行政院國家科學委員會補助專題研究計畫　■成果報告

台灣新移民女性血中鉛及 DNA 損傷程度之調查研究

Assess the Blood Lead Concentrations and the Association with DNA Damage Levels in Immigrant women

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中文摘要

近年來，美國疾病控制及預防中心(CDC)與美國國家健康營養調查(NHANES)分別指出移民族群為鉛暴露的高危險族群，鑒於國內目前新移民女性人數持續增加(根據中華民國內政部 2007 年統計全台新移民女性已達 360,288 人，大部份來自大陸及東南亞國家)。鉛會造成中樞神經、造血與生殖系統等危害，更會將危害傳給下一代，但國內目前尚未建立新移民女性世代血中鉛值，以及探討過去與現在環境因素之影響。

本研究招募中部地區之新移民女性 239 位及台籍女性 189 位，進行結構式問卷訪視及收集血液檢體，使用感應耦合電漿質譜儀分析血液中重金屬濃度(鉛(Pb)、鎘(Cd)、汞(Hg)、鋅(Zn)、銅(Cu)、硒(Se)，並分析重金屬相關基因型 *ALAD, HFE, TF,* 與 *VDR*。氧化傷害指標部分則使用硫代巴比妥酸反應(TBARS Assay) 與超氧化物歧化反應(SODs Assay)來進行分析。

來台前五年的新移民女性有較高的血中重金屬濃度(鉛, 鎘, 錳, 銅, 和 鋅)。但在基因多型性分析中發現 *ALAD, HFE (H63D), TF (P570S),* 與 *VDR (folk, bsml, apal)*基因型在本三組研究族群分布上皆相似，且無統計上差異，表示基因型在本研究上並不會影響血中重金屬的分布。血中鉛、鎘與銅會隨著來台時間而減少，但血中硒則是相反，因此證實來台年數對於新移民女性體內血中重金屬與氧化傷害程度是一個重要因子。

建議公共衛生單位對於此族群應該提供初步重金屬的篩檢與預防，已減少相關重金屬所帶來的慢性疾病。

中文關鍵詞：新移民女性、血中重金屬 、氧化傷害

Abstract

Background: International immigration has had an impact on the public health systems of countries receiving immigrants. However, seldom studies with extensive data have been conducted to confirm the impact of migration on metal exposure and oxidative stress among this vulnerable population.

Objective: The objectives of this study were to (a) explore the differences in lead-associated genotypes, metals levels in blood, and oxidative stress between immigrant and native women and (b) examine if the duration of residence is an important determinant in the changes in blood metal levels and oxidative stress.

Methods: We used a structured questionnaire to collect data on socio-demographic status from (a) 239 immigrant women who had resettled in 2000 in central area of Taiwan and (b) 189 native women who live in the same area. Each study participant provided blood samples for metals measurements. They were also genotyped for *ALAD, HFE, TF, and VDR* variants. The TBARS Assay and SODs Assay were used to measure oxidative stress.

Results: Immigrant women were at risk for elevated blood metal levels (lead, cadmium, manganese, copper, and zinc) in the first five years after immigrating to Taiwan. The genetic variation of *ALAD, HFE (H63D), TF (P570S), and VDR (folk, bsml, apal)* were similar among those in our study populations and did not affect the blood metal levels. Decreased levels of lead, cadmium, and copper, and increased levels of selenium in the blood, were significantly associated with duration of residence.

Conclusions: This study confirmed that the duration of residence among immigrants is an important determinant in the change in blood metal levels and oxidative stress levels. The immigrant population in Taiwan is growing, and early prevention and screening programs may represent an important opportunity to prevent metal-related chronic illnesses in this vulnerable population.

KEY WORDS: Immigrants, Blood Metal levels, Oxidative stress

1. INTRODUCTION

International migration has recently emerged as a global priority issue, and the public health of immigrants in their new countries is also an issue. Migration patterns in Asia and the Pacific Rim are growing in scope and complexity (Nations 2005). Through December 2009, 408,079 immigrant women reported resettled in Taiwan; among these 274,617 were from Mainland China and 133,462 persons from countries, mostly in Southeast Asia. Newly married couples with different nationalities peaked at 28.4% in 2003 (Ministry of the Interior 2007). The immigrant population has altered the population structure in Taiwan and will affect the future of Taiwanese society.

Most immigrant women arrive in Taiwan from resource-limited countries, which may not have strict environmental policies. Thus, these women were exposed to elevated risks of pollution such as particulate matter and metals in their home countries (Yoshitsugu Hayashi 2004). Recently, a study suggested that exposure to combustion particles is consistently associated with oxidative DNA and lipids damage in humans, and such oxidative damage measurements may be used as biomarkers to determine the biologically effective dose of exposure (Moller and Loft 2010). This study chooses lipid peroxidation (Malondialdehyde (MDA)) and cellular antioxidant (Superoxide dismutases (SODs)) to represent environmental oxidative stress. According to our pilot study, there are variations in the blood lead levels (BLLs) in the immigrants of Asian nationalities, and BLLs decreased with an increasing in the length of time the immigrants resided in Taiwan (Wu et al. 2009). Many studies reported that environmental lead emissions resulted in significant health effects on the central nervous system, haem-synthesis, reproductive system, and psychological and neurobehavioral functions (Tong et al. 2000; Fewtrell et al. 2004; Bellinger 2005; ATSDR 2007). Therefore, we believe that migration may influence the interaction between genetics and environmental stress. Until now, however, there have been no studies with large datasets to confirm the effect of migration on metal exposure among this vulnerable population.

