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Original Article

Extra ordinary high blood lead levels in Mashhad, Iran: a one-year study in a referral center

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ABSTRACT

Introduction: Lead is a heavy metal with vast usage in the industry. Lead toxicity affects any organ in the body. It causes various clinical presentations, which leads to diagnostic complexity. Regarding recent increased observation of cases with lead toxicity in our center, we aimed to evaluate the frequencies of lead toxicity in patients referred to Imam-Reza Hospital's laboratory and find a possible relationship between the blood lead level (BLL) and hematological and biochemical tests.

Methods: From 2016 to 2017, the patients referred to Imam-Reza hospital's laboratory to detect BLL enrolled in the study. Among them, 254 adult cases with BLLs≥10 µg/dl were selected. Complete blood counts and peripheral blood smear were done. Other lab data were extracted from hospital files.

Results: The mean BLL of 1649 participants was 59.11±116.25 µg/dl, ranging from 0 to 1580. Sixty nine percent of them had lead toxicity. Eighty-one percent (n=1341) of patients were males and 18.7% (n=308) were females. In 254 selected cases, the mean BLL was 138.17±189.98 µg/dl. There were significant inverse correlations between BLL and red blood cell counts, hemoglobin, mean cell hemoglobin, total iron-binding capacity, target shape and basophilic stippling, as well as positive correlations between BLL and white blood cell counts, red cell distribution width, neutrophil counts and iron.

Conclusion: Lead toxicity seems to be more frequent than it is expected. Patients with unexplained anemia with increased iron and decreased total iron-binding capacity are better to be evaluated for BLL.

Keywords:
Lead toxicity
Opium
Hematological tests
Biochemical tests
Blood lead level

Introduction

Lead is a heavy metal that was widely used in the industry because of its special chemical and physical properties including malleability, resistance to corrosion and poor conductibility (Wani et al., 2015). Lead toxicity has affected individuals since historical times. It was postulated that the Roman Emperor collapse may be a consequence of dementia attributed to lead-containing wines (Wani et al., 2015). Lead toxicity affects any organ in the body including central nervous

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system, blood, gastrointestinal tract and reproductive system. Consequently, it can be presented with non-specific signs and symptoms such as nausea, abdominal pain, weakness, neuropathy and even coma as well as unconsciousness (Gidlow, 2015; Wani et al., 2015). Therefore, the diagnosis may be missed until sever toxicity occur. Lead can cause sideroblastic anemia. Sideroblastic anemias are defined by an increase in marrow sideroblasts as a result of some disruption in iron incorporation to the hemoglobin (McPherson, 2017). Through interfering with some enzymes involved in the biosynthesis of heme as well as enzymes work in maintaining red blood cell (RBC) membrane integrity, lead can cause anemia by reduction in production and hemolysis (Halmo and Nappe, 2019). The anemia of lead poisoning is mostly of normochromic normocytic and sometimes hypochromic microcytic (Gidlow, 2015). Lead is stored in the kidney and liver. It can result in a reduction of renal glomeruli as well as renal tubular damage (Kshirsagar et al., 2015; Buser et al., 2016; Nakhaee et al., 2019). In addition, lead can cause oxidative liver damage (Dadpour et al., 2016; Nakhaee et al., 2019).

The limitation of lead use in the industry has decreased the prevalence of lead toxicity. Lead-based paint and lead-contaminated dust in old buildings are the main sources of lead toxicity in children; other sources include some occupations as well as contaminated air or water (Gidlow, 2015; Wani et al., 2015). Lead contaminated opium was recently introduced as a new source of lead toxicity in Iran and some authors alarmed about the lead outbreak between opium users (Meybodi et al., 2012; Hayatbakhsh et al., 2017; Ghane et al., 2018; Karrari et al., 2012). Khorasan province sharing a common border with Afghanistan, one of the major opium producers, suffers widely from opium related health problems. We evaluated the frequency of lead toxicity in patients referred to Imam Reza university hospital's central laboratory, Mashhad, Iran and searched for correlations between patient's blood lead level (BLL) and their hematological and biochemical tests. Imam Reza university hospital is the biggest general hospital in the east of Iran which is the referral hospital in many fields, including toxicology.

Material and methods

The study was conducted at Imam Reza university hospital, Mashhad University of Medical Sciences, Mashhad, Iran. Between September 2016 and September 2017, all patients referred to the Imam Reza university hospital's central laboratory, Mashhad, Iran for detecting BLL enrolled in the study. The study protocol was approved by Research Ethics Committee in Mashhad University of Medical Sciences (IR.MUMS.fm.REC.1396.162).

