ORIGINAL ARTICLES

Pilot survey on blood lead levels in non-occupationally exposed workers at a CDC in Vietnam using the GF-AAS technique

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ABSTRACT

Objective: The present study aimed to develop an analytical method for detecting trace amounts to elevated levels of lead in human blood using an atomic absorption spectrophotometer (GF-AAS) technique and to apply this method in evaluating blood lead levels (BLLs) of non-occupationally exposed workers at a CDC in Vietnam in 2023.

Methods: A cross-sectional study design was applied. Validation of a GF-AAS method was performed on the basis of the Association of Analytical Chemists (AOAC) guidelines, and BLLs of 30 non-occupationally exposed workers were measured.

Results: The results showed that all validation parameters of the analytical method in this study meet the requirements of the Association of Analytical Chemists (AOAC). Evaluation of BLLs of non-occupationally exposed workers found that most workers has lead in their blood with the proportion of 93.0%. The min and max value of BLLs was in the range of 0 to 2.693 µg/dL. There was 13.3% of workers with the BLLs > 5.0 µg/dL, which is the level used for indicating an elevated BLL for surveillance purposes.

Conclusions: The GF-AAS method has both high accuracy and precision and meets the AOAC requirements for analysis of BLLs. The measured BLLs of non-occupationally exposed workers suggests that surveillance purposes for a large population in Vietnam are needed for health risk assessment in the future.

Keywords: *ASS, blood lead levels.*

INTRODUCTION

Metal induced toxicity is very well reported across the world. Metals like lead, copper, cadmium, mercury, nickel, iron and arsenic have ability to generate reactive radicals, leading to cellular damage, lipid bilayer, DNA and also depletion of enzyme activities. These metals generate reactive species, which in turn may cause neurotoxicity, hepatotoxicity, nephrotoxicity and infertility in human beings. Elements like manganese, selenium, nickel and molybdenum, although toxic at high levels, are actually required nutrients at lower levels. However, lead has no nutritional value or positive biological effect even at lower concentration. Exposure to lead can produce a negative impact on health of all age groups (1).

Lead persists in various environmental mediums, such as soil, air, drinking water, and homes, where it accumulates and does not degrade. The primary sources that significantly contribute to lead exposure include gasoline additives; food can solder; lead-based paints; ceramic glazes; drinking water systems; and

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cosmetic and folk remedies. Other significant exposures include inadequately controlled industrial emissions from lead smelters and battery recycling plants, contaminating both the environment and people in the vicinity. The highest level of environmental contamination is found to be associated with uncontrolled recycling operations, with the most highly exposed adults being those who work with lead (2-3).

The Institute for Health Metrics and Evaluation estimated that in 2019 lead exposure accounted for 0.90 million deaths and 21.7 million years lost to disability and death due to long-term health effects, with the highest burden in developing regions (4). Greater BLLs are linked to increased all-cause mortality in both men and women. Within the past decade, there have been numerous reports of lead poisoning in humans, particularly from developing countries faced with environmental and occupational lead exposure. Although the World Health Organization (WHO) has set a standard BLLs of 5.0 μg/dL for adults, the Environmental Health Committee of the Council of State and Territorial Epidemiologists (CSTE) indicated that a blood lead reference value (BLRV) >3.5 μg/dL is considered high. BLRV is used to identify patients with the highest BLLs in the population but is not indicative of a toxicity threshold. Adult lead toxicity is typically considered at mean BLL ≥10.0 μg/dL, but there is evidence linking long-term risks to chronic lead exposure below 10.0 μg/dL. Other studies indicate a correlation between higher BLLs and increased cardiovascular mortality in adults. In addition, lead is a strong inhibitor of δ-aminolevulinic acid dehydratase, affecting the spleen and hematopoietic system (5-7).

The common spectroscopic methods in trace element analysis in biological fluids are dithizone extraction, polarography, spectral analysis, atomic absorption spectrometry (AAS), and inductively coupled plasma atomic emission spectrometry. A graphite furnace atomic absorption spectrophotometer (GF-AAS) is a valuable, simple, and cost-effective spectrometric technique for the identification of lead absorbance in the human system. The GF-AAS method can be employed for the measurement of lead percentage in whole blood and urine, and the results acquired are helpful in biological monitoring and clinical diagnostic of work related to surrounding lead exposure. The GF-AAS method has been used frequently in laboratories and selected as the primary method for determination of BLLs in biochemical guidance of the Ministry of Health, Vietnam (8-11). Therefore, development of analytical methods using the GF-AAS technique is necessary and suitable with facilities in Centers for Disease Control and Prevention (CDCs) in provinces in Vietnam. Accordingly, the present study was conducted with 2 objectives: 1) to validate an analytical method for detecting trace amounts to elevated levels of lead in human blood using the GF-AAS technique and 2) to evaluate blood lead levels in non-occupationally exposed workers at the CDC of Bac Ninh in Vietnam.