Previous studies on immigrants have selected native women as control group (Wu et al. 2009; Baron-Epel and Kaplan 2001). Because of major differences in socioeconomic status and race, native women are not a good comparison group. In our study, we selected recent (<=5 years) immigrants as the research group and less recent (>5 years) as a comparison group. The objectives of this study were to (a) explore differences between immigrant women and native women in lead-related genotypes, blood metal levels, and oxidative stress levels, and (b) explored if the duration of residence is an important determinant in changes in blood metal levels or oxidative stress levels after immigration.

2. METHODS

2.1 Study subjects and data collection

From August 2006 to December 2009, 239 immigrant women who had resettled in central Taiwan were recruited for this study at the Public Health Center (67 were from Mainland China, and 172 from Southeast Asia). We also invited 189 native women of a similar age ranges who live in the same area at the Center to participate. This study was approved by the Institutional Review Board of China Medical University Hospital, Taichung, Taiwan. Upon giving consent, the subjects were interviewed in person using a structured questionnaire to collect information on: (a) demographic characteristics including originating countries, years living in Taiwan, educational level, occupation, (b) lifestyle behaviors, including smoking status, environmental tobacco exposure, and drinking, and (c) uses of Chinese herbal medicine and contraceptive drugs. Each participant also underwent a blood draw with two vacutainer lead-free plastic tubes with/without K_2EDTA after an overnight fast (>10 h). The blood was collected into one EDTA sample tube for plasma and another for serum, and these tubes were centrifugation at 1500 g for 10min. Plasma and serum samples were stored in aliquots at -80°C until analysis. The blood was assessed for the concentration of Triglyceride (TG), Total Cholesterol (T-CHOL), low-density lipoprotein (LDL), and high-density lipoprotein (HDL) (Hitachi 912 autoanalyser).

2.2 Measurement of blood metals levels

The blood metals levels (lead, cadmium, manganese, copper, zinc, and selenium) were analyzed using an inductively coupled plasma mass spectrometer (Perkin Elmer SCIEX DRC II ICP-MS, Waltham, Massachusetts, U.S.A). The multi-element analytical method of whole blood was performed based on US CDC 2004 Blood Lead, Cadmium and Mercury ICPDRCMS Method No. ITB001A, following standard quality control procedures (CDC 2004). An ICP multi-element standard solution Ⅳ

(23 elements in 1 mol/L nitric acid, 1000±10 mg/L, MERCK, Darmstadt, Germany) was used to prepare the standard solution and to validate the metals content in the blood as part of quality control.

2.3 Oxidative Stress indices

The measurement of the Thiobarbituric Acid Reactive Substances (TBARS) is a well-established method for screening and monitoring MDA, a naturally occurring product of lipid peroxidation. Lipid peroxidation is a well-established mechanism of cellular injury and is used as an indicator of oxidative stress (Armstrong and Browne 1994; Yagi 1998). The MDA analysis in plasma was performed with a kit purchased from Cayman chemicals (Catalog No. 10009055—Cayman Chemical, Ann Arbor, MI, USA). In this procedure, the MDA-Thiobarbituric Acid (TBA) adduct formed through the reaction of MDA and TBA under high temperature (90-100°C) and acidic conditions were measured fluorometrically at an excitation wavelength of 530 nm and an emission wavelength of 550 nm using a Plate Chameleon Multi-technology Plate Reader (Hidex, Turku, Finland).

SODs are metalloenzymes that catalyze the dismutation of the superoxide anion to molecular oxygen and hydrogen peroxide and thus, form a crucial part of the cellular antioxidant defense mechanism. The amount of SOD present in cellular and extracellular environments is crucial for the prevention of diseases linked to oxidative stress (Marklund 1980). SOD activity in plasma was determined using the SOD Assay Kit (Catalog No.: 706002—Cayman Chemical, Ann Arbor, MI, USA). The SOD Assay Kit utilizes a tetrazolium salt for detect superoxide radicals generated by xanthine oxidase and hypoxanthine. The SOD Assay Kit measures all three types of SOD (Cu/Zn, Mn, and FeSOD). Activity was expressed as units per mini liter (U/mL) SOD. Absorbance at 450 nm was measured in the Microplate Reader (UVM340; Asys Hitech GmbH, Eugendorf, Austria).

