Body Iron Stores and Dietary Iron Intake in Relation to Diabetes in Adults in North China

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OBJECTIVE — To evaluate the association between body iron stores, dietary iron intake, and risk of diabetes in northern China.

RESEARCH DESIGN AND METHODS — The data of a cross-sectional household survey in 2002 in Liaoning Province in northern China was used. The final sample in our study contained 2,997 subjects aged ≥18 years. Fasting plasma glucose and serum ferritin were measured. Dietary information was collected by 3-day food records.

RESULTS — Serum ferritin was associated with elevated risk of diabetes even adjusted for age, sex, nondietary factors, and dietary factors. No association among total iron intake, nonheme iron intake, and diabetes risk was found. However, higher heme iron intake was significantly associated with elevated risk of diabetes after adjusting for known factors.

CONCLUSIONS — In Chinese, associations among higher serum ferritin level, higher heme iron intake, and elevated risk of diabetes were found.

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The 2002 China National Nutrition and Health Survey is a nationally representative cross-sectional survey (1). Data presented in this article are based on subsamples from Liaoning Province in northern China. A multistep cluster-sampling method was used for subject selection (1). Sampling involved a total of 12,059 subjects aged 1–96 years, representing the population of Liaoning Province. Written consent was obtained from all participants. In the study presented here, only adults, who were selected for dietary assessments and blood sample collection, aged ≥18 years old were involved.

Trained interviewers went to the subjects' homes to collect information on food intake using the 24-h dietary recall method for 3 consecutive days. Total iron, heme iron, nonheme iron, and other nutrient intakes were calculated using data of dietary intake in conjunction with the China Food Composition Table (2).

A health status questionnaire and a 1-year physical activity questionnaire were adopted to collect the information of health behavior and lifestyle. An individual who had smoked daily for at least 6 months during his/her life was defined as a smoker. A drinker was defined as one who drank an alcohol product at least once a week. Sedentary time was total time spent watching TV, reading, playing electric games, and operating a computer during leisure time. Family history of diabetes was defined as the presence of known family members with diabetes in any of three generations.

At the study site, all anthropometric measurements were made by trained investigators using standard techniques. Plasma glucose level was measured with a spectrophotometer within 4 h after a fasting blood sample was obtained. Serum ferritin was analyzed in the laboratory of the National Institute for Nutrition and Food Safety (Beijing, China) using a commercially available radioimmunoassay kit (Beijing North Institute of Biological Technology). Plasma total cholesterol, triacylglycerols, and HDL cholesterol were measured enzymatically with an Hitachi 7060 7180 auto-analyzer (Hitachi, Tokyo, Japan) (1). Diabetes was defined as fasting plasma glucose ≥7.0 mmol/l.

All statistical analyses were performed with SAS software (SAS Institute, Cary, NC). We divided all subjects into four quartiles according to serum ferritin level, total iron intake, heme iron intake, or nonheme iron intake. Logistic regression was used to analyze association among serum ferritin, total iron intake, heme iron intake, nonheme iron intake, and risk of diabetes. Tests of linear trend across quartiles were conducted by assigning the median value for each quartile and fitting this continuous variable in the model. Subjects who were known to have diabetes and had fasting plasma glucose <7.0 mmol/l were excluded from this study.

RESULTS — In total, 1,618 women and 1,379 men were involved in this study. Mean ± SD age was 46.5 ± 14.7 years. Prevalence of diabetes was 4.9%. Mean serum ferritin level, total iron intake, heme iron intake, and nonheme iron intake were 105.4 ± 87.5 μg/l and 19.6 ± 8.8, 2.7 ± 3.3, and 16.1 ± 8.4 mg/l, respectively.

Serum ferritin was associated with elevated risk of diabetes even adjusted for age, sex, nondietary factors, and dietary factors (Table 1). No association among total iron intake, nonheme iron intake, and diabetes risk was found after adjusting for known factors. However, heme iron intake was positively associated with risk of diabetes adjusted for known factors (Table 1).

