

Letter to the Editor



Nickel-exposed Workers in China: A Cohort Study

BAI Ya Na^{1,2,#}, YAGN Ai Min¹, PU Hong Quan^{3,#}, HE Jie⁴, CHENG Ning⁵, ZHENG Tong Zhang⁶,
DAI Min⁴, ZHANG Ya Wei⁶, BASSING Bryan A.⁶, and WANG Qiu Ying³

There are more than 50 000 workers in *Jinchuan Group Co, Ltd (JNMC)*. Since all staff in JNMC are eligible for a medical examination every two years, only 23 484 nickel-exposed subjects who participated in medical examination were included in this study. Their data, collected from June 22, 2011 to September 28, 2012, in a comprehensive epidemiological survey and during medical examinations, permitted an extensive evaluation of the relation between metal exposure, gene, epigenetics and risk of human diseases. Their lifestyle investigation showed that the overall prevalence of current smokers, alcohol drinkers, and tea drinkers was 39.1%, 19.7%, and 55.2%, respectively. The prevalence of hypertension, allergic rhinitis and cholecystitis, the top 3 prevalent diseases, was 11.7%, 11.0%, and 8.9%, respectively.

Nickel (Ni) is one of the most widely distributed and used metals in the world^[1]. Occupational exposure to nickel occurs predominantly in mining, refining, alloy production, electroplating, and welding and is considered as an occupational hazard^[1]. It has been demonstrated that nickel metal dusts and some nickel compounds are extremely potent carcinogens after inhalation following occupational exposure^[2]. Nickel compounds are designated as carcinogenic to humans (group 1) by the International Agency for Research on Cancer, based on their association with lung cancer and cancer of the nasal cavity and paranasal sinuses in humans^[2]. However, their underlying mechanisms are still not fully understood.

The cohort study (Jinchang cohort) of nickel-exposed workers in China was started in June 2011. Jinchang City is located in Gansu Province, China. Jinchuan Group Co., Ltd. (JNMC) is the largest producer of nickel in China and its nickel output accounts for more than 90% of the total production

in China. Workers in the JNMC are routinely exposed to nickel and several other contaminants, including industrial dust, particulate matter and gaseous pollutants, cobalt, covellite, and chromium. Many of which are considered as definite or possible carcinogens^[2]. The Jinchang cohort study was initiated in order to create a large cohort with comprehensive epidemiological and biological data. Therefore, the cohort provided an opportunity to evaluate the effects of joint exposure to nickel and other metals and contaminants on health. The Jinchang cohort was a collaborative study of Lanzhou University, Workers' Hospital of JNMC, National Cancer Centre of China, and Yale University. The study was approved by The Ethical Committee of College of Public Health, Lanzhou University, and The Ethical Committee of Workers' Hospital of JNMC.

There are more than 50 000 workers in JNMC. Since all staff in JNMC is eligible for a medical examination every two years, only those who participated in the medical examination were included in the present cohort study. The initial medical examination began in June 2011 and ended in December 2013. The first examination of individuals in the cohort study will start immediately after the baseline survey from 2013-2015 because JNMC required a biannual medical examination for all of its employees. A total of 23 136 subjects received a medical examination from June 22, 2011 to September 28, 2012. Their baseline characteristics are shown in Table 1. It is anticipated that about 50 000 workers will complete their medical examination and epidemiological interviews in December 2013.

Data are available about nickel-exposed workers in JNMC from 2001 to 2010. Papers on the mortality study are going to be published. A study on health status and disease burden was conducted in nickel-exposed workers of JNMC to collect the data about

doi: 10.3967/bes2014.042

1. College of Earth and Environmental Sciences, Lanzhou University, Lanzhou 730000, Gansu, China; 2. School of Public Health, Lanzhou University, Lanzhou 730000, Gansu, China; 3. Workers' Hospital of Jinchuan Group Co., Ltd., Jinchang 737103, Gansu, China; 4. Cancer Institute and Hospital, Chinese Academy of Medical Sciences, Beijing 100021, China; 5. Key Laboratory of Preclinical Study for New Medicine, College of Basic Medicine, Lanzhou University, Lanzhou 730000, Gansu, China; 6. School of Public Health, Yale University, New Haven, CT, USA

Table 1. Baseline Characteristics of Participants in Jinchang Cohort

Items	Men (n=14 598)		Women (n=8 538)		Total (n=23 136)	
	n	%	n	%	n	%
Age group (years)						
20-25	381	2.6	247	2.9	628	2.7
25-30	1 063	7.3	472	5.5	1 535	6.6
30-35	761	5.2	397	4.6	1 158	5.0
35-40	2 135	14.6	1 647	19.3	3 782	16.3
40-45	3 369	23.1	3 071	36.0	6 440	27.8
45-50	2 736	18.7	1 899	22.2	4 635	20.0
50-55	1 027	7.0	274	3.2	1 301	5.6
55-60	965	6.6	223	2.6	1 188	5.1
60-65	846	5.8	158	1.9	1 004	4.3
65-70	516	3.5	60	0.7	576	2.5
70-75	427	2.9	57	0.7	484	2.1
≥75	372	2.5	33	0.4	405	1.8
Highest level of education						
Primary schooling completed	1 457	10.0	208	2.4	1 665	7.2
Secondary school	3 697	25.3	2 597	30.4	6 294	27.2
High school	4 227	29.0	2 637	30.9	6 864	29.7
Professional college	3 176	21.8	1 990	23.3	5 166	22.3
Bachelor degree or above	2 041	14.0	1 106	13.0	3 147	13.6
Monthly household income						
<1 000	2 561	17.5	423	5.0	2 984	12.9
1 000-2 000	5 756	39.4	3 815	44.7	9 571	41.4
2 000-3 000	4 529	31.0	3 366	39.4	7 895	34.1
≥3 000	1 752	12.0	934	10.9	2 686	11.6

the direct economic burden of disease from 2001 to 2010. The purpose was to understand the burden of their disease. Papers based on this study are available^[3-5] and the Jinchang cohort can thus be established.