2.4 Genotyping of polymorphisms

Genomic DNA was extracted from whole blood by using High Pure PCR Template Preparation Kit (Roche Diagnostics, Penzberg, Germany). Genotyping of *ALAD*, *HFE (H63D)*, *TF (P570S)*, and *VDR* (*folk*, *bsml*, *apal)* were performed using commercially available Pre-made TaqMan® Genotyping assays (Applied Biosystems Inc.). The TaqMan® PCR was performed according to the manufacturer's standard PCR protocol. Each sample underwent 50 amplification cycles using the ABI GeneAmp® PCR System 9700. Fluorescent signals of the two probes were analyzed using the end-point fluorescent data from the ABI PRISM® 7900HT Sequence Detection System (Applied Biosystems Inc.). Genotype was determined automatically by Sequence Detection Software (Applied Biosystems Inc.). About 5% of samples were repeated as a quality control.

2.5 Statistical analysis

The mean resettlement time of the 239 immigrant women was five years at the time of blood lead sampling. We divided immigrants who were recent (≤5 years, n=137) and less recent (>5 years, n=102). In the data analyses, we compared the recent immigrants, less recent immigrants, and native women. We first compared the socio-demographic characteristics, menstruation status, and lifestyle factors among the three groups. The blood metal levels exhibited left-skewed distributions; therefore, we used and presented the nonparametric analysis and natural logarithm. We used the t-test and trend analysis to assess the difference between means, and we used the χ^2-test to compare the frequency distributions among groups. A linear regression model was used to assess the association between different groups and metals levels while also controlling for covariates. A logistic regression model was used to assess the association between different groups and oxidative stress levels while also controlling for covariates. The statistical analyses were performed using SPSS, version 15.0, for Windows. All statistical tests were two-sided with $p<0.05$ as the level of statistical significance.

3. RESULTS

In our analyses, we compared the recent immigrants (≤5 years, research group 1), less recent immigrants (>5 years, control group 1) and native women (control group 2). Compared with native study participants, recent immigrant women were slightly younger (mean age 27.9 vs. 30.0 years, p=0.09), had lower BMI (p<0.001), less education (p=0.002) and lower family income (p=0.001). Compared with natives, they also had statistically significantly less cigarette use, environmental tobacco smoke exposure, and alcohol use. Recent immigrants and less recent immigrants had similar socioeconomic state and life habits, but not family income (Table 1).

We selected lead-related genotypes including *ALAD, HFE (H63D), TF (P570S)*, and *VDR* (*folk, bsml, apal)* to study the gene that originated differed by race. As shown in table 2, there were no statistically significant differences in these genotypes between the three groups. Therefore, the genetic variations in our study populations were similar and could not affect blood metal levels in the comparison of the three groups.

As shown in table 3, compared with native women, recent immigrants had lower TG (76.50 ± 38.70 vs. 136.20 ± 99.59 μg/dl; p=<0.001) and higher HDL-CHOL (58.01 ± 12.24 vs. 53.35 ± 12.86 mg/l; p=0.015). Compared with less recent immigrants and native women, immigrants exhibited a significant decreasing trend in TG and significantly increasing trend in HDL-CHOL as they resided for a longer period of time in Taiwan.

In the analysis on the levels of metals in the blood, the group of recent immigrants had higher blood metal levels (lead, cadmium, manganese, and copper) and lower blood selenium level than native women. Among the three groups, we found a significantly decreasing trend in blood metal levels (lead, cadmium, and copper) and significantly increasing trend in blood selenium level. In the oxidative stress results, recent immigrants had a higher MDA concentration than less recent immigrants (3.77 ± 3.36 vs. 2.48 ± 2.83 μM; p=0.001).

We performed multiple linear regression analysis to identify significant predicators of blood metals levels. We adjusted for city of data collection (Nantou County/Taichung city), age (≥30yrs or <30yrs), BMI (≥23 or <23), education level, cigarette smoking, environmental tobacco smoke exposure, alcohol use, and we found that compared with natives, recent immigrants had higher blood metal levels (lead, manganese, and copper), and slight lower blood selenium levels. The blood lead and manganese levels in less recent immigrants were not different from those in the native women; however, the blood copper and selenium levels were still higher in the less recent immigrants than in the native women (Table 4).

Multiple logistic regression analysis showed that, compared with natives, recent immigrants had significantly higher odds of having ≥ 3.40 μM MDA the average level for the entire study population (odds ratio (OR) = 2.855; 95% confidence interval (CI), 1.071–7.611); however, less recent immigrants were not at increased odds compared with natives. Compared with subjects with BMI <23, the subjects with BMI ≥23 also had higher odds (OR = 1.915; 95% CI, 0.985–3.720) (Table 5).

4. DISCUSSION

This study confirms duration of residence is an important determinant in the change of blood metal levels and oxidative stress levels after immigration. During their first five years in Taiwan, immigrant women are at risk for elevated blood metal levels (lead, cadmium, manganese, copper, and zinc). A significantly decreasing trend in blood metals levels (lead, cadmium, and copper) and significantly increasing trend in blood selenium level was observed with the duration of residence. This phenomenon of “when in Rome, do as the Romans do” also appeared in the evolution of environmental stress in these vulnerable population.