METHODS

Study Design: The experimental and cross-sectional study.

Research subjects: Materials included standard lead solution (1g/L) with purity of 99.9% from Merk company, Seronorm™ Trace Elements Whole Blood, and blood samples (2.0 mL) of non-occupationally exposed workers obtained through an anual health check program at the CDC of Bac Ninh Province. The workers had no history of lead exposure in the working evironment. All the materials were stored at at 0^oC in a laboratory freezer until analysis.

Study site and time: This cross-sectional study was conducted from April to October 2023 at the CDC of Bac Ninh Province.

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Sample size and sampling method: For validation purpose: The samples included 1 sample of lead standard solution 20 µg/dL, 10 blood samples added with 0.5 µg/dL lead standard solution, 1 blood sample spiked with lead standard concentrations of 2.0; 4.0; 8.0 µg/dL, 1 standard material sample (Trace Elements Whole Blood L-1 of SERO).

For measurement of BLLs of non-occupationally exposed workers: 30 blood samples were obtained from all of the laboratory workers at the CDC

Study variables: For validation purpose: Calibration curve, limit of detection (LOQ), limit of quantitation (LOQ), the relative level of detection (R_{LOD}), the relative standard deviations for repeatability (RSDr), the relative standard deviations for reproducibility (RSD_R), recovery, and bias were measured based on the guidelines of AOAC.

For measurement of BLLs in workers: Blood lead levels were determined by GF-AAS method; and characteristics such as sex, age, living area, working units, and history of lead exposure were obtained from medical records.

Tools and methods of data collection: Blood samples (2.0 mL) were collected under sterile conditions using EDTA tubes for BLL measurements. Immediately after sampling, the blood had to be thoroughly mixed to avoid clotting during storage. The samples were stored in the laboratory refrigerator at 0°C until analysis. At the laboratory, the samples were processed accordingly. In a 100 mL volumetric flask, 5.0 mL of 10% Triton X-100, 2 mL of NH_4PO_4, and four drops of 70% HNO_3 were mixed and diluted to volume with deionized water to form the matrix modifier.

To prepare a multipoint calibration curve, 0; 1.0; 5.0; 10.0; 30.0, and 60.0 µg/dL working standard lead containing solutions were prepared in 1% HNO_3 solution. The final standard solutions were prepared by mixing 100 µL of each of the working standard solutions with 900 µL of matrix modifier in autosampler vessels to produce 1.0, 4.0, 8.0, 16.0, and 20.0 µg/dL, respectively. These standard solutions were set aside until the bubbles dissipated. The samples were then prepared by mixing 100 µL of whole blood (with anticoagulant) with a 900 µL matrix modifier. BLLs were estimated using a graphite furnace atomic absorption spectrophotometer (GF-AAS). The BLL measurement method has been validated with an estimated detection limit of < 1.0 µg/L, which is suitable for evaluating lead levels in human blood.

Processing and analyzing data: Data were entered in and analyzed by Microsoft Excel. The continuous variables in the study (i.e., BLLs) were summarized as mean ± SD. The categorical variables, including age, gender, and occupational exposure, were presented as frequency or percentage.

Research ethics: This study was approved by the Ethics Committee of the University of Public Health under Decision No. 327/2023/YTCC-HD3 on 12 June 2023.

RESULTS

Analytical method validation

The analytical method is described by the validation parameters shown in Table 1. The calibration line for human plasma analysis was evaluated. The linearity is in the range of 1-20 µg/dL, and the regression coefficient (R^2) is of 0.999. By gradually increasing amount of lead in human blood sample, the determined LOD and LOQ values were 0.17 and 0.56 µg/dL, respectively. All the validated parameters meet the requirements of the Association of Analytical Chemists (AOAC) for the purpose of blood lead evaluation (12).