In model building, it was found that abnormal blood lipid, family history of diabetes, central obesity, and dietary intake of fat mainly confounded the association between iron status and diabetes

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Table 1—*Odds ratios (95% CIs) for diabetes by quartiles of serum ferritin level and heme iron intake in subjects*

	Quartile 1	Quartile 2	Quartile 3	Quartile 4	P_{trend}
Serum ferritin					
n	739	739	741	740	—
Ferritin (μg/l)	20.3 ± 9.6	59.2 ± 12.9	112.9 ± 18.8	229.1 ± 72.4	—
Age and sex adjusted	1.00 (ref.)	2.02 (1.06–3.85)	1.15 (0.57–2.33)	4.34 (2.31–8.14)	<0.0001
Nondietary factors adjusted*	1.00 (ref.)	1.84 (0.96–3.53)	0.91 (0.44–1.88)	3.19 (1.68–6.07)	<0.0001
Dietary and nondietary factors adjusted†‡	1.00 (ref.)	1.69 (0.87–3.28)	0.90 (0.43–1.87)	2.96 (1.53–5.72)	0.0002
Heme iron					
n	743	756	753	745	—
Intake (mg/day)	0.3 ± 0.3	1.3 ± 0.3	2.6 ± 0.4	6.4 ± 4.6	—
Age and sex adjusted	1.00 (ref.)	1.36 (0.77–2.39)	2.23 (1.33–3.73)	2.62 (1.56–4.40)	0.0030
Nondietary factors adjusted*	1.00 (ref.)	1.42 (0.77–2.60)	1.97 (1.12–3.44)	2.39 (1.36–4.18)	0.0119
Dietary and nondietary factors adjusted†§	1.00 (ref.)	1.32 (0.72–2.45)	1.85 (1.04–3.31)	2.30 (1.26–4.19)	0.0292

Data are odds ratios (95% CIs) or means ± SD unless otherwise indicated. *Nondietary factors include age (10-year categories), sex, smoking (yes/no), drinking (yes/no), and quartiles of sedentary time (h/day), family history of diabetes (yes/no), central obesity (waist circumference ≥90 cm for men and ≥80 cm for women), high blood pressure (diastolic blood pressure ≥90 mmHg, systolic blood pressure ≥140 mmHg, or using antihypertensive drugs), abnormal blood lipid (total cholesterol ≥5.20 mmol/l and/or HDL cholesterol ≤0.91 mmol/l and/or triacylglycerols ≥1.70 mmol/l and/or LDL cholesterol ≥3.15 mmol/l). †Dietary factors include intake of calories (kcal/day), fiber (g/day) (all quartiles), and high percentage of energy from fat (≥30%). ‡In this model, odds ratios of abnormal blood lipid, central obesity, family history of diabetes, and dietary intake of fat were 2.12 (1.42–3.17), 1.69 (1.12–2.53), 2.68 (1.61–4.47), and 1.61 (1.07–2.44), respectively. §In this model, abnormal blood lipid, central obesity, family history of diabetes, and dietary intake of fat yield odds ratios of 2.16 (1.47–3.16), 1.78 (1.20–2.65), 2.85 (1.75–4.65), and 1.36 (0.89–2.08), respectively.

risk and might replace the effects of iron (Table 1). For example, if blood lipid was not adjusted, total iron intake was significantly associated with elevated risk of diabetes in women (odds ratio 1.00 [referent], 1.29 [95% CI 0.62–2.67], 2.04 [0.93–4.51], and 2.71 [1.12–6.56] for quartiles 1–4, respectively; P_{trend} = 0.0192), consistent with the recent study in southern China (3). However, nonheme iron intake remained unassociated with diabetes risk.

CONCLUSIONS— Increasing evidence suggests that high body iron stores (4–5) and only heme iron in diet (6–8) are associated with elevated risk of diabetes in Western countries. However, Chinese dietary pattern is unique in that it consists of more plant food and less animal food. A recent study in southern China (3) reported that serum ferritin and total iron intake were significantly associated with elevated diabetes risk. But without data analysis, they concluded that nonheme iron intake may play a role in association between iron status and diabetes in the Chinese context. To confirm these results, we conducted this study.

Though racial background of the Chinese population differs from that in Western countries, the positive association between serum ferritin (a biomarker of body iron store) and diabetes risk was also found in our study. As to dietary iron, we only found that heme iron intake was associated with elevated diabetes risk, consistent with several studies in Western countries (6–8). However, there was little difference between our results and those of the study in southern China (3). We could have had a similar association between total iron and diabetes risk if we did not adjust for blood lipid. But blood lipid, family history of diabetes, waist circumference, and dietary intake of fat were main confounders that should be adjusted. We only found that heme iron plays a role in association between total iron and diabetes; nonheme iron intake didn't affect the association.

Our study confirmed earlier findings (3) that body iron associates with glucose homeostasis in the Chinese population and identified intake of heme iron as a potential causal factor. However, a cohort study is needed to confirm the causal relation.

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