The age, sex and BLL of patients were extracted from hospital files. The BLL was detected using PerkinElmer atomic absorption spectrophotometer (Perkin-Elmer AAnalyst, USA). the BLL of 10 μg/dl or more was regarded as lead toxicity (Wani et al., 2015). Among the patients, 254 adult cases with BLL≥ 10μg/dl were selected non-randomly. Complete blood counts (CBC) and peripheral blood smear (PBS) were done on the same blood sample used to detect BLL. The CBC was done using Sysmex KX21 hematology analyzer (Sysmex Co., Japan). The PBS stained using the Geimsa method (Kuhlmann, 2018). An experienced technologist evaluated RBC morphology, including hypochromia, microcyte, macrocyte, target shape and basophilic stippling. The presence of each morphologic change was assessed according to the ICSH guideline (Palmer et al., 2015). Biochemical lab data of cases including blood urea nitrogen (BUN), creatinine (Cre), aspartate amino transferase (AST), alanine amino transferase (ALT), lactate dehydrogenase (LDH), alkaline phosphatase (ALK), iron and total iron-binding capacity (TIBC) were extracted from hospital electronic files. Biochemical lab tests were done using BS 300 autoanalyzer (Biotecnica instruments S.P.A., Italy). Finally, correlations between BLL and CBC, PBS findings, as well as other lab data were evaluated. Anemia was defined as hemoglobin (Hb) levels less than 12.3g/dl and 14g/dl in females and males, respectively. As RBC counts as well as Hb and hematocrit (Hct) show different reference levels in males and females, these parameters were separately evaluated in two sexes. A WBC counts ≥11000/μl was considered leukocytosis, whereas WBC counts ≤4400/μl was defined as leukopenia (McPherson, 2017).

Statistical analysis

Data analysis was performed using SPSS 11.5 software (SPSS, Chicago, IL). As the BLL of patients did not show normal distribution, non-parametric tests were employed. Spearman's correlation was used to find

TABLE 1: The demographic data of patients

Variable name	Categories	Mean±SD, or n(%)
Age (years)	-	45.61±20
Sex	Males	1341 (81.3%)
	Females	308 (18.7%)
BLL (µg/dl)	-	59.11±116.25

BLL: blood lead level

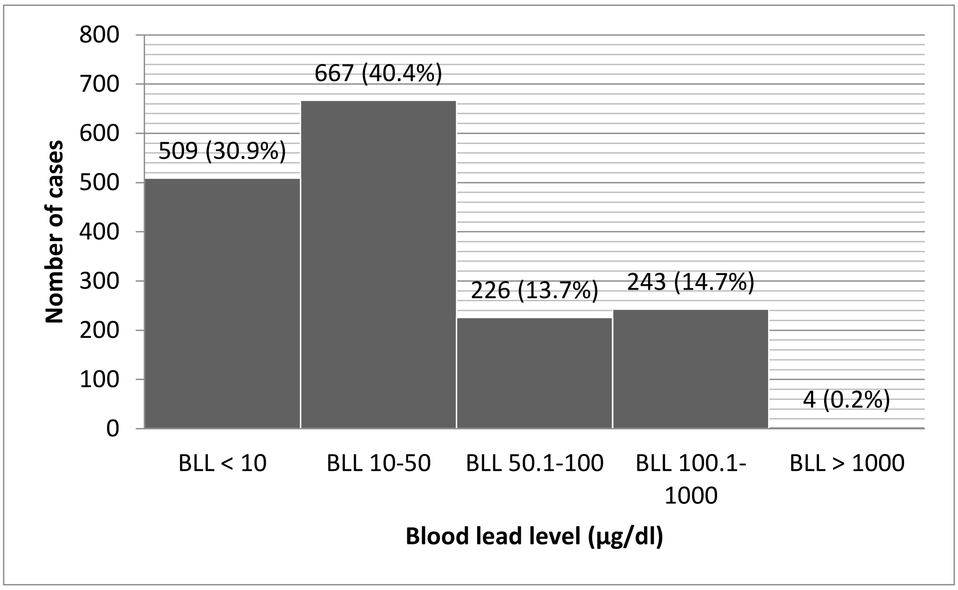

FIGURE 1. Blood lead level of the studied cases. Four cases showed BLLs of more than 1000µg/dl.

correlations between BLL and quantitative variables, including CBC parameters, BUN, Cre, ALT, AST, LDH, ALK, iron and TIBC. To find any association between BLL and PBS findings, the Mann-Whitney test was employed. The *P* values less than 0.05 were considered statistically significant.

