IJOEM
International Journal of Occupational and Environmental Medicine

Original Article

Occupational Lead Poisoning in Workers of Traditional Tile Factories in Mashhad, Northeast of Iran

M Balali-Mood,[1] S Shademanfar,[2] J Rastegar Moghadam,[2] R Afshari,[1] M Namaei Ghassemi,[1] H Allah Nemati,[3] MR Keramati,[4] J Neghabian,[1] B Balali-Mood,[5] G Zare[1]

Abstract

Background: Occupational lead poisoning is a health problem in Iran. It has not previously been studied in traditional tile makers.

Objective: To determine the prevalence of lead poisoning and its complications in traditional tile workers in Mashhad, Northwest of Iran.

Methods: We visited workers in two traditional tile factories and collected data by direct history taking and physical examination. Blood and urine lead concentrations were measured by heated graphite atomization technique.

Results: Overall, 108 men with mean±SD age of 37±7.8 years were studied. The mean±SD length of daily lead exposure was 9.8±6 years. The mean±SD blood lead concentration was 520.5±323.2 µg/L. The main objective clinical findings were the presence of lead line (64.8%), peripheral neuropathy of the upper extremities (37%), depressed deep tendon reflexes in the upper extremities (25.7%), tremor (23.3%), peripheral neuropathy of the lower extremities (17%) and abdominal tenderness (15.1%). The subjective findings were mainly attributed to the central nervous system and included loss of memory (57%), moodiness (56.1%), agitation (47.7%), drowsiness (36.4%) and headache (29.9%). There was no statistically significant correlation between the blood lead concentration and glomerular filtration rate. However, there were significant correlations between the blood lead concentration and each of the urine lead concentration ($p<0.001$), diastolic blood pressure ($p=0.04$), serum triglyceride level ($p=0.043$), high density lipoprotein level ($p=0.012$), and basophilic stippling ($p=0.048$). Blood lead level, however, did not have any significant correlation with the presence of lead line.

Conclusion: In traditional tile workers, lead toxicity is not uncommon and the toxic effects of lead were found more often on the teeth (bone), central and peripheral nervous system, hematological and lipid profiles than on the renal function.

Keywords

Occupational exposure, toxicology, lead poisoning, nervous system, Iran.

[1]Medical Toxicology Research Centre,
[2]Department of Medicine,
[3]Department of Neurophysiology,
[4]Department of Hematology and Blood Banking, Mashhad University of Medical Sciences, Mashhad, Iran and
[5]Department of Chemistry, Imperial College, London, UK.

Correspondce to
M. Balali-Mood, BSc, MD, PhD, Professor of Medicine and Clinical Toxicology, Director, Medical Toxicology Research Centre, Imam Reza Hospital, Mashhad 91735-348, Iran
Tel: +98-511-881-9301 and 859-8973
Fax: +98-511-881-3714 and 852-5315
E-mail: BalalimoodM@mums.ac.ir

Introduction

Occupational lead poisoning has been a well-known health hazard for more than 2000 years.[1] The most common exposure to lead among adults is occupational.[1,2] Approximately, 95% of lead poisoning among US adults results from occupational exposure.[3] Lead poisoning has become the most common disease of environmental origin and is still increasing very rapidly in developing countries.[4]

Lead is a soft, ductile, heavy metal which is obtained from the primary smelting of lead containing ores or from the secondary smelting of recycled lead scrap. The risk of lead poisoning is highest after inhalation or ingestion of lead in soluble and absorbable forms of fumes, particulates and glaze composed of lead oxides. Lead products with lower solubility, such as elemental lead, lead sulfide and lead chromate, pose less acute risk, but may still result in toxicity, if the absorbed dose is high or when certain factors such as fine particle size, prolonged intestinal retention, or intra-articular contact exist. Organolead compounds such as tetra-ethyl lead which has been used as fuel additive are slightly soluble in water, but are well absorbed by the skin, oral mucosa and the respiratory tract.[1-4]