A baseline survey was conducted to recruit the cohort. The recruitment process included an in-person epidemiological survey, a comprehensive physical and biochemical examination, and a collection of biological samples. The epidemiologic survey included an in-person interview with a standard and structured questionnaire, including questions about occupational exposure history, medical history, family history of CVD or cancer, reproductive factors, and other demographic, socioeconomic, and lifestyle factors.

The workers in JNMC underwent physical examination immediately after the epidemiological survey was completed. Their body weight, body height and blood pressure were measured. A fasting blood sample (6 mL) was collected from each participant and stored for laboratory tests of tumor

biomarkers such as WBC, RBC, HGB, PLT, TP, ALT, AST, TC, HDL, LDL-C, and TG. Findings in B-type ultrasound, chest X-ray, and electrocardiograms were recorded and used in the diagnosis of gallstones, and liver, lung, heart and other related diseases. The plasma and serum samples were preserved at -80 °C, and the hemocytes, blood clots and urine samples were preserved at -40 °C.

The causes of death and mortality of the workers in JNMC were analyzed, indicating that cancer is the most important disease affecting the health of workers, accounting for 35.9% of the total cancer-related deaths with the highest standard mortality of 163.62/10⁵. The lung cancer deaths accounted for 33.4% (309/925) of the total cancer-related deaths with a standard mortality of 54.22/10⁵. It has been shown that exposure to nickel is closely related with an increase lung cancer risk, especially in nickel-exposed workers^[2,6-8].

The baseline biochemical and hematological data and the prevalence of disease are listed in Tables 2 and 3.

Table 2. Lifestyle Characteristics of Participants in Jinchang Cohort

Characteristics	Men (n=14 598)		Women (n=8 538)		Total (n=23 136)	
	n	%	n	%	n	%
Tobacco smoking						
Current smokers	8 946	61.3	101	1.2	9 047	39.1
Former smokers	1 789	12.3	11	0.1	1 800	7.8
Never smokers	3 863	26.5	8 426	98.7	12 289	53.1
Alcohol drinking						
Current drinkers	4 419	30.3	149	1.7	4 568	19.7
Former drinkers	885	6.1	11	0.1	896	3.9
Never drinkers	9 294	63.7	8 378	98.1	17 672	76.4
Tea drinking						
Current drinkers	9 913	67.9	2 866	33.6	12 779	55.2
Former drinkers	208	1.4	51	0.6	259	1.1
Never drinkers	4 477	30.7	5 621	65.8	10 098	43.6

Table 3. Prevalence of Main Diseases in Participants of Jinchang Cohort

Diseases	Men (n=14 598)		Women (n=8 538)		Total (n=2 3136)	
	n	%	n	%	n	%
Hypertension	2 172	14.9	524	6.1	2 696	11.7
Allergic rhinitis	1 410	9.7	1 128	13.2	2 538	11.0
Cholecystitis	1 120	7.7	949	11.1	2 069	8.9
Gallstone	1 058	7.2	780	9.1	1 838	7.9
Faucitis	901	6.2	710	8.3	1 611	7.0
Fatty liver	1 307	9.0	225	2.6	1 532	6.6
Hyperlipidemia	1 131	7.7	280	3.3	1 411	6.1
Gastritis	654	4.5	310	3.6	964	4.2
Diabetes mellitus	586	4.0	99	1.2	685	3.0
Prostatoses disease	592	4.1	—	—	592	2.6

The lifestyle investigation showed that the overall prevalence of current smokers, alcohol drinkers, and tea drinkers was 39.1%, 19.7%, and 55.2%, respectively. It was reported that smoking and nickel exposure have multiple effects on lifestyle^[9]. The lifestyle risk factors and health outcomes in these workers need to be further studied.

The prevalence of hypertension, allergic rhinitis and cholecystitis, the top 3 diseases in the 23 136 workers, was 11.7%, 11.0%, and 8.9%, respectively. Hypertension, a common disease of the cardiovascular system with a high incidence, results from multiple factors. Nickel is a potent coronary vasoconstrictor in animal models. However, whether exposure to nickel increases the prevalence of

cardiovascular diseases remains unclear^[10], thus needing to be further studied.

The data obtained in our study can provide a population-based platform to examine the biological indicators that are closely correlated with metal exposure and illness.

ACKNOWLEDGEMENTS

The authors thank all the participants for their collaboration in this study, and the Government of Gansu Province, Lanzhou University, INMC, National Cancer Centre of China, and Yale University for their support.

[#]Correspondence should be addressed to BAI Ya Na,

Tel: 86-931-8915526, E-mail: baiyana@lzu.edu.cn; and Prof. PU Hong Quan, E-mail: phq@jnmc.com

Biographical note of the first author: BAI Ya Na, female, born in 1959, professor, majoring in occupational epidemiology.

Received: October 21, 2013;

Accepted: December 24, 2013

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