Results

From September 2016 to September 2017, 1649 cases were referred to Imam Reza hospital's central laboratory to detect BLL. The demographic characteristics of the patients are presented in Table 1. Most patients were males (81.3%, n=1341). The patients' ages ranged from 0 to 92 years, with a mean±SD of 45.61±20 years. Their mean±SD of BLL was 59.11±116.25 µg/dl, ranging from 0 to 1580µg/dl. Figure 1 shows the distribution of different levels of blood lead in studied cases. According to a cut-off level of 10µg/dl, 69.1% (n=1140) of patients showed toxic levels of lead in their blood. The BLL in 15% (n=247) was above 100µg/dl and 5 patients had BLLs of more than 1000µg/dl.

There was a statistically significant but weak correlation between age and BLL (P=0.002, Spearman's correlation coefficient: 0.09). The differences between BLL in men (mean±SD: 60.86±117.8 µg/dl) and women (mean±SD: 51.70±109.18 µg/dl) were statistically significant (P<0.001). In 254 selected cases with BLL ≥10µg/dl, the mean±SD of BLL was 138.17±189.98 µg/dl. The results of the CBC and biochemical tests of these patients, as well as correlations between BLL and lab results are summarized in Table 2. There were significant inverse correlations between BLL and RBC count, Hb, Hct, mean cell hemoglobin (MCH) and TIBC (Table 2). Besides, significant positive correlations were found between BLL and WBC count, red cell distribution width (RDW), absolute neutrophil counts and iron. Two hundred six patients (81.1%) were anemic. Thirty-eight cases (15%) showed leukocytosis, whereas 17 (6.7%) exhibited leukopenia.

As RBC counts, as well as Hb and Hct show different reference levels in males and females, these parameters were separately evaluated in two sexes and their correlation with BLL was re-evaluated (Table 3). There were significant correlations between BLL and

TABLE 2: The summary of laboratory data of 254 selected cases and their correlation with blood lead level

Variable name	Mean±SD	Correlation	P value
WBC Counts (×10³ per µl)	8.56±3.74	0.39	**<0.001**
RBC Counts (×10³ per µl)	4.04±0.76	-0.31	**<0.001**
Hemoglobin (g/dl)	11.31±2.53	-0.3	**<0.001**
Hematocrit (%)	35.61±7.63	-0.24	**<0.001**
MCV (fL)	88.35±8.42	-0.08	0.21
MCH (pg)	27.83±2.60	-0.14	**0.02**
MCHC (g/dl)	31.44±1.64	-0.12	0.06
RDW (%)	15.63±2.87	0.26	**<0.001**
Plt count (×10³ per µl)	271.55±97.95	0.08	0.27
PDW (%)	14.88±2.41	0.74	0.32
MPV (fL)	11.14±1.04	0.49	0.51
P-LCR (%)	34.54±8.52	0.06	0.46
ANC (×10³ per µl)	5.40±3.33	0.38	**0.001**
ALC (×10³ per µl)	2.14±1.17	-0.06	0.45
BUN (mg/dl)	15.17±7.23	0.02	0.9
Cre (mg/dl)	0.98±0.32	-0.09	0.61
AST (U/L)	58.47±80.20	0.1	0.45
ALT (U/L)	54.51±54.41	0.12	0.39
LDH (U/L)	633.27±625.93	-0.23	0.21
ALK (U/L)	278.18±190.72	-0.24	0.16
Iron (µg/dl)	88.16±53.08	0.34	**0.04**
TIBC (µg/dl)	315.71±72.28	-0.38	**0.03**

MCV: mean cell volume, MCH: mean cells hemoglobin, MCHC: mean cells hemoglobin concentration, RDW: red cells distribution width, PDW: platelets distribution width, MPV: mean platelets volume, P-LCR: platelets large cell ratio, ANC: absolute neutrophil counts, ALC: absolute lymphocytes counts, BUN: blood urea nitrogen, Cre: Creatinin, AST: aspartate amino transferase, ALT: alanin amino transferase, LDH: lactate dehydrogenase, ALK alkaline phosphatase, TIBC: total iron binding capacity.