Affinity of lead for proteins in the erythrocyte is very high and thus, in low to moderate concentrations, more than 99% of lead in whole blood is associated with erythrocyte. Toxicokinetic studies on humans consuming stable lead isotopes over a period of months indicated that only 1% of lead is found in the blood, which is consistent with a final volume of distribution of 7 L/kg. Lead clearance from the blood is greater after acute than chronic exposure. Almost 70% of total lead clearance occurs in the urine; the remainder is excreted in the feces, sweat, hair and nails. Lead removal after a chronic exposure usually follows a multicompartment kinetic model—a fast compartment in the blood and soft tissues with a half life of 1–2 months, and a few slower compartments in the skeleton with a half life of years to decades.[3-5]

Lead toxicity induces various effects on many organs. In acute poisoning, it may cause acute encephalopathy, foot drop, wrist drop, headache, insomnia, tiredness, seizure and coma. Two cases of acute lead poisoning due to occupational exposure who engaged in stripping off antirust materials composed of lead were reported from Japan. Both patients presented with colic, arthralgia, and anemia. Their blood lead levels were 73.1 and 96.3 μg/dL.[6] While acute poisoning is very rare, subacute and chronic poisonings (occupational) are not uncommon.[1-3,7,8] Psychiatric disorders such as fatigue, loss of memory and concentration, headache and depression are the initial symptoms of chronic occupational lead poisoning.[1,8] Peripheral neuropathy can also be observed in occupational lead poisoning. Motor nerves are more affected than sensory ones.[9] Occupational lead poisoning may result in anemia and nephropathy, particularly in heavily exposed workers.[10-12] Lead poisoning may cause tubular atrophy and interstitial fibrosis of the kidneys.[11,12] Dark blue pigmentation in gingival margin which is called “lead line” or Burton line, is reported occasionally in adults with heavy lead exposure and poor oral hygiene.[1,4,8]

Battery plant workers, painters, workers involved in welding, and tile making factories are at risk of lead toxicity.[1] Lead toxicity has been relatively controlled in industrialized countries, but it is still a

health problem in developing countries such as Iran. Occupational lead exposure with or without symptoms, has not been thoroughly investigated in Iranian workers who exposed to lead. In particular, workers that are involved in glazing the traditional tiles are heavily exposed to lead. The objective of this research was to study the possible toxic effects of lead in workers of two traditional tile making factories, both clinically and paraclinically. We especially studied the association between the clinical findings and blood lead levels. Moreover, the possible toxic effects of lead on different organs, particularly the nervous system, kidneys, hematological values and serum lipid profiles were investigated.

Patients and Methods

Following the agreement of managers of the factories and the approval of the Medical Ethics Committee of Mashhad University of Medical Sciences, we visited the workers in the factories in three sessions—on July 2003, July to August 2004, and August to September 2005. Informed consents were taken from each participant prior to the study. Standard documentation of the history taken and the physical examination performed were described for the research team prior to the start of the study. The workers were examined by two trained physicians (SS and JRM). Demographic and clinical findings were recorded in predesigned data collection forms. Blood and urine samples were taken in three consecutive years from all available workers and administrative staff. The only female clerk was excluded from the study.

Venous blood sample (14 mL) was taken from each participant and processed according to the type of analysis. Blood and urine lead concentrations were determined by an atomic absorptiometer (Perkin-Elmer model 3030, USA) using heated graphite atomization (HGA) method in the Toxicology Laboratory of the Center. Biochemical tests on sera were performed by an auto-analyzer (Hitachi, 9002, Japan) in the Laboratory of Biochemistry of Imam Reza Hospital. Hematological tests were performed in the Hematology Laboratory of the Hospital using standard equipment such as Hemocounter. The lead clearance for each individual was calculated using the following conventional formula:

$$LC_{(mL/min)} = \frac{ULL_{(\mu g/L)} \times 24 - hr\ UV_{(mL)}}{1440_{(min)} \times BLL_{(\mu g/L)}}$$

where LC, ULL, UV, and BLL represent lead clearance, urine lead level, urine volume, and blood lead level, respectively. Blood lead level (BLL) was categorized into four grades: 0–200 µg/L as "normal;" 201–400 as "mild toxicity;" 401–600 as "moderate toxicity;" and >600 µg/L as "severe toxicity." Those participants with mild or

Table 1: Demographic data of 80 subjects studied at their first visit in year 2004.

