Original Article

Metal Exposure and Risk of Diabetes and Prediabetes among Chinese Occupational Workers*

YANG Ai Min[1,2], CHENG Ning[3], PU Hong Quan[4], LIU Si Min[2], LI Juan Sheng[1], BASSIG Bryan A.[5], DAI Min[6], LI Hai Yan[4], HU Xiao Bin[1], REN Xiao Wei[1], ZHENG Tong Zhang[2,#], and BAI Ya Na[1,#]

1. Institute of Epidemiology and Statistics, School of Public Health, Lanzhou University, Lanzhou 730000, Gansu, China; 2. Department of Epidemiology, School of Public Health, Brown University, Providence, RI 02912, USA; 3. Center of Medical Laboratory, Lanzhou University, Lanzhou 730000, Gansu, China; 4. Workers' Hospital of Jinchuan Group Co., Ltd., Jinchang 730000, Gansu, China; 5. Department of Environmental Health Sciences, School of Public Health, Yale University, New Haven, CT 06511, USA; 6. Cancer Hospital, Chinese Academy of Medical Sciences, Beijing 100021, China

Abstract

Objective To study the association between metal exposure and risk of diabetes and prediabetes among Chinese workers exposed to metals.

Methods We used data obtained from the baseline survey of the Jinchang Cohort Study of workers in Jinchang Industry, the largest nickel production company in China. A total of 42,122 workers ≥20 years of age were included in the study. A standardized, structured questionnaire was used to collect epidemiological information. Physical examinations and laboratory tests were conducted to evaluate the health status of the participants and to measure various biomarkers including blood sugar, lipids, and urinary metal concentrations. Logistic regression was used to study the association between occupational groups categorized according to the measured metal levels (office workers, low-level; mining/production workers, mid-level; and smelting/refining workers, high-level) and risk of diabetes and prediabetes.

Results The overall prevalence of diabetes and prediabetes was 7.5% and 16.8%, respectively. The adjusted odds ratios for diabetes among mining/production workers and smelting/refining workers compared to office workers were 1.5 (95% CI: 1.3, 1.7) and 3.8 (95% CI: 3.4, 4.3), respectively. No association was observed between these occupational groups and prediabetes in this study.

Conclusion Occupations associated with higher levels of metal exposure were associated with an increased risk of diabetes in this cohort. More studies are needed to confirm this observed association.

Key words: Metals; Occupational exposure; Diabetes; Prediabetes; Risk factors

Biomed Environ Sci, 2015; 28(12): 875-883 *doi: 10.3967/bes2015.121* *ISSN: 0895-3988*

www.besjournal.com (full text) *CN: 11-2816/Q*

*This work was supported by the Project of Employees Health Status and Disease Burden Trend Study in Jinchuan Nonferrous Metals Corporation, Grant JKB20120013; Fogarty training grants D43TW 008323 and D43TW 007864-01 from the US National Institutes of Health.

#Correspondence should be addressed to BAI Ya Na, Tel: 86-931-8915526, E-mail: baiyana@lzu.edu.cn; ZHENG Tong Zhang, Tel: 1 (401) 863-6365, E-mail: Tongzhang_Zheng@Brown.edu

Biographical note of the first author: YANG Ai Min, Visiting Research Fellow of Brown University, majoring in environmental and occupational health.

INTRODUCTION

Diabetes mellitus is a major public health and socioeconomic challenge that affects nearly all countries[1]. Every year, 3.2 million people worldwide die from complications associated with diabetes[2]. Diabetes is a metabolic disorder characterized by deficient insulin secretion or insulin receptor insensitivity that results in fasting hyperglycemia[3]. The prevalence of diabetes is likely to rise with changing lifestyles characterized by reduced physical activity and increased obesity[1,4-5]. Besides traditional lifestyle-related risk factors, environmental exposures such as heavy metals may contribute to the development of diabetes[6-7]. Thus, there is considerable interest in understanding the role of metal exposure in the development of diabetes[8].