TABLE 3: RBC counts, hemoglobin and hematocrit in males (n=217) and females (n=37), and their correlation with blood lead level

Variable name	Sex	Mean±SD	Correlation	P value
RBC counts (per µl)	Male	4.03±0.77	-0.32	<0.001
	Female	4.13±0.76	-0.22	0.2
Hemoglobin (g/dl)	Male	11.30±2.57	-0.32	<0.001
	Female	11.35±2.37	-0.3	0.07
Hematocrit (%)	Male	35.31±7.13	-0.25	<0.001
	Female	37.46±9.99	-0.2	0.25

RBC count, Hb and Hct only in men. The results of the morphologic evaluation of PBS are shown in Table 4. About 88% of patients had abnormal morphology. There were significant associations between higher BLLs and the presence of hypochromia, anisocytosis, target shape, as well as basophilic stippling (*P* values: 0.013, 0.006,

TABLE 4: RBC Morphologic findings of the patients and their relation with blood lead level

Variable name		percent	P value
Morphologic abnormality	Present	87.6	0.14
	Absent	12.4	
Hypochromia	Present	78.9	0.013
	Absent	21.1	
Anisocytosis	Present	53.9	0.006
	Absent	46.1	
Target shape	Present	70.1	0.008
	Absent	29.9	
Basophilic stippling	Present	5	0.003
	Absent	95	

0.008 and 0.003, respectively).

Discussion

This study evaluated the mean BLL of 1649 patients referred to Imam Reza University Hospital, Mashhad, Iran and found a mean±SD of BLL was 59.11±116.25 µg/dl. About 69% of patients showed BLLs above the toxic level (10µg/dl). These results are much higher than the mean BLL of the population in Mashhad (Farhat et al., 2006; Deldar et al., 2008; Mansoori et al., 2009). In a study of 80 mothers in Mashhad, mean BLLs of 10.49 and 12.46 were reported for two groups based on their infants' birth weight (Mansoori et al., 2009). Other studies reported mean BLLs of 12.19 and 16.38 for children aged from 1 to 7 years living in Mashhad (Farhat et al., 2006; Deldar et al., 2008). Even in the industrialized, polluted city of Tehran, reported BLLs are much lower (Farzin et al., 2008; Hassanian-Moghaddam et al., 2018). Farzin et al. (2008) in a study of 101 volunteers resident in Tehran, Iran, found a BLL of 12.37±5.64µg/dl. Besides, occupationally exposed workers in Mashhad did not show such high BLLs (Balali-Mood et al., 2010; Keramati et al., 2010). Keramati et al. (2010) in a study on 105 battery manufacturing workers, reported a mean BLL of 32.27±13.7µg/dl. Balali-Mood et al. (2010) reported a mean BLL of 52.05±32.32 µg/dl in 108 workers of Mashhad traditional tile factories. In addition, the participants in this study were not occupationally exposed workers referring for their routine checkups. Lead contaminated opium was recently introduced as a new source of lead toxicity in Iran (Meybodi et al., 2012; Hayatbakhsh et al., 2017; Ghane et al., 2018). Hayatbakhsh et al. (2017) reported an increase in opium-related lead poisoning in the Kerman province and alarmed this emerging lead source's awareness. Ghane et al. (2018) reported an outbreak of lead toxicity in Tehran. BLLs of 37.15±22.75 to 57.04 µ/dl in opium addicts are reported by some authors (Amiri and Amini, 2012; Ahmadinejad et al., 2019; Froutan et al., 2011). The reported BLLs in addicts are in line with our results. Furthermore, according to the feedback from the clinicians, many of our studied cases were opium addicts. Therefore, the lead contaminated opium may be the source of the extraordinary high BLLs observed in the present study. Further studies exploring the BLL as well as possible causes of lead toxicity (e.g. addiction) simultaneously, are needed to confirm this claim. The highest BLL found in the present study was 1580µg/dl. Even in symptomatic patients who are reported as cases, BLL was ranging from 50 to 323µg/dl (Mohsen Masoodi et al.; Beigmohammadi et al., 2008; Fatemi et al., 2008; Jalili and Azizkhani, 2009; Moharari et al., 2009; Verheij et al., 2009; Salman-Roghani and Foroozan, 2011; Soltaninejad et al., 2011; Meybodi et al., 2012; Alinejad et al., 2018; Soltaninejad and Shadnia, 2018). Regarding the possible role of opium addiction as the cause of lead toxicity in this study, the unexpected extraordinary BLLs could be related to the location of Khorasan province at the common border with Afghanistan, a main producer of opium. This can influence opium availability to addicts and consumption of higher amounts of lead contaminated opium by patients.

