

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

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Running title: Body Iron, Dietary Iron and Diabetes

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ABSTRACT

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

RESEARCH DESIGN AND METHODS — The data of a cross-sectional household survey in 2002 in Liaoning Province in North China was used. Final sample contained 2997 subjects aged 18 years old above in our study. Fasting plasma glucose and serum ferritin were measured. Dietary information was collected by three-day food records.

RESULTS – Serum ferritin was associated with elevated risk of diabetes even adjusted for age, gender, 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 the association among higher serum ferritin level, higher heme iron intake and elevated risk of diabetes were also found.

RESEARCH DESIGN AND METHODS

The 2002 China National Nutrition and Health Survey (CNHS2002) is a nationally representative cross-sectional survey (1). The data presented in this article are based on subsamples from the Liaoning Province in North China. A multi-step cluster sampling method was used for subject selection (1). Sampling involved a total of 12059 subjects aged 1-96 years representing the population of Liaoning Province. Written consent was obtained from all the participants. In the study presented here, only adults, who were selected for dietary assessments and blood sample collection, aged 18 years old above were involved.

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

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

At study site, all anthropometric measurements were made by trained investigators using standard techniques. Plasma glucose level was measured with a spectrophotometer within 4 hours after a fasting blood sample was obtained. Serum

ferritin was analyzed in the laboratory of National Institute for Nutrition and Food Safety in Beijing using a commercially available radioimmunoassay kit(Beijing North Institute of Biological Technology). Plasma total cholesterol, triacylglycerols and HDL-C were measured enzymatically with a Hitachi 7060, 7180 auto-analyzer (Hitachi, Tokyo, Japan) (1). Diabetes was defined as fasting plasma glucose (FPG) ≥ 7.0 mmol/l.

All statistical analyses were performed with SAS software (SAS Institute Inc., Cary, NC). We divided all subjects into four categories (quartiles) according to their serum ferritin level, total iron intake, heme iron intake or nonheme iron intake, respectively. Logistic regression was used to analyze association among serum ferritin, total iron intake, heme iron intake, nonheme iron intake and the 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 FPG<7.0mmol/l were excluded from this study.

RESULTS

In total, 1618 women and 1379 men were involved in this study. The mean \pm SD of age was 46.5 \pm 14.7. The prevalence of diabetes was 4.9%. The mean \pm SD of serum ferritin level, total iron intake, heme iron intake and nonheme iron intake were 105.4 \pm 87.5 μ g/l, 19.6 \pm 8.8mg/l, 2.7 \pm 3.3mg/l and 16.1 \pm 8.4mg/l, respectively.

Serum ferritin was associated with elevated risk of diabetes even adjusted for age, gender, 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 the 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 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 (Q1-Q4: 1.00; 1.29(95%CI 0.62-2.67), 2.04(95%CI 0.93-4.51), 2.71(95%CI 1.12-6.56), $P_{\text{trend}}=0.0192$). It was consistent with the recent study in South China (3). But nonheme iron intake still remained no association with diabetes risk.

CONCLUSIONS

Increasing evidence has suggested 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 that consists of more plant food and less animal food. A recent study in South 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 above results, we conducted

this study.

Though the race in China is different from 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. It was consistent with several studies in western countries (6-8). But there was little difference with the result of the study in South China (3). We could have the similar association between total iron and diabetes risk if not adjusting 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 play a role in association between total iron and diabetes. But nonheme iron intake didn't affect the association.

Our study confirmed the earlier findings (3) that body iron associates with glucose homeostasis also 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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Table 1 – OR and 95% CIs for diabetes by quartiles of serum ferritin level and heme iron intake in subjects

		Q1	Q2	Q3	Q4	<i>P</i> _{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 gender adjusted	1.00	2.02 (1.06-3.85)	1.15 (0.57-2.33)	4.34 (2.31-8.14)	<.0001
	Nondietary factors adjusted†	1.00	1.84 (0.96-3.53)	0.91 (0.44-1.88)	3.19 (1.68-6.07)	<.0001
	Dietary and nondietary factors adjusted ‡§	1.00	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 gender adjusted	1.00	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	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	1.32 (0.72-2.45)	1.85 (1.04-3.31)	2.30 (1.26-4.19)	0.0292

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