The general population is primarily exposed to metals through the air, water, and food ingestion. Occupational exposure to metals occurs predominantly in mining, refining, alloy production, electroplating, and welding[9]. Data from animal and human studies have suggested that exposure to metals may be associated with an increased risk of diabetes. Specifically, several animal studies have reported that nickel exposure can induce hyperglycemia[10-11]. Some human studies have further demonstrated that other metals, and nickel in particular, may play a role in the development of diabetes[12-13]. Liu et al. observed that nickel exposure was associated with the prevalence of diabetes in a study of 2155 Chinese adults[7]. Lai et al. reported an association between arsenic and diabetes in a cross-sectional study of 891 subjects in Taiwan[14]. However, most of the previous population-based studies included diabetes patients that were based on self-reports, and the sample size or number of individuals with diabetes was small[8]. There have been limited large-scale population-based studies on metal exposure and risk of diabetes[7].

In order to provide additional insight into the role of occupational metal exposure on a variety of health outcomes, we initiated a large prospective cohort study of about 45,000 metal exposed workers in Jinchang city, Gansu province, China (Jinchang Cohort Study) in 2011. This study collects comprehensive epidemiological and biological data in order to understand the environmental toxicity of metal exposure and the associations between metal exposure and risk of cancer and other diseases. The current analysis used data obtained from the baseline Jinchang Cohort Study survey to explore the associations between occupational groups that were categorized according to their measured urinary metal levels and risk of diabetes and prediabetes.

METHODS

Study Population

The Jinchang Industry, the largest nickel production company in China, is a large mining group of about 45,000 workers engaged in mining, concentrating, metallurgy, and deep processing. The primary focus of the company is the smelting and processing of nickel, copper, and cobalt as well as the chemical processing of materials. The company has become the third-largest nickel and second-largest cobalt manufacturing enterprise in the world, and the third-largest copper and largest platinum group metal manufacturing enterprise in China. The rationale, design, and methods of the Jinchang cohort have previously been described in detail[15-16]. Since 2011, all workers in the company have been eligible for a medical exam every two years, which includes in-person interviews, comprehensive physical exams, laboratory-based tests, and biosample collection. Only those who participated in the medical examinations were eligible to enter the Jinchang Cohort Study. We established the Jinchang Cohort Study with a cross-sectional baseline survey from June 2011 to December 2013.

Of 46,295 workers, 44,947 (97.1%) underwent medical examinations and completed the baseline survey. Of these subjects, 42,122 (93.7%) were included in the current study; 2825 (6.3%) were excluded because they did not complete the full medical examination (including the in-person interview, physical exams, laboratory tests, and donation of a blood sample). Thus, a total of 42,122 workers with a mean age of 46±13 years (61.7% men, 38.3% women) were included in this study.

Data Collection

Several types of data were collected for analysis, including questionnaire data obtained from in-person interviews, clinical data from physical and biochemical examinations, and biosample collection. In-person interviews were conducted at the hospital by trained interviewers, who completed a standardized and structured questionnaire that included an assessment of lifetime occupational history, medical history, family history of tumors and chronic diseases, and other demographic, socioeconomic, and lifestyle factors. Comprehensive physical examinations were performed by clinicians at the Workers' Hospital of the Jinchang Company using standard protocols and techniques[17] after completion of the in-person interviews. The examinations included measurements of weight, height, and blood pressure. Body-mass index (BMI) was calculated as weight in kilograms divided by the square of height in meters. All participants provided blood samples and 20% of participants provided urine samples. Plasma and serum were cryopreserved at -80 °C, while hemocytes, blood clots, and urine samples were cryopreserved at -40 °C. The cryopreserved blood and urine samples were stored in 1.8 mL cryogenic tubes for future study. The biochemical examinations were performed using a clinical chemistry automatic analyzer (Hitachi 7600-020, Kyoto, Japan) in the morning after an overnight fast of at least 8 hours. Six mL of fasting blood sample was taken from each participant and stored for laboratory testing of fasting blood glucose (FPG), total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C).