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Table 1. Validation parameters by GF-AAS

Validation parameters	Results	AOAC guidelines
Calibration curve	R = 0.999 (y = 0.0161x + 0.0003)	$0.995 \leq R \leq 1$
Limit of detection (LOQ)	0.17 µg/dL	$4 < R_{LOD} < 10$
Limit of quantitation (LOQ)	0.56 µg/dL	
R_{LOD}	0.96 µg/dL	
The relative standard deviations for repeatability (RSDr)	1.7% (at 2 µg/dL)	< 15%
	0.9% (at 4 µg/dL)	
	1.2% (at 8 µg/ dL)	
The relative standard deviations for reproducibility (RSD_R)	3.7% (at 2 µg/ dL)	< 15%
	2.1% (at 4 µg/ dL)	
	1.8% (at 8 µg/ dL)	
Recovery	91.6	80 - 110%
Bias	4.8%	< 20%

Determination of blood lead levels

General characterictics of the non-occupationally exposed workers

The characteristics of the non-occupationally exposed workers at the CDC of Bac Ninh are presented in Table 2. Approximately 90% of workers were less than 50 years old, with a mean age of 39 ± 7 years old, ranging from 29 to 58 years old. As for gender, 73.3% of workers were females. Majority of the workers lived in city area (76.7%). All workers had no history of lead exposure.

Table 2. General characteristics of subjects study

Characteristics		n	%
Sex	Male	8	26.7
	Female	22	73.3
Age	< 30	1	3.3
	30 – 50	26	86.7
	> 50	3	10.0
Living area	City	23	76.7
	Urban	7	23.3
Working units	Test laboratory	20	66.7
	Imaging laboratory	4	13.3
	Functional Examination laboratory	6	20.0
History of lead exposure	Yes	0	0
	No	30	100

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Blood lead levels of workers

Blood lead levels (BLLs) of the non-occupationally exposed workers at the CDC of Bac Ninh were evaluated by the validated GF-AAS method, and the results are presented in Table 3. Most workers had lead in their blood with the proportion of 93%. The mean, min and max of BLLs was 2.693 µg/dL, 0 µg/dL and 7.9 µg/dL, respectively. According to the regulations and recommendations for blood lead levels of the USA CDC shown in Table 4 (7), there were no workers with BLLs > 10.0 µg/dL, which is considered toxic level. However, there was 13.3% of workers with the BLLs > 5.0 µg/dL, which is the level used for indicating an elevated BLL for surveillance purposes (7).

Table 3. Blood lead levels

No	Values	Blood lead level (µg/dL) (n = 30)
1	Mean	2.693
2	Median	2.150
3	SD	2.091
4	Min	0
5	Max	7.9

Table 4. Regulations and recommendations for blood lead levels (BLLs)

No	Blood lead levels (µg/dL)	Regulations and recommendations
1	0	Ideal concentration
2	0.855	The typical BLL among adults in the United States
3	3.5	It is advisable for women who are or may become pregnant to avoid occupational lead exposure that would elevate the BLLs greater than or equal to 3.5 µg/dL
4	5.0	The level is used for indicating an elevated BLLs for surveillance purposes
5	< 10.0	The level increases blood pressure, the risk of hypertension, and the incidence of essential tremor
6	≥10.0	Lead poisoning

DISCUSSION

Analytical method validation

Laboratory diagnostic and screening studies of trace elements in biological fluids can be simple and more effective and can help diagnose metal toxicity. The preferred methods for such studies are Graphite Furnace Atomic Absorption Spectrometry (GF-AAS). Whole blood lead levels are the most widely used method to determine the absorbed dose in the human system. GF-AAS is simple, quick, repeatable, reliable, and cost-effective spectrometric technique for the identification of lead absorbance in human system. Therefore, the

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GF-AAS is a valuable method for biological monitoring and clinical diagnostic of work related or surrounding lead exposure (8-10).

Validation method is a routine process that demonstrates that analytical procedures are suitable for intended use. The analytical method is described by the validation parameters. According to AOAC/IEC 17025 guidelines (12), validations parameters such as calibration curve, limit of detection (LOQ), limit of quantitation (LOQ), the relative level of detection (R_{LOD}), the relative standard deviations for repeatability (RSDr), the relative standard deviations for reproducibility (RSD_R), recovery, bias were calculated and meet the requirements of the AOAC for the purpose of blood lead evaluation (12). In the present study, the obtained results (Table 1) were also similar to the validated data reported in previous studies (8-10). The working range of this method was designed by the lowest and highest concentration of lead in the sample for which it has been established that the procedure has an appropriate level of precision, accuracy, and linearity, which could be applied for determination of lead levels in blood samples with the highest concentration of 7.9 µg/dL.

Determination of blood lead levels of non-occupationally exposure workers

Blood lead tests are used to check a person's blood lead level to ensure workers are protected from lead exposure. Any amount of lead in the blood means a person was exposed to lead. A small amount of lead in the human body is vulnerable to affect physical as well as mental health. High BLLs can have significant negative health effects on the human body. Lead is particularly harmful to the central nervous system and cardiovascular system. High BLLs can have significant negative health effects on the human body. Lead is particularly harmful to the central nervous and cardiovascular system and can accumulate in the kidneys over time, leading to kidney damage. In addition, lead can also interfere with the development and maintenance of healthy bones (5-7).