The recent immigrant women were at risk for elevated BLLs. According to previous studies, BLLs in Asian women have varied; reported rates are 19.4 μg/dl in Lucknow City, India, in 1994, to 5.7 μg/dl in Mainland China in 1997, 3.4 μg/dl in Manila, Philippines in 1998, 6.5 μg/dl in Kuala Lumpur, Malaysia in 1999, and 3.2 μg/dl in Bangkok, Thailand in 1999, 3.4 μg/dl in Tainan, Taiwan in 1996 and 2.6 μg/dl in Kaohsiung, Taiwan in 2003 (Ikeda et al. 2000; Yang et al. 2007). These data agree with our finding that BLLs were slighter higher in immigrant population than in native people. The study indicated that some Asian countries ban the use of leaded gasoline in vehicles, while others do not (Hayashi et al. 2004). Because leaded petroleum has contaminated air, dust, soil, drinking water and food crops, it increased the human blood lead burden to harmful levels (Landrigan 2002). To our knowledge, the measurement of lead level in bone is the representative method to assess long-term lead exposure. Although our study did not measure the bone lead, many studies have revealed a high correlation between blood lead and bone lead (ATSDR 2007; Kehoe 1961; Rabinowitz et al. 1976; Papanikolaou et al. 2005). Blood lead measurements should parallel to the long-term lead accumulated in the bone or soft-tissues among subjects. In the article entitled “Blood lead in the 21st Century:

The sub-microgram challenge", the authors mentioned that immigrants from industrial or late-industrial nations may unknowingly carry a locally acquired endogenous bone lead burden that will be a potential source of blood lead for decades (Amaya et al. 2010).

We also observed that the duration of residence in Taiwan was a determinant of the decrease in BLLs among immigrants. These resulted differed from those of a previous urban pollution study. Hernandez et al. observed that time living in Mexico City was a significant linear predictor of bone lead. Compared to women who had lived 5 years or less in the Mexico City area, those who had lived 20 or more years in Mexico City had significantly higher levels of bone lead (9.6 pig Pb/g more in the patella and 4.8 more in the tibia) (Hernandez-Avila et al. 1996). Our study suggested that the environmental lead exposure in Taiwan was lower than in the immigrants' country of origin and that the immigrants' blood lead measurements decreased with increased time spent in Taiwan. Medical treatment of individuals with overt lead intoxication, these involves decontamination, supportive care, and judicious use of chelating agents (Kosnett et al. 2007). We believe that by leaving their original countries, immigrants undergo a type of decontamination process as well. According to a previous study, however, pregnant women are advised to avoid occupational or avocational lead exposure that would result in blood lead concentrations of > 5 μg/dL (Kosnett et al. 2007). Elevated BLLs among immigrant women is a problem for the health of their offspring.

Immigrant women who had lived five years or less in Taiwan had 2.8 times the risk of oxidative damage than natives. Lipid peroxidation is a well-established mechanism of cellular injury and is used as an indicator of oxidative stress (Armstrong and Browne 1994; Yagi 1998). Air pollution, nutritional status, chronic diseases and genetic factors are main candidates to determine susceptibility to oxidative stress-related effects (Romieu et al. 2008). The subjects in this study were normal and younger, and our study population was homogeneous with regard to genetic variations. Hence, past pollution exposure and different nutritional statuses were the main factors affecting oxidative damage in this population. However, more data on the possible pathways of oxidative damage in this vulnerable population are needed.

Lax environmental regulations or badly enforced laws in developing countries are the main factor in pollution exposure (Hayashi et al. 2004; Amaya et al. 2010). These may also be reasons why recent immigrant women have elevated blood metal levels (cadmium, manganese, copper, and zinc) when migrating to Taiwan, and then, their blood metal levels gradually decline the longer they stay in Taiwan. In addition, immigrants have lower TG, and lower blood selenium levels, which reflect their poor home environment, poor nutrition, and low socioeconomic status (Goel et al. 2004).

This study confirmed that the duration of residence is an important determinant in the change in blood metal levels and oxidative stress levels after immigration. Elevated BLLs in immigrant women may serve as a warning sign for health care providers to be aware of problems that may occur in the offspring of these women. With the growing immigrant population in Taiwan, early public health intervention strategies, including screening and prevention programs, are an important opportunity to prevent metal-related chronic illnesses in this vulnerable population. We suggest that this vulnerable population should delay having children for a period of time after immigration.

REFERENCES

Nations U. 2005. Socially Vulnerable Groups: Selected Issues: Tackling Emerging Issues in International Migration. United Nations publication.

Ministry of the Interior ROC. 2007. The Statistics of Marriage Registration and Number of Birth by Bride's Nationality in Taiwan. (Affairs tdoHR, ed).

Yoshitsugu Hayashi KD, Masaharu Yagishita, and Masako Kuwata. 2004. Urban Transport Sustainability: Asian Trends, Problems and Policy Practices. European Journal of Transport and Infrastructure Research 4(1): 27-45.