Variable Definitions

Diabetes and Prediabetes Based on World Health Organization (WHO) standards[18], participants were classified as diabetic (*n*=3161) in the study if they were taking anti-diabetic medications (*n*=541), or if their baseline FPG levels were high (≥7.0 mmol/L) at the time of cohort entry (*n*=2620). Prediabetes was defined as a FPG between 5.6 and 7.0 mmol/L in workers without prior diabetes diagnosis (*n*=7068).

BMI, Hypertension, and Abnormal Lipid Measurements Based on WHO classifications[19], normal weight, overweight, and obesity were defined as BMIs less than 25, 25 to 29.9, and ≥30, respectively. Hypertension was defined as systolic blood pressure ≥140 mm Hg or diastolic blood pressure ≥90 mmHg, or self-reported treatment for hypertension. Abnormal lipid measurements were defined as[20]: TG ≥1.70 mmol/L (150 mg/dL) or HDL-C <0.9 mmol/L (35 mg/dL) in men and <1.0 mmol/L (39 mg/dL) in women.

Smoking and Drinking Participants were categorized as current, former, and non-smokers. Current smokers were defined as those who had smoked at least one cigarette per day in the last six months. Former smokers were defined as those who used to be smokers, but who had smoked less than one cigarette per day or stopped smoking for at least the past six months. The rest of the participants were defined as non-smokers. Current drinkers were defined as those participants who drank hard liquor, beer, or wine at least once per week during the past six months. Former drinkers were those who used to be drinkers, but who had drank less than once per week or stopped drinking for at least the past six months. Non-drinkers were defined as those who always drank less than once per week or not at all.

Estimation of Occupational Metal Exposure Levels

The Jinchang Industry contains 32 production and auxiliary service units; the layout includes the complete product industry chain for mine, ore dressing and smelting, and related diverse auxiliary industries such as engineering construction and mechanical and automation engineering. Workers are routinely exposed to nickel as well as several other metals, including copper and cobalt. Estimation of likely metal exposure levels for each subject was based on their occupation/production process within the Industry. Levels of metal exposure were divided into three categories, namely office workers (low-levels), mining/production workers (mid-levels), and smelting/refining workers (high-levels). Data collected from the occupational history assessment on the baseline questionnaire were used to assign cohort members into these three categories. Among subjects who reported having been diagnosed with diabetes, 853 (49.5%) had only one occupation in their lifetimes, 604 (35.0%) had two occupations in their lifetimes, and 262 (15.5%) had more than two occupations in their lifetimes. Among workers with more than one occupation in their lifetimes (*n*=866), only 37 (4.3%) had worked in different categories among the three evaluated in this study (i.e., mining/production, smelting/refining, and office workers). The occupational categorization for those with diabetes was based on the patients' occupation at the time they were diagnosed. Among 40,398 subjects who did not have diabetes, 23,565 (58.3%) had only one occupation in their lifetimes, 11,301 (28.0%) had only two occupations in their lifetimes, and 5,532 (13.7%) had more than two occupations in their lifetimes. Among the non-diabetic workers with >1 occupation in their lifetimes (*n*=16,833), 609 (3.6%)

had worked in different occupational categories among the three evaluated in this study. Those subjects that did not have diabetes were assigned to the occupational category in which they had spent the longest time working, based on their occupational histories. Office workers included service staff and managers in the company. The mining/production worker category included chemical and metal products manufacturing workers and workers involved in mining and ore dressing. Finally, all smelting and refining workers were included in the smelting/refining workers category.

Assessment of Metal Exposure Levels

In order to determine the relative metal exposure levels among specific occupational groups and to assess whether participants in each of the three categories had been exposed to different metal levels, we measured urinary levels of nickel, copper, and cobalt in a subgroup of workers. Urine samples from a total of 300 workers were obtained from the biobank of the Jinchang Cohort Study. These 300 workers (150 men and 150 women) were between 20 and 50 years of age and consisted of three age-matched subgroups based on their occupations: service staff and managers with presumed low metal exposure levels (*n*=100); workers involved in the manufacturing of metal products and workers involved in mining and ore dressing with presumed intermediate metal exposure levels (*n*=100); and smelting/refining workers with presumed high levels of metal exposure (*n*=100).