Variable	Mean±SD
Age (yrs)	37±7.8
Period of working (yrs)	9.8±6.0
Daily time at work (hrs)	7.4±1.8
Weight (kg)	72.9±13.2
Smoking (%)	31.4
Opium addiction (%)	2.9
Alcohol use (%)	1.0

Table 2: Clinical findings of occupational lead poisoning in workers of two traditional tile factories.

Clinical manifestations	Frequency	
	n	%
Lead line	91	64.8
UEPN*	100	37.0
Tremor	90	23.3
LEPN†	100	17.0
Pallor	90	16.7
Abdominal tenderness	105	15.1
Babinski sign	100	6.7
LDMS‡	104	2.9
Wheezing	90	1.1
UDMS**	104	0.0
LPMS††	104	0.0
LDMS‡‡	104	0.0

*Upper extremity polyneuropathy; †Lower extremity polyneuropathy; ‡Lower distal muscle strength; **Upper distal muscle strength; ††Lower proximal muscle strength; ‡‡Lower distal muscle strength.

moderate toxicity was considered as having "low BLL" and persons with severe toxicity was considered as having "high BLL."

In 2004 and 2005, all patients with severe toxicity who also had signs of lead poisoning (*e.g.*, lead line) were hospitalized and treated with the standard dosages[8] of calcium edetate ($CaNa_2$-EDTA) and British antilewisite (BAL). Those with mild or moderate toxicity were treated with the standard dosages[8] of dimercaptosuccinic acid (DMSA), succimer or D-penicillamine, when succimer was not available.

Statistical analyses were done using SPSS® for Windows® ver 11.5. The means of two normally-distributed variables were compared with *Student's t* test for independent data. Categorical variables were compared with χ^2 or Fisher's exact test when appropriate. A p value <0.05 was considered statistically significant.

Results

A total of 80 and 108 workers were studies in 2004 and 2005, respectively. Eighty-one blood samples from these persons were also assessed for BLL in 2003. Demographic findings of participants at their first visit in 2004 are summarized in Table 1.

Clinical findings

The workers were complaining of restlessness (56%), fatigue (50.5%), weakness in upper extremities (36.4%), neurologic problems (39.3%), decreased libido (38.3%), numbness in legs (38.3%) and hands (31.8%), and paresthesia in legs (38.3%) and hands (30.8%). The objective clinical findings of workers studied in summers 2004 and 2005 are summarized in Table 2.

Hematology, biochemistry, and blood lead level

The distribution of BLL is shown in Figure 1, and the distribution of blood lead clearance in the studied workers is presented in Figure 2. The mean±SD lead clearance (n=42) was 0.73±0.81 mL/min.

Hematological and biochemical finding are presented in Tables 3 and 4, respectively. The mean±SD BLL varied from 337.2±208.7 µg/L in 2003 to 520.5±323.3 in 2004 and to 361.6±179.9 µg/L in 2005. The results of the categorized BLLs are summarized in Table 5.

Associations

Table 3: Hematological findings of occupational lead poisoning in the studied workers

Hematological parameters	n	Mean±SD	n	Mean±SD
	Year 2004		Year 2005	
WBC (10^3/mm^3)	72	6.62±1.38	80	6.94±1.3
RBC (10^6/mm^3)	72	5.2±0.5	80	5.0±0.4
Hb (g/dL)	72	15.8±1.2	80	14.5±1.3
HCT (%)	72	46.2±3.6	80	44.5±3.0
MCV (fL)	72	88.8±6.6	80	89.4±7.1
MCH (pg)	72	30.3±2.5	80	29.1±3.1
MCHC (g/dL)	72	34.1±0.9	80	32.5±1.4
Platelets (10^3/mm^3)	72	238.1±459.2	80	194±404
Reticulocyte count (%)	72	1.3±0.7	0	–
ESR (mm/h)	60	6.2±4.2	1	5.0

In this study, the BLL was positively correlated with urine lead levels (r=0.594, p<0.001, n=72) and serum cholesterol-HDL level (r=0.344, p=0.012, n=52); it was negatively correlated with serum triglyceride concentration (r=-0.282, p=0.043, n=52), diastolic blood pressure (r=-0.268, p=0.040, n=85), 24-hour urine uric acid (r=-0.769, p=0.043, n=7) and 24-hour urine creatinine (r=-0.757, p=0.049, n=7).