Moller P, Loft S. 2010. Oxidative Damage to DNA and Lipids as Biomarkers of Exposure to Air Pollution. Environmental Health Perspectives 118(8): 1126-1136.

Wu WT, Liou SH, Lin KJ, Liu TE, Liu SH, Chen CY, et al. 2009. Changing blood lead levels and DNA damage (comet assay) among immigrant women in Taiwan. Sci Total Environ 407(23): 5931-5936.

Tong S, McMichael AJ, Baghurst PA. 2000. Interactions between environmental lead exposure and sociodemographic factors on cognitive development. Arch Environ Health 55(5): 330-335.

Fewtrell LJ, Pruss-Ustun A, Landrigan P, Ayuso-Mateos JL. 2004. Estimating the global burden of disease of mild mental retardation and cardiovascular diseases from environmental lead exposure. Environ Res 94(2): 120-133.

Bellinger DC. 2005. Teratogen update: lead and pregnancy. Birth Defects Res A Clin Mol Teratol 73(6): 409-420.

ATSDR, ed. 2007. Toxicological Profile for Lead: Agency for Toxic Substances and Disease Registry.

Baron-Epel O, Kaplan G. 2001. Self-reported health status of immigrants from the former Soviet Union in Israel. Isr Med Assoc J 3(12): 940-946.

CDC. 2004. Laboratory Procedure Manual- Lead, Cadmium, and Mercury in Whole Blood. Atlanta, GA 30333: Centers for Disease Control and Prevention.

Armstrong D, Browne R. 1994. The analysis of free radicals, lipid peroxides, antioxidant enzymes and compounds related to oxidative stress as applied to the clinical chemistry laboratory. Adv Exp Med Biol 366: 43-58.

Yagi K. 1998. Simple assay for the level of total lipid peroxides in serum or plasma. Methods Mol Biol 108: 101-106.

Marklund S. 1980. Distribution of CuZn superoxide dismutase and Mn superoxide dismutase in human tissues and extracellular fluids. Acta Physiol Scand Suppl 492: 19-23.

Ikeda M, Zhang ZW, Shimbo S, Watanabe T, Nakatsuka H, Moon CS, et al. 2000. Exposure of women in general populations to lead via food and air in East and Southeast Asia. Am J Ind Med 38(3): 271-280.

Yang YH, Liou SH, Yang CY, Sung FC, Wu CC, Wu TN. 2007. Increased blood lead concentration during menstruation in teen female students. Sci Total Environ 382(2-3): 224-227.

Hayashi Y, Doi K, Yagishita M, Kuwata M. 2004. Urban Transport Sustainability: Asian Trends, Problems and Policy Practices. Europ J Transp Infrast Res 4: 27-45.

Landrigan PJ. 2002. The worldwide problem of lead in petrol. Bull World Health Organ 80(10): 768.

Kehoe RA. 1961. The metabolism of lead in man in health and disease. Arch Environ Health 2: 418-422.

Rabinowitz MB, Wetherill GW, Kopple JD. 1976. Kinetic analysis of lead metabolism in healthy humans. J Clin Invest 58(2): 260-270.

Papanikolaou NC, Hatzidaki EG, Belivanis S, Tzanakakis GN, Tsatsakis AM. 2005.

Lead toxicity update. A brief review. Med Sci Monit 11(10): RA329-336.

Amaya MA, Jolly KW, Jr NEP. 2010. Blood lead in the 21st Century: The sub-microgram challenge. Journal of Blood Medicine 1: 71-78.

Hernandez-Avila M, Gonzalez-Cossio T, Palazuelos E, Romieu I, Aro A, Fishbein E, et al. 1996. Dietary and environmental determinants of blood and bone lead levels in lactating postpartum women living in Mexico City. Environ Health Perspect 104(10): 1076-1082.

Kosnett MJ, Wedeen RP, Rothenberg SJ, Hipkins KL, Materna BL, Schwartz BS, et al. 2007. Recommendations for medical management of adult lead exposure. Environ Health Perspect 115(3): 463-471.

Romieu I, Castro-Giner F, Kunzli N, Sunyer J. 2008. Air pollution, oxidative stress and dietary supplementation: a review. Eur Respir J 31(1): 179-197.

Goel MS, McCarthy EP, Phillips RS, Wee CC. 2004. Obesity among US immigrant subgroups by duration of residence. Jama-Journal of the American Medical Association 292(23): 2860-2867.