All urine samples were coded and analyzed by laboratory personnel blinded to their origins. One mL of each urine sample was mixed with 3.0% HNO_3 to a final volume of 2.5 mL for overnight nitrification. Urinary nickel, copper, and cobalt were analyzed by inductively coupled plasma mass spectrometry (iCAP Q ICP-MS, Thermo Scientific). Standard reference material human urine (SRM2670a, National Institute of Standards and Technology, Gaithersburg, MD, USA) was used as an external quality control, and sample spike-recoveries were used to confirm analytical recovery, which was 95%. The intra- and inter-day coefficient of variation was within 5%.

Statistical Analysis

Descriptive statistics were used to describe the frequency and proportion, mean (M) and standard deviation (SD), and median and interquartile range of the demographic and clinical characteristics. We used the Kruskal-Wallis test to compare urine metal levels between the three occupational groups. Logistic regression analysis was used to estimate the unadjusted and adjusted odds ratio (OR) between mining/production workers and smelting/refining workers and risk of diabetes and prediabetes, using office workers as the reference group. Models were adjusted for other known diabetes risk factors, including age, smoking, alcohol drinking, BMI, hypertension, and family history of diabetes. As diabetes and insulin resistance are associated with a clustering of interrelated plasma lipid levels[21], abnormal lipids were also adjusted in the models. We also performed sensitivity analyses that excluded workers who had worked in >1 of the occupational categories assessed in our study, in order to mitigate the potential influence of exposure misclassification on the associations between occupation, prediabetes, and diabetes risk. All reported *P*-values were made on the basis of two-sided tests with a significance level of 0.05. SAS software version 9.3 was used for all the statistical analyses.

RESULTS

The overall prevalence of diabetes and prediabetes in the study population was 7.5% (9.0% in men and 5.2% in women) and 16.8% (19.0% in men and 13.3% in women), respectively. The characteristics of participants overall and according to gender in the Jinchang Cohort are summarized in Table 1. The prevalence of overweight (25≤BMI<30) and obesity (BMI≥30) participants was 27.9% and 3.2%, respectively. Current and former smokers accounted for 72.6% of men, whereas most women were non-smokers (98.4%).

Table 2 shows the urine metal concentrations in occupational workers according to their job titles. The median urinary nickel concentrations among office workers, mining/production workers, and smelting/refining workers were 4.75 μg/L (4.15 μg/L in males and 5.63 μg/L in females), 7.03 μg/L (7.82 μg/L in males and 6.83 μg/L in females), and 9.89 μg/L (9.89 μg/L in males and 9.88 μg/L in females), respectively (Kruskal-Wallis test: *P*=0.002; 0.001 for males and 0.044 for females). The corresponding median urinary copper concentrations were 118.25 μg/L, 209.19 μg/L, and 393.77 μg/L, respectively (*P*=0.001 in Kruskal-Wallis test). The corresponding median urinary cobalt concentrations were 0.76 μg/L, 0.72 μg/L, and 0.97 μg/L, respectively (*P*=0.213 in Kruskal-Wallis test). Compared with those who had

Table 1. Baseline Survey Participant Characteristics

Characteristics	Male	Female	Overall
Participants, *n* (%)	26,008 (61.7)	16,114 (38.3)	42,122 (100.0)
Age (M±SD)	46.8±14.1	45.8±11.8	46.4±13.3
Education, *n* (%)			
Middle School or Less	9,362 (36.0)	6,250 (38.8)	15,612 (37.0)
High School	7,244 (27.9)	4,165 (25.9)	11,409 (27.1)
College or Higher	9,402 (36.2)	5,699 (35.4)	15,101 (35.9)
Monthly Household Income (¥)			
<2000	14,214 (52.1)	7,928 (45.0)	22,142 (49.3)
2000-4999	12,576 (46.0)	9,335 (53.0)	21,911 (48.8)
≥5000	529 (1.9)	365 (2.1)	894 (2.0)
BMI, *n* (%)			
Normal (<25)	16,411 (63.1)	12,646 (78.5)	29,057 (69.0)
Overweight (25-30)	8,709 (33.5)	3,024 (18.8)	11,733 (27.9)
Obesity (≥30)	888 (3.4)	444 (2.8)	1,332 (3.2)
Current smoker	15,323 (58.9)	218 (1.4)	15,541 (36.9)
Former smoker	3,556 (13.7)	48 (0.3)	3,604 (8.6)
Current drinker	7,841 (30.2)	342 (2.1)	8,183 (19.4)
Former drinker	1,670 (6.4)	38 (0.2)	1,708 (4.1)