In our study, we could not find any correlations between BLL and neither of hemoglobin concentration, hematocrit, MCV, MCH, MCHC, platelet count, reticulocyte count, erythrocyte sedimentation rate (ESR), serum uric acid, blood urea nitrogen (BUN), creatinine level, alkaline phosphatase (AlP), calcium, serum iron, luteinizing hormone (LH), follicle stimulating hormone (FSH), ferritin, and urine indices.

BLL also had no correlation with glomerular filtration rate (GFR), creatinine clearance, and uric acid clearance. However, uric acid fraction excretion was negatively correlated with GFR (r=-0.600, p=0.004, n=21), creatinine clearance (r=-0.348, p=0.024, n=42), and uric acid clearance (r=0.447, p=0.025, n=22).

Comparison of subjects with high and low lead levels

Fifty-four percent of those with lead line and 34% of workers without lead line had high BLL. The distribution of basophilic stippling in those with and without high BLL, is presented in Figure 3.

Deep tendon reflex, in both the upper and lower extremities, was decreased more frequently in those with higher than lower BLLs (p<0.001).

Discussion

Many of the examined workers had clinical signs of occupational lead poisoning (*e.g.*, lead line). Nevertheless, we failed to show any significant positive correlations

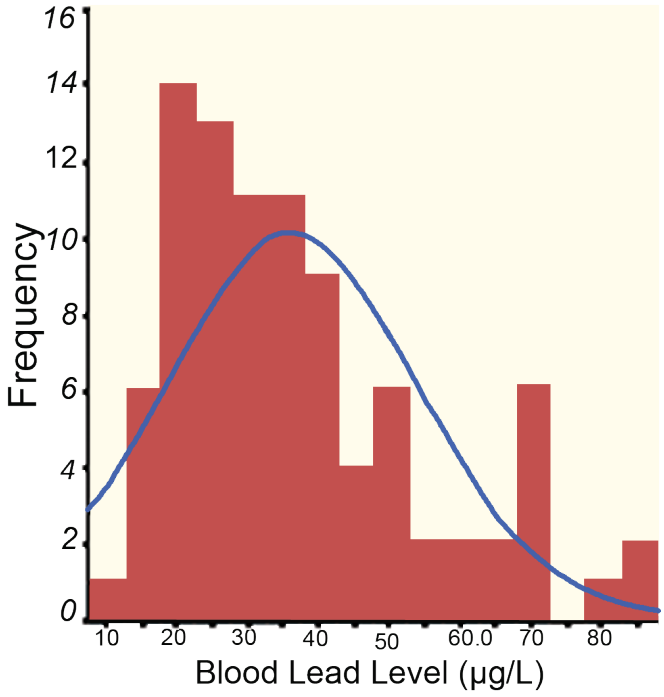

Figure 1:. Histogram of the distribution of blood lead level in the studied workers in 2005 (n=90). The curve represents the best normal curve fit.