There are several regulations/recommendations related to blood lead testing, blood lead levels, and lead exposure in the workplace. The Occupational Safety and Health Administration (OSHA) and a few state agencies regulate BLLs in workers. Other government agencies and non-government groups offer recommended lead exposure limits. BLLs of 0.855 µg/dL was the typical BLL among adults in the United States in 2017-2018. Regarding the BLLs of 3.5 µg/dL, the Council of State and Territorial Epidemiologists' (CSTE) blood lead reference value is 3,5 µg/dL. This value is used to identify adults and children whose blood lead levels are higher than the 97.5th percentile of adults and children nationwide. The California Department of Public Health (CDPH) recommends that, if the BLL is between 3.5 to 9.0 µg/dL, the BLL tests be repeated every 3 months for adults until their BLLs is less than 3.5 µg/dL. The American College of Occupational and Environmental Medicine (ACOEM) states it is advisable for women who are or may become pregnant to avoid occupational lead exposure that would elevate the BLLs greater than or equal to 3.5 µg/dL (7).

Considering the BLLs of 5.0 µg/dL, the ABLES program uses 5.0 µg/dL to indicate an elevated BLLs for surveillance purposes. If pregnant, the pregnant women should not exceed 5.0 µg/dL. The National Toxicology Program (NTP) concluded that people who are pregnant with BLLs even lower than 5.0 µg/dL can result in reduced fetal growth. The WHO has established a reference value of 5.0 µg/dL BLL as the threshold at which public health action is recommended. Below 10.0 µg/dL, the NTP concluded lead increases blood pressure, the risk of hypertension, and the incidence of essential tremor. For the BLLs of 10.0 µg/dL, ACOEM and CDPH recommend repeat BLL tests every two months (7).

In the present study, the median concentration of lead in participants was 2.15 μg/dL which was similar several studies which reported BLLs of around 2.40 μg/L (13-15). However, this concentration was in contrary to other studies which reported higher BLLs (16-17). The differences in BLLs among countries may be due to other factors such as lifestyles, dietary habits and different inter individual metabolism and variation in eliminating foreign intermediates.

In the present study, the non-occupationally exposed workers are primary health-care workers at CDC of Bac Ninh, Vietnam. Notably, while not being exposed to occupational lead or air pollution zones, most workers had lead in their blood (93%) and there was 13.3% of workers with the BLLs exceeding 5.0 μg/dL. This may be due to potential confounding factors affecting BLL measurements , such as lifestyles, smoking, dietary habits. The WHO has established a reference value of 5.0 μg/dL BLLs as the threshold at which public health action is recommended (7). One of the primary reasons for the presence of BLLs in non-occupationally exposed workers could be due to lead-contaminated dust in contaminated air, water or soil. So far, there is no large-scale monitoring of blood lead levels (BLLs) in the Vietnamese general population. Therefore, the identification of lead in the blood samples of most non-occupationally exposed workers is significant for public health notice.

The present study was not without limitations. It involved a relatively small study samples (n = 30) due the available number of laboratory workers at the CDC center. In addtion, BLLs were also not measured by another method for comparison due the availability of instrument in the laboratory. Also, all of the workers resided in an area of a province in Vietnam, so the results may not be representative of the general population of Vietnam. To improve the representative of results, more extensive data sets, and enhanced data collection methods are suggested in the future. In addition a follow-up study can be useful to evaluate the trend of lead concentration in the large population of non-occupationally exposed workers in other areas.

CONCLUSION

This paper presents simple and fast method of lead determination in blood samples using the GF-AAS method, which could be applied for lead determination in CDCs. The findings showed that lead levels in the blood of non-non-occupationally exposed workers did not exceed the toxic blood lead reference levels (>10.0 μg/dL) and did not pose a major threat to the respondents' health. However, knowing the BLLs in non-occupationally exposed workers offers necessary information to health policymakers for public health measures, and preventive interventions in the community as the monitoring of heavy metals concentrations in the community is important to assess their impact on human health. In addition, it also provides baseline data for future researches on lead exposure in a large population in Vietnam. For future study, evaluation of the trend of lead concentration in the large population of non-occupationally exposed workers in other areas should be investigated. In addition, policy regulation related to lead exposure, monitoring frequency and program should be considered for proper revision or update.

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