Table 1　Demeographic charateristics between immigrant women and natives

Dependent variables	Immigrants Residing years<=5 yrs (N=137)		Immigrants Residing years>5 yrs (N=102)		Natives (N=189)		*P*-value [a]	*P*-value
	Mean	*(SD)*	*Mean*	*(SD)*	*Mean*	*(SD)*		
Age (years)	27.90	(6.26)	30.63	(5.10)	30.04	(8.33)	0.090	0.454
BMI	21.17	(2.88)	21.78	(2.88)	23.46	(4.83)	<0.001	<0.001
Residing years in Taiwan (years)	2.18	(1.23)	8.42	(3.94)			<0.001	
	N	*(%)*	*N*	*(%)*	*N*	*(%)*		
Education							0.822	0.002
≦junior high school	30	(21.9)	24	(23.5)	10	(5.3)		
senior high school	49	(35.8)	42	(41.2)	33	(17.5)		
≧junior college	44	(32.1)	31	(30.4)	57	(30.2)		
Family income per month (NT$)							0.010	0.001
≦19999	20	(14.6)	29	(28.4)	64	(33.9)		
20000~39999	50	(36.5)	37	(36.3)	49	(25.9)		
≧40000	52	(38.0)	24	(23.5)	73	(38.6)		
Cigarette smoking							0.082	0.013
Passive smoker	3	(2.2)	5	(4.9)	17	(9.0)		
Nonsmoker	129	(94.2)	94	(92.2)	169	(89.4)		
Former smoker	5	(3.6)	0	(0.0)	2	(1.1)		
Environmental tobacco smoke							0.849	0.040
Yes	41	(29.9)	29	(28.4)	78	(41.3)		
No	95	(69.3)	71	(69.6)	111	(58.7)		
Alcohol use							0.427	<0.001
Yes	6	(4.4)	6	(5.9)	35	(18.5)		
No	132	(96.4)	94	(92.2)	151	(79.9)		
Former used	0	(0.0)	1	(1.0)	4	(2.1)		
Ever worked in lead factories [c]							0.607	0.702
Yes	11	(8.0)	10	(9.8)	13	(6.9)		
No	128	(93.4)	92	(90.2)	178	(94.2)		
Traditional Chinese medicine							0.984	0.135
Yes	17	(12.4)	13	(12.7)	36	(19.0)		
No	116	(84.7)	88	(86.3)	153	(81.0)		

[a] Immigrants that residing years<=5yrs compared with those residing years >5yrs

[b] Immigrants that residing years<=5yrs compared to natives.

[c] Lead battery factory, metal smelting factory, solder factory, printing factory, PVC stabilizers manufactory, glass manufacturing.

Table 2　Genotype between immigrant women and natives

Dependent variables	Immigrants Residing years<=5 yrs (N=137)		Immigrants Residing years>5 yrs (N=102)		Natives (N=189)		*P*-value [a]	*P*-value [b]
	n	*(%)*	*n*	*(%)*	*n*	*(%)*		
Genotype								
*ALAD*_rs1800435							0.471	0.301
Wildtype C/C	112	(81.8)	76	(74.5)	148	(78.3)		
Variant G/C	11	(8.0)	5	(4.9)	9	(4.8)		
*HFE*_rs1799945							0.173	0.057
Wildtype C/C	108	(78.8)	74	(72.5)	147	(77.8)		
Variant C/G+G/G	15	(10.9)	5	(4.9)	8	(4.2)		
*TF*_rs1049296							0.331	0.890
WildtypeC/C	75	(54.7)	45	(44.1)	97	(51.3)		
Variant C/T	43	(31.4)	34	(33.3)	52	(27.5)		
Variant T/T	5	(3.6)	1	(1.0)	8	(4.2)		
*VDR*_rs7975232							0.607	0.332
WildtypeC/C	55	(40.1)	42	(41.2)	75	(39.7)		
Variant C/A	52	(38.0)	30	(29.4)	70	(37.0)		
Variant A/A	16	(11.7)	9	(8.8)	12	(6.3)		
*VDR*_rs1544410							0.350	0.462
Wildtype C/C	107	(78.1)	73	(71.6)	141	(74.6)		
Variant C/T	16	(11.7)	7	(6.9)	16	(8.5)		
*VDR*_rs10735810							0.160	0.081
Wildtype G/G	39	(28.5)	34	(33.3)	54	(28.6)		
Variant A/G	50	(36.5)	33	(32.4)	76	(40.2)		
Variant A/A	34	(24.8)	14	(13.7)	26	(13.8)		

[a] Immigrants that residing years<=5yrs compared with those residing years >5yrs
[b] Immigrants that residing years<=5yrs compared to natives.

Table 3 Blood metals levels and Oxidative stress between immigrant women and natives