Table 2. Urinary Metal Levels Based on Metal Exposure According to Job Title (μg/L)

Metal Levels	Nickel			Copper			Cobalt		
	Office workers	Mining/ Production workers	Smelting/ Refining workers	Office workers	Mining/ Production workers	Smelting/ Refining workers	Office workers	Mining/ Production workers	Smelting/Refining workers
Overall (*n*=300)									
Mean	5.79	9.290	17.17	156.69	221.880	469.67	1.15	0.990	1.44
Median	4.75	7.030	9.89	118.25	209.190	393.77	0.76	0.720	0.97
25th percentile	2.66	4.880	5.79	75.85	144.370	199.79	0.50	0.510	0.7
75th percentile	6.89	12.050	17.92	153.93	273.410	651.89	1.40	1.170	1.58
H*		12.600			14.241			3.097	
P value		0.002			0.001			0.213	
Male (*n*=150)									
Mean	4.31	10.140	12.27	91.03	228.130	577.82	0.57	0.720	1.07
Median	4.15	7.820	9.89	87.78	209.190	542.88	0.51	0.640	0.83
25th percentile	2.26	5.220	6.58	48.11	146.070	233.34	0.40	0.420	0.58
75th percentile	5.86	13.110	17.92	125.97	290.510	775.87	0.73	0.840	1.05
H*		15.103			10.888			11.579	
P value		0.001			0.004			0.003	
Female (*n*=150)									
Mean	7.09	8.440	21.98	222.36	215.640	361.51	1.74	1.270	1.81
Median	5.63	6.830	9.88	142.62	207.260	262.05	1.36	1.050	1.48
25th percentile	3.03	4.560	5.53	101.96	138.440	173.04	0.88	0.690	0.85
75th percentile	9.05	11.430	15.85	259.84	264.090	551.44	2.13	1.700	2.34
H*		6.312			12.994			3.080	
P value		0.044			0.002			0.214	

Note. *Using the Kruskal-Wallis test.

low metal exposure levels based on job title, subjects with high likely metal exposure levels had elevated urinary nickel and copper concentrations either overall or in men and women. We also calculated Pearson's correlations to assess interrelationships among the metals. Levels of urinary nickel among workers showed a strong positive correlation with copper (r=0.40, P=0.001) and cobalt (r=0.61, P=0.001). Furthermore, urinary copper concentration showed a moderate positive correlation with cobalt (r=0.37, P=0.001).

The association between the occupational groups and risk of diabetes and prediabetes are shown in Table 3. After controlling for gender, age, education, BMI, smoking, drinking, abnormal lipids, hypertension, and family history of diabetes, the adjusted ORs for diabetes among mining/ production workers and smelting/refining workers were 1.5 (95% CI: 1.3, 1.7) and 3.8 (95% CI: 3.4, 4.3), respectively, compared to office workers. No significant association was observed for risk of prediabetes in either of the occupational groups.

Table 4 shows the associations between occupation and risk of diabetes and prediabetes in male and female participants. The adjusted ORs were 1.4 and 3.7 among male mining/production (95% CI: 1.2, 1.6) and smelting/refining (95% CI: 3.2, 4.3) workers, compared to office workers. Female mining/production (OR=2.0, 95% CI: 1.5, 2.5) and smelting/refining (OR=4.2, 95% CI: 3.4, 5.2) workers also had a significantly increased risk of diabetes compared to office workers. There was also no association between occupation and prediabetes risk in males or females separately.

In order to mitigate the potential influence of exposure misclassification on the associations between occupation, prediabetes, and diabetes risk, we also performed sensitivity analysis that excluded workers who had worked in >1 of the occupational categories assessed. The association was not materially changed when these workers were excluded from the analysis (Table 5).