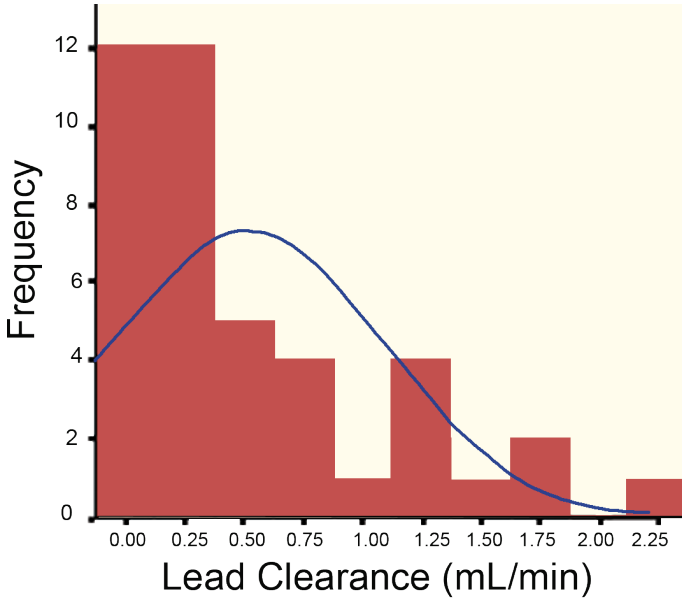

Figure 2:. Histogram of the distribution of lead clearance in the studied workers (n=42). The curve represents the best normal curve fit.

between presence of these signs and BLL. This might be due to different level of oral hygiene of the studied workers and different level of lead exposure. The younger workers were more educated and thus, had a better oral hygiene. However, they were working in areas with higher lead hazards. Only in a few young cases with very high BLLs, despite of their good oral hygiene, clinical signs of lead toxicity were apparent which may suggest that there is a particular BLL at which the ability of kidneys to excrete the element would be saturated.

Although the mean BLL of the studied workers was higher than the upper normal limit, blood red cell indices were not affected. Similar findings have also been reported previously.[11]

Deep tendon reflex in both the upper and lower extremities was significantly more depressed in workers with higher BLL than those with lower BLL. Subclinical damage to the peripheral nervous system causing neurogenic abnormal changes on electromyogram (EMG) and sympathetic skin response (SSR) have been previously reported.[12] Another study showed that these patients also had degrees of sensory and autonomic neuropathies rather than the motor neuropathy classically seen in patients with lead toxicity.[9]

The correlation between BLL and serum total cholesterol has been reported differently in previous studies;[13,14] we found no correlation, which is consistent with some of the reports.[15,16] The correlation between BLL and serum HDL-cholesterol level, observed in our study, has also been reported earlier.[13] Another study, nonetheless, could not show it.[9] What we found about the correlation between BLL and serum triglyceride concentration is not in keeping with some reports,[13,14] but is consistent with the reported effect of high lead con-

Table 4: Biochemical findings of occupational lead poisoning in the studied workers

Biochemical parameters	n	Mean±SD	n	Mean±SD
	Year 2004		Year 2005	
BUN (mg/dL)	72	15.7±3.5	0	–
Creatinine (mg/dL)	72	0.9±0.2	78	1.0±0.2
Uric acid (mg/dL)	71	5.0±1.1	78	4.7±1.1
ALP (U/L)	71	94.4±22.9	0	–
Calcium (mg/dL)	64	9.2±0.3	0	–
Phosphorus (mg/dL)	64	3.6±0.5	0	–
Serum iron (µg/dL)	70	120.3±46.0	0	–
TIBC (µg/dL)	18	357.6±126.8	0	–
LH (mIU/mL)	72	2.6±2.1	0	–
FSH (mIU/mL)	72	6.8±3.6	0	–
Ferritin (ng/mL)	72	100.9±66.9	0	–
Urine pH	51	5.5±0.9	14	5.6±1.1
Urine WBC (per HPF)	51	0.0±0.0	14	0.0±0.0
Urine RBC (per HPF)	51	0.0±0.0	14	0.0±0.0
Blood lead level (µg/L)	76	520.5±323.3	90	361.6±176.9
Urine lead level (µg/L)	75	237.8±291.7	62	206.5±131.9
24-h Urine creatinine (g/L)	9	1.2±0.6	64	1.2±0.5
24-h Urine uric acid (mg/L)	9	495.2±291.2	65	363.7±170.1
24-h Urine volume (mL)	9	1397.8±686.5	65	1317.4±540.2
Glucose (mg/dL)	0	–	79	77.9±19.0
Total cholesterol (mg/dL)	0	–	53	200.8±40.0
TG (mg/dL)	0	–	53	133.9±104.2
HDL (mg/dL)	0	–	53	45.3±6.3
LDL (mg/dL)	0	–	53	126.2±39.2