Dependent variables	Immigrants Residing years<=5 yrs (N=137)		Immigrants Residing years>5 yrs (N=102)		Natives (N=189)		*P*-value [a]	*P*-value [b]	*P*-value for trend
	Mean	*(SD)*	*Mean*	*(SD)*	*Mean*	*(SD)*			
Blood lipids test									
TG (mg/dl)	76.50	(38.70)	83.54	(56.06)	136.20	(99.59)	0.359	<0.001	<0.001
T-CHOL (mg/dl)	177.83	(37.28)	169.83	(32.46)	182.63	(40.66)	0.149	0.418	0.311
HDL-CHOL (mg/dl)	58.01	(12.24)	53.00	(9.52)	53.35	(12.86)	0.005	0.015	0.012
LDL-CHOL (mg/dl)	101.99	(31.93)	97.10	(28.31)	99.31	(36.51)	0.305	0.607	0.629
Blood metals levels									
Pb (μg/dl)	2.67	(1.28)	2.40	(0.96)	2.33	(1.11)	0.070	0.003	0.003
Cd (μg/l)	0.85	(0.54)	0.74	(0.44)	0.74	(0.64)	0.166	0.027	0.029
Mn (μg/l)	16.72	(5.67)	14.23	(4.78)	15.76	(6.87)	<0.001	0.046	0.066
Cu (μg/l)	932.4	(752.9)	879.9	(272.1)	774.3	(316.6)	0.701	<0.001	<0.001
Zn (μg/l)	8039.2	(7407.6)	9165.4	(3483.1)	6920.8	(2760.5)	<0.001	0.800	0.495
Se (μg/l)	148.1	(41.4)	181.7	(40.4)	179.2	(43.9)	<0.001	<0.001	<0.001
Oxidative stress levels									
MDA (μM)	3.77	(3.36)	2.48	(2.83)	3.67	(2.87)	0.001	0.832	0.613
SOD (U/mL)	13.43	(4.59)	13.81	(4.91)	12.98	(4.72)	0.321	0.375	0.236

[a] Immigrants that residing years<=5yrs compared with those residing years >5yrs

[b] Immigrants that residing years<=5yrs compared to natives.

Table 4 Multiple linear regression model for determinants of blood metals levels

Variables	B	SE	*p*-value
Dependent varables: Ln Pb[a] (Enter)			
Intercept	0.755	0.144	<0.001
Cities of data collection (Nantou County/Taichung city)	-0.165	0.067	0.014
Age (age>=30yrs /age<30yrs)	0.025	0.056	0.651
BMI (BMI>=23 /BMI<23)	0.033	0.061	0.588
Education of subjects			
senior high school /<junior high school	0.093	0.073	0.208
≧senior college /<junior high school	0.045	0.075	0.548
Cigarette smoking			
Passive smoker/ Nonsmoker	0.009	0.116	0.937
Former smoker/ Nonsmoker	0.275	0.204	0.178
Environmental tobacco smoke (Yes/No)	-0.084	0.060	0.165
Alcohol use			
Yes/No	0.018	0.090	0.845
Former used/No	0.124	0.222	0.576
Residing years			
Immigrants residing years>5 yrs/ Natives	0.130	0.076	0.090
Immigrants residing years<=5 yrs/ Natives	0.329	0.088	<0.001
Dependent varables: Ln Cd[a] (Enter)			
Intercept	-0.716	0.211	0.001
Cities of data collection (Nantou County/Taichung city)	0.147	0.107	0.169
Age (age>=30yrs /age<30yrs)	0.199	0.084	0.018
BMI (BMI>=23 /BMI<23)	0.142	0.091	0.120
Education of subjects			
senior high school /<junior high school	-0.034	0.108	0.754
≧senior college /<junior high school	-0.054	0.111	0.627
Cigarette smoking			
Passive smoker/ Nonsmoker	0.481	0.180	0.008
Former smoker/ Nonsmoker	0.139	0.294	0.637
Environmental tobacco smoke (Yes/No)	0.040	0.089	0.655
Alcohol use			
Yes/No	0.024	0.133	0.858
Former used/No	0.181	0.321	0.574
Residing years			
Immigrants residing years>5 yrs/ Natives	0.020	0.116	0.860
Immigrants residing years<=5 yrs/ Natives	0.072	0.136	0.595

Table 4 Multiple linear regression model for determinants of blood metals levels

Variables	B	SE	*p*-value
Dependent varables: Ln Mn[a] (Enter)			
Intercept	2.716	0.108	<0.001
Cities of data collection (Nantou County/Taichung city)	-0.118	0.055	0.032
Age (age>=30yrs /age<30yrs)	0.062	0.043	0.152
BMI (BMI>=23 /BMI<23)	0.024	0.047	0.605
Education of subjects			
senior high school /<junior high school	-0.136	0.056	0.016
≧senior college /<junior high school	-0.034	0.058	0.556
Cigarette smoking			
Passive smoker/ Nonsmoker	0.112	0.093	0.229
Former smoker/ Nonsmoker	0.222	0.151	0.144
Environmental tobacco smoke (Yes/No)	-0.055	0.046	0.227
Alcohol use			
Yes/No	-0.149	0.069	0.031
Former used/No	-0.043	0.165	0.796
Residing years			
Immigrants residing years>5 yrs/ Natives	0.044	0.059	0.454
Immigrants residing years<=5 yrs/ Natives	0.266	0.070	<0.001
Dependent varables: Ln Cu[a] (Enter)			
Intercept	6.403	0.122	<0.001
Cities of data collection (Nantou County/Taichung city)	0.016	0.056	0.779
Age (age>=30yrs /age<30yrs)	0.045	0.047	0.341
BMI (BMI>=23 /BMI<23)	-0.071	0.052	0.171
Education of subjects			
senior high school /<junior high school	-0.011	0.062	0.860
≧senior college /<junior high school	-0.006	0.064	0.922
Cigarette smoking			
Passive smoker/ Nonsmoker	0.063	0.099	0.522
Former smoker/ Nonsmoker	0.703	0.157	<0.001
Environmental tobacco smoke (Yes/No)	0.102	0.051	0.046
Alcohol use			
Yes/No	-0.325	0.076	<0.001
Former used/No	-0.042	0.185	0.822
Residing years			
Immigrants residing years>5 yrs/ Natives	0.172	0.065	0.008
Immigrants residing years<=5 yrs/ Natives	0.155	0.075	0.038