DISCUSSION

Diabetes is rapidly becoming one of the most common non-communicable diseases worldwide.[1] Understanding the role of environmental and occupational exposures in the development or progression of diabetes is an emerging issue in environmental health[8]. The Diabetes Strategic Plan issued by the US National Institutes of Health in February 2011 recognized the need to understand the role of environmental exposures as part of future research and prevention strategies for diabetes[22]. Metal exposure may play a role in the development of diabetes, but little is known about its association with diabetes and prediabetes in among workers exposed to metal in their occupations[7]. We thus conducted a large-scale occupational study and found that occupational groups with elevated metal exposure levels had a significantly increased risk of diabetes, whereas no

Table 3. Participant Metal Exposure and Risk of Diabetes and Prediabetes

Occupation Category	***n* (42,122)**	**Adjusted OR* (95% CI)**	
		Prediabetes	Diabetes
Office workers	14,114	Reference	Reference
Mining/Production workers	16,364	1.0 (1.0, 1.1)	1.5 (1.3, 1.7)
Smelting/Refining workers	11,644	1.0 (0.9, 1.0)	3.8 (3.4, 4.3)

Note. *Adjusted for gender, age, BMI, abnormal lipid, hypertension, family history of diabetes, education, smoking and drinking.

Table 4. Metal Exposure and Risk of Diabetes and Prediabetes by Gender

Occupation Categories	**ORa* of Male (Total 26,008)**			**ORa* of Female (Total 16,114)**		
	n	Prediabetes (95% CI)	Diabetes (95% CI)	*n*	Prediabetes (95% CI)	Diabetes (95% CI)
Office workers	7210	Reference	Reference	6904	Reference	Reference
Mining/Production workers	11,450	1.0 (0.9, 1.1)	1.4 (1.2, 1.6)	4914	1.2 (1.1, 1.3)	2.0 (1.5, 2.5)
Smelting/Refining workers	7348	1.0 (0.9, 1.1)	3.7 (3.2, 4.3)	4296	0.9 (0.8, 1.0)	4.2 (3.4, 5.2)

Note. *Adjusted for age, BMI, abnormal lipid, hypertension, family history of diabetes, education, smoking, and drinking.

significant risk was observed for prediabetes. The association with diabetes was independent of traditional diabetes risk factors including age, education, BMI, smoking, drinking, abnormal lipids, and family history of diabetes.

Copper is considered an essential trace element in humans[23]. Workers in certain occupational settings, such as mining, smelting and welding, may be exposed to higher levels of copper[24]. Urinary levels of nickel and cobalt mainly reflect recent exposure. Substantial occupational exposure may result in elevated urinary cobalt levels that may persist for many weeks[25]. The median urinary nickel concentration of office workers participating in this study was 4.75 μg/L. The median urinary nickel levels in the Chinese general population was reported to be 3.63 μg/L (interquartile range: 2.29-5.89 μg/L) in a previous study[7]. The United States Centers for Disease Control Agency for Toxic Substances and Disease Registry currently uses 1-3.0 μg/L as a reference value for the general population[26]. However, there are no acceptable values for urinary nickel in the general population or in occupational workers. In our study, urinary levels of nickel and copper were elevated in smelting/refining workers compared with office workers, both overall and in male and female workers separately. Workers in the Jinchang Cohort Study are routinely exposed to multiple metals, including nickel, copper, and cobalt. Previous human and experimental studies on metal exposure have reported nickel and arsenic exposure to be associated with diabetes risk[6,27-28]. Several studies have suggested that nickel might damage insulin function, induce hyperglycemia, increase hepatic glycolysis and pancreatic glucagon release, decrease peripheral utilization of glucose, induce gluconeogenesis, and increase plasma glucose levels[10-11,29-30]. Similar findings for diabetes risk have been shown in the art glass industry and in copper smelter workers[6,14,31-32]. Copper, the third-most abundant essential transition metal in the human body, may play an important role in the pathogenesis of diabetes, including the induction of pancreatic islet cell degeneration and facilitation of hydrogen peroxide generation from amylin[33]. Wei et al. reported that urinary cobalt was associated with altered FPG or diabetes risk[34]. Little is known about the relationship between urinary cobalt and risk of diabetes. A number of *in vitro* studies have also showed that arsenic can influence insulin sensitivity, including oxidative stress, glucose uptake and transport, adipocyte differentiation, and gluconeogenesis[35-36]. It is possible that the other metals to which workers are exposed may be associated with development of diabetes in this occupational population. Further studies are needed to explore these associations.