Continued

Table 4: Biochemical findings of occupational lead poisoning in the studied workers

Biochemical parameters	n	Mean±SD	n	Mean±SD
	Year 2004		Year 2005	
Lead clearance	–	–	42	0.5±0.6
Uric acid clearance (mL/min)	–	–	54	6.8±3.0
Creatinine clearance (mL/min)	–	–	53	100.4±48.2
GFR (mL/min)	–	–	53	111.3±22.5

centration on serum triglyceride level in rats.[17]

As expected, the blood and urine lead levels were correlated. We did not, however, find any correlation between the BLL and creatinine clearance, serum uric acid, and diastolic blood pressures. These are in contrast with previous reports,[18-21] In fact, diastolic blood pressure was negatively associated with BLL (r=-0.268, p=0.04). This finding is not consistent with previous studies in which BLL did not have any association with blood pressure.[22]

We also determined the range of lead clearance in 108 patients. To the best of our knowledge, the lead clearance has not been used as an index earlier. However, whether this index has a clinical implication is a question that should wait to be answered by future studies.

TAKE-HOME MESSAGE

- Occupational lead poisoning has been a well-known health hazard.
- Lead poisoning has become the most common disease of environmental origin and is still increasing very rapidly in developing countries.
- We conducted this study to determine the prevalence of lead poisoning among traditional tile workers in northeastern Iran.
- Lead toxicity is not uncommon among our tile workers and the toxic effects of lead were found more often on the teeth, central and peripheral nervous system, hematological and lipid profiles.

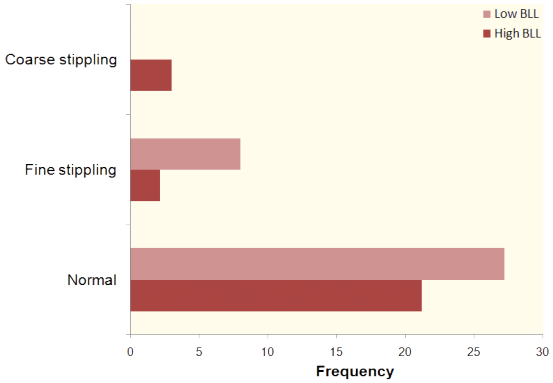

Figure 3: Distribution of different levels of basophilic stippling in those with and without high blood lead level (BLL, n=90).

Table 5: Means±SD of blood lead levels (BLL) of the studied workers from 2003–2005.

	Mean±SD in Year		
BLL (µg/L)	**2003 (n=81)**	**2004 (n=76)**	**2005 (n=102)**
0–200	159.6±30.0 (27%)	167.3±30.5 (11%)	169.5±25.3 (13.7%)
201–400	277.7±51.7 (47%)	309.9±57.9 (37%)	287.0±59.9 (46.1%)
401–600	482.2±51.8 (14%)	483.8±61.5, (24%)	574.9±135.2 (28.4%)
>600	793.8±147.2 (12%)	946.9±259.2 (29%)	714.4±79.0 (11.8%)

One of the limitations of our study was the low sample size. However, as a preliminary study, it showed that in traditional tile workers in Iran, lead poisoning is not uncommon. The toxic effects are frequently seen on teeth, nervous system and hematological and lipid profiles. The results underline the importance of using protective measures for traditional tile workers in such factories.

Acknowledgements

The authors would like to thank the financial support of the Research Council of Mashhad University of Medical Sciences and kind cooperation of the managers of the Astan-e-Ghods and Goharshad tile factories.