Table 4 Multiple linear regression model for determinants of blood metals levels

Variables	B	SE	*p*-value
Dependent varables: Ln Zn[a] (Enter)			
Intercept	8.979	0.164	<0.001
Cities of data collection (Nantou County/Taichung city)	-0.137	0.076	0.073
Age (age>=30yrs /age<30yrs)	0.121	0.064	0.060
BMI (BMI>=23 /BMI<23)	-0.095	0.069	0.174
Education of subjects			
senior high school /<junior high school	-0.048	0.083	0.569
≧senior college /<junior high school	0.022	0.086	0.798
Cigarette smoking			
Passive smoker/ Nonsmoker	0.290	0.133	0.029
Former smoker/ Nonsmoker	-0.502	0.212	0.018
Environmental tobacco smoke (Yes/No)	-0.011	0.068	0.867
Alcohol use			
Yes/No	-0.126	0.102	0.221
Former used/No	0.346	0.249	0.167
Residing years			
Immigrants residing years>5 yrs/ Natives	0.133	0.087	0.127
Immigrants residing years<=5 yrs/ Natives	-0.059	0.100	0.557
Dependent varables: Se[a] (Enter)			
Intercept	180.312	12.988	<0.001
Cities of data collection (Nantou County/Taichung city)	2.134	5.998	0.722
Age (age>=30yrs /age<30yrs)	-5.200	5.051	0.304
BMI (BMI>=23 /BMI<23)	0.023	5.492	0.997
Education of subjects			
senior high school /<junior high school	-14.962	6.617	0.025
≧senior college /<junior high school	-13.432	6.780	0.049
Cigarette smoking			
Passive smoker/ Nonsmoker	15.943	10.496	0.130
Former smoker/ Nonsmoker	-38.897	16.743	0.021
Environmental tobacco smoke (Yes/No)	-2.191	5.438	0.687
Alcohol use			
Yes/No	-0.312	8.109	0.969
Former used/No	21.406	19.744	0.279
Residing years			
Immigrants residing years>5 yrs/ Natives	20.367	6.888	0.003
Immigrants residing years<=5 yrs/ Natives	-14.687	7.932	0.065

Table 5 Multiple linear regression model for determinants of oxidative stress levels.

Variables	B	SE	ORs	95%CI
Dependent varables: MDA(high/low)[a] (Enter)				
Cities of data collection (Nantou County/Taichung city)	0.733	0.376	2.082	0.997 - 4.348
Age (age>=30yrs /age<30yrs)	-0.281	0.312	0.755	0.410 - 1.391
BMI (BMI>=23 /BMI<23)	0.649	0.339	1.915	0.985 - 3.720
Education of subjects				
senior high school /<junior high school	0.048	0.389	1.049	0.489 - 2.250
≧senior college /<junior high school	-0.140	0.399	0.869	0.398 - 1.900
Cigarette smoking				
Passive smoker/ Nonsmoker	-1.262	1.104	0.283	0.033 - 2.465
Former smoker/ Nonsmoker	0.275	0.974	1.316	0.195 - 8.886
Environmental tobacco smoke (Yes/No)	0.253	0.319	1.288	0.690 - 2.405
Alcohol use				
Yes/No	-0.981	0.618	0.375	0.112 - 1.258
Former used/No	1.500	1.073	4.482	0.547 - 36.743
Residing years				
Immigrants residing years>5 yrs/ Natives	0.324	0.446	1.382	0.577 - 3.312
Immigrants residing years<=5 yrs/ Natives	1.049	0.500	2.855	1.071 - 7.611

計畫成果自評

本研究結果發現在新移民女性高血鉛的比例高於本地女性，截至目前為止台灣尚未有完整建立新移民女性體內重金屬，在應用上亦能提供政府機關有利的依據及參考，考慮不同國籍的差異點，對現今台灣多元化族群提供更有效率的生理危害的篩檢及早期治療的預防工作，已減少相關重金屬所帶來的慢性疾病。此外本研究亦證實來台年數對於新移民女性體內血中重金屬與氧化傷害程度是一個重要因子，未來也可考量新移民女性來台時生產的時間點，相信藉由環境的改善與生活適應性可以更加有利於下一代的健康。本研究為已將目前研究結果整理完畢並投稿至 SCI 雜誌上。