We did not observe an association between occupation and prediabetes either overall or in men and women separately. There have been limited occupational studies of metal exposure and risk of prediabetes. However, Wallia et al.[37] has reported that urinary cadmium excretion is associated with a non-linear increased risk of prediabetes. In our study, the diagnosis of prediabetes was based on a single blood glucose measurement. Disease misclassification in this baseline examination may have led to an underestimation of the prevalence of prediabetes

Table 5. Sensitivity Analyses for Metal Exposure and Risk of Diabetes and Prediabetes (ORa*)

Gender	Office Workers	Mining/Production Workers	Smelting/Refining Workers
Male (Total 25,637)			
n	6,956	11,423	7,258
Prediabetes (95% CI)	Reference	1.0 (0.9, 1.0)	0.9 (0.8, 1.0)
Diabetes (95% CI)	Reference	1.3 (1.1, 1.5)	2.9 (2.6, 3.3)
Female (Total 15,839)			
n	6,699	4,902	4,238
Prediabetes (95% CI)	Reference	1.2 (1.1, 1.3)	0.9 (0.8, 1.0)
Diabetes (95% CI)	Reference	1.9 (1.6, 2.4)	4.0 (3.3, 4.8)
Overall (Total 41,476)			
N	13,656	16,324	11,496
Prediabetes (95% CI)	Reference	1.0 (1.0, 1.1)	0.9 (0.8, 1.0)
Diabetes (95% CI)	Reference	1.4 (1.3,1.6)	3.2 (2.9, 3.6)

Note. *Adjusted for age, BMI, abnormal lipid, hypertension, family history of diabetes, education, smoking and drinking.

in this population. Consequently, disease misclassification is one possible explanation for the null findings. Additional prospective studies are necessary to clarify the role of metal exposure in the pathogenesis of prediabetes and diabetes.

The main limitation of this study was that disease information was based on the baseline questionnaire within the Jinchang Cohort Study. The relationship between metal exposure and diabetes will be further evaluated within this ongoing prospective study with continued follow-up assessments. A second limitation of the present study was the lack of data on actual levels of metal exposure in the air of the workplace. Instead, metal exposure was determined based on occupation. However, exposure misclassification was mitigated by using sensitivity analysis that excluded workers who had worked in >1 of the occupational categories. Another limitation was that we could not identify which individual metals might be driving the increased risk of diabetes. Other relevant exposures aside from metals could also increase the risk of diabetes in this population. Additional studies are therefore necessary to explore metal exposure and risk of diabetes.

In conclusion, this large-scale population-based study of metal exposure and risk of diabetes and prediabetes in metal exposed workers showed that mining/production workers and smelting/refining workers had elevated risks of diabetes. More studies will be carried out to examine the relationship between metal exposure, epigenetics, and risk of diabetes in the population-based platform provided by the Jinchang Cohort Study.

ACKNOWLEDGEMENTS

As a visiting research fellow of Brown University, Yang Ai Min would thank the support from the China Scholarship Council (CSC).

CONTRIBUTOR SHIP

Mr. YANG Ai Min performed the data analyses and wrote the manuscript; Prof. CHENG Ning, Prof. PU Hong Quan, Prof. LIU Si Min, Prof. ZHENG Tong Zhang, Prof. DAI Min, and Prof. BAI Ya Na developed the study design and help with implementation; Dr. Bryan A. Bassig, Prof. LI Juan Sheng, Dr. LI Hai Yan, Prof. HU Xiao Bin, and Prof. REN Xiao Wei helped in the analysis with constructive discussions.

Received: September 21, 2015;
Accepted: November 23, 2015

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