Conflict of Interest: None declared

References

1. Staudinger KC, Roth VS. Occupational lead poisoning. *Am Fam Physician* 1998;**57**(4)**:**719-26, 731-2.
2. Hettmansberger TL, Mycyk MB. Lead poisoning presents a difficult diagnosis. *Am Fam Physician* 2002;**66**(10)**:**1839-40.
3. Adult blood lead epidemiology and surveillance--United States, 2002. *MMWR Morb Mortal Wkly Rep* 2004;**53**(26)**:**578-82.
4. Kosnet MJ. Lead. In: Brent J, Wallace KL, Burkhart KK, Phillips SD, Donovan JW, eds. Critical Care Toxicology. Philadelphia: Elsevier-Mosby, 2005: 821-836.
5. Henreting F. Lead. In: Goldfrank L, ed. Goldfrank's Toxicologic Emergencies. New York: McGraw-Hill, 2002: 1200-1221.
6. Ogawa M, Nakajima Y, Kubota R, Endo Y. Two cases of acute lead poisoning due to occupational exposure to lead. *Clin Toxicol (Phila)* 2008;**46**(4)**:**332-5.
7. Srianujata S. Lead--the toxic metal to stay with human. *J Toxicol Sci* 1998;**23 Suppl 2:**237-40.
8. Ellenhorn M, Schonwald S. Lead poisoning. In: Ellenhorn M, ed. Ellenhorn's Medical Toxicology: Diagnosis and Treatment of Human Poisoning. New York: Williams and Wilkins, 1997: 1564-1579.
9. Rubens O, Logina I, Kravale I, Eglite M, Donaghy M. Peripheral neuropathy in chronic occupational inorganic lead exposure: a clinical and electrophysiological study. *J Neurol Neurosurg Psychiatry* 2001;**71**(2)**:**200-4.

10. Fontana V, Baldi R, Franchini M, et al. Adverse haematological outcome and environmental lead poisoning. *J Expo Anal Environ Epidemiol* 2004;**14**(2)**:**188-93.

11. Nolan CV, Shaikh ZA. Lead nephrotoxicity and associated disorders: biochemical mechanisms. *Toxicology* 1992;**73**(2)**:**127-46.

12. Khalil-Manesh F, Gonick HC, Cohen AH, et al. Experimental model of lead nephropathy. I. Continuous high-dose lead administration. *Kidney Int* 1992;**41**(5)**:**1192-203.

13. Chuang HY, Tsai SY, Chao KY, et al. The influence of milk intake on the lead toxicity to the sensory nervous system in lead workers. *Neurotoxicology* 2004;**25**(6)**:**941-9.

14. Ito Y, Niiya Y, Kurita H, Shima S, Sarai S. Serum lipid peroxide level and blood superoxide dismutase activity in workers with occupational exposure to lead. *Int Arch Occup Environ Health* 1985;**56**(2)**:**119-27.

15. Hami J GD. Correlations between blood lead level and serum lipoproteins. *J Birjand Unive. Med Sci.* 2005;**2:**26-30.

16. Tarugi P, Calandra S, Borella P, Vivoli GF. Heavy metals and experimental atherosclerosis. Effect of lead intoxication on rabbit plasma lipoproteins. *Atherosclerosis* 1982;**45**(2)**:**221-34.

17. Nawrot TS, Thijs L, Den Hond EM, Roels HA, Staessen JA. An epidemiological reappraisal of the association between blood pressure and blood lead: a meta-analysis. *J Hum Hypertens* 2002;**16**(2)**:**123-31.

18. Den Hond E, Nawrot T, Staessen JA. The relationship between blood pressure and blood lead in NHANES III. National Health and Nutritional Examination Survey. *J Hum Hypertens* 2002;**16**(8):563-8.

19. Dolenc P, Staessen JA, Lauwerys RR, Amery A. Short report: low-level lead exposure does not increase the blood pressure in the general population. Cadmibel Study Group. *J Hypertens* 1993;**11**(5)**:**589-93.

20. Staessen JA, Lauwerys RR, Buchet JP, et al. Impairment of renal function with increasing blood lead concentrations in the general population. The Cadmibel Study Group. *N Engl J Med* 1992;**327**(3):151-6.

21. Ukaejiofo EO, Thomas N, Ike SO. Haematological assessment of occupational exposure to lead handlers in Enugu urban, Enugu State, Nigeria. *Niger J Clin Pract* 2009;**12**(1):58-64.

22. Bennett WM. Lead nephropathy. *Kidney Int* 1985;**28**(2):212-20.