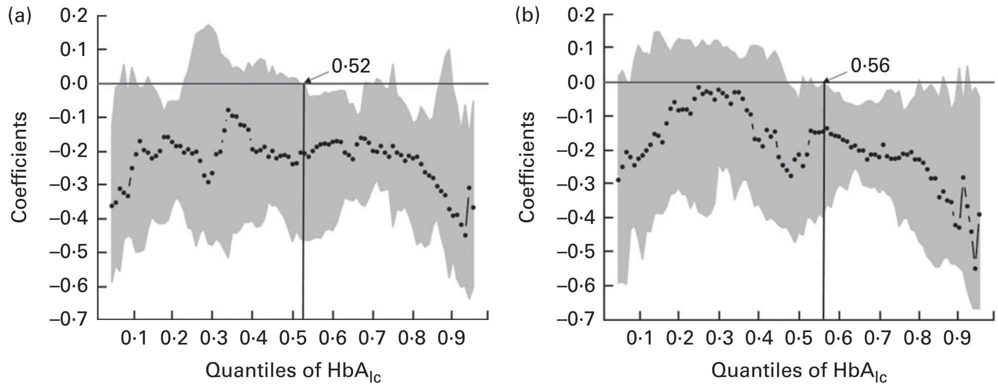

Fig. 1. Coefficients (β) for the associations of glycosylated Hb (HbA_{1c}) levels with insoluble dietary fibre intake across the quantile levels of HbA_{1c}. The coefficients indicate the change in HbA_{1c} levels (%) with one unit (g/1000 kJ per d) increase in insoluble fibre. The black solid horizontal line represents $\beta = 0$, 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 HbA_{1c} 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).

were more evident after the quantile of 0·56 (HbA_{1c} 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 HbA_{1c} levels changed across the selected quantile levels of HbA_{1c} among Chinese adults with type 2 diabetes. We found that both insoluble dietary fibre intake and GI value were significantly associated with subsequent HbA_{1c} levels among diabetic patients, especially among those with high HbA_{1c} 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 HbA_{1c} 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 HbA_{1c} 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

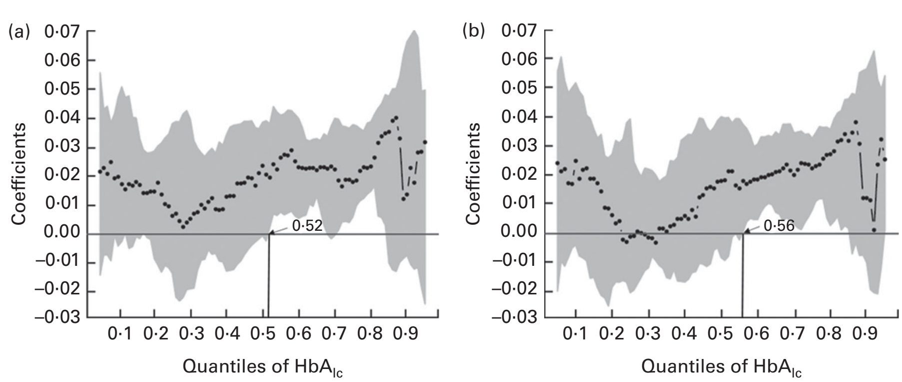

Fig. 2. Coefficients (β) for the associations of glycosylated Hb (HbA_{1c}) levels with dietary glycaemic index (GI) value across the quantile levels of HbA_{1c}. The coefficients indicate the change in HbA_{1c} levels (%) with one unit increase in dietary GI. The black solid horizontal line represents $\beta = 0$, 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 61·9, 58·9, 60·8, 57·0, 60·4, 58·5, 62·3, 61·7 and 68·2, 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 HbA_{1c} 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).

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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 HbA_{1c} levels, especially among patients who did not have their blood glucose under control. Unlike the parametric logistic regression method used in our previous study[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 HbA_{1c} and provided a more complete picture of how the dietary factors and HbA_{1c} levels are associated[14].

The results of the present study are somewhat consistent with those reported by Livesey *et al.*[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/1000 kJ per d) was found to be associated with a 0·174 % decrease in HbA_{1c} content at a HbA_{1c} level of 7·2 % and with a 0·221 % decrease at a HbA_{1c} 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[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 HbA_{1c} levels within a few months. The possible differentiated changes in patients with low or high HbA_{1c} levels could bias the results of the study in both directions. In the present study population, the κ coefficient for regular exercise between the two surveys was 0·22 ($P<0·001$) for patients with low HbA_{1c} levels, but was 0·01 ($P>0·05$) for patients with high HbA_{1c} levels, indicating more evident changes in regular exercise among patients with high HbA_{1c} 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 HbA_{1c} 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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