Among 254 selected cases with BLL ≥10µg/dl, 206 (81.1%) were anemic. We found a significant correlation between BLL and decrease in RBC counts, Hb, Hct, MCH, as well as an increase in RDW. Sideroblastic anemias are a group of anemias characterized by an increase in iron stores and the presence of ring sideroblasts in the marrow. They are caused by various etiologies including lead toxicity (McPherson, 2017). Lead can cause anemia by interfering with some enzymes involved in the biosynthesis of heme, as well as enzymes work in maintaining RBC membrane integrity. So, it can lead to anemia by reduction in production and hemolysis (Halmo and Nappe, 2019). The Anemia of lead poisoning is mostly of normochromic normocytic and sometimes hypochromic microcytic (Gidlow, 2015). Domeneh et al. (2014) reported that 41% of their addict patients were anemic. The mean BLL of their patients was 11.75±6.06 and 7.07±3.61 for oral or inhalational users, respectively. The lower percentage of anemia in their study could be related to the lower BLLs of their patients. In line with our results, Nakhaee et al. (2019) in a study on 200 subjects divided into two high BLL and Low BLL groups, showed significantly lower RBC counts, Hb, HCT and MCH in their high BLL group. Hayatbakhsh et al. (2017) also found a significant correlation between BLL and Hb. In contrast, some studies failed to find a significant correlation between BLL and Hb or Hct (Abbasi et al., 2009; Kianoush et al., 2013). The lower BLLs in their studies could explain these results.

The present study showed a significant association between higher BLL and the presence of hypochromia, anisocytosis, target shaped RBCs and basophilic stippling in PBS. Basophilic stippling is characterized by the presence of deep blue granules in red cells as a result of instability of RNA. Basophilic stippling can be seen in various disorders including lead toxicity, B12 deficiency and other severe anemias (McPherson, 2017). Only 5% of our patients showed basophilic stippling. In a study on 40 addict patients, fakoor et al. (2019) found basophilic stippling in 55% of their opium-addicted subjects. The BLL of basophilic stippling-positive subjects was significantly higher than basophilic stippling-negative subjects. Finding low frequencies of basophilic stippling in our study may be related to the fact that EDTA blood tubs were used to prepare peripheral blood smears. Besides, preparation of the results of BLL sometimes lasts for more than 24 hours. Then, smears were prepared which may have influenced their quality. However, it might be attributed to it in many opium addict patients, lead toxicity is a recent problem, and the sub-acute nature of the disease does not give enough time to erythroid precursors to exhibit expected morphologic findings.

Leukocytosis was found in 15% of patients in the current study. In addition, there was a significant positive correlation between BLL and WBC counts, as well as the percent of neutrophils in peripheral blood. In line with our study, Nakhaee et al. (2019) as well as Patil et al. (2006) reported significantly higher WBC counts in their lead-exposed participants. In contrast Kianoosh et al. (2013) did not find a significant correlation between BLL and WBC or neutrophil counts. Further studies are needed to elucidate the association between lead toxicity and WBC count. The observed higher WBC counts may be related to other additives other than lead, which are sometimes included in opium.

Lead toxicity, like other sideroblastic anemias, is associated to an increase in iron stores and serum iron as well as a decrease in TIBC. In this study, there were significant correlations between BLL and an increase in blood iron and a decrease in TIBC. Some authors report a negative correlation between BLL and serum Iron (Wibowo et al., 1977; Kim et al., 2003). Competition between lead and iron in occupying metal-binding proteins in plasma was mentioned as a possible explanation. A study on 111 smelter workers found no significant correlation between BLL, Iron and TIBC (Lilis et al., 1978). Lead can cause various effects on iron metabolism (Leikin and Eng, 1963; Carvalho et al., 1995). It mostly depends on the severity of lead toxicity. Iron deficiency was reported to be related to increased BLL (Carvalho et al., 1995). While, peoples heavily exposed to lead did not show correlations between BLL and serum iron (Lilis et al., 1978). Further studies are needed to elucidate the interrelations between lead and iron.

Lead is stored in the kidney and liver. It can result in a reduction of renal glomeruli as well as renal tubular damage (Kshirsagar et al., 2015; Buser et al., 2016; Nakhaee et al., 2019). In addition, lead can cause oxidative liver damage (Dadpour et al., 2016; Nakhaee et al., 2019). Some studies have shown a correlation between BLL and renal dysfunction (Wang et al., 2002; Alasia et al., 2010; Nakhaee et al., 2019). In contrast, others did not find such correlations (Gerhardsson et al., 1992; Balali-Mood et al., 2010; Kianoush et al., 2013).

In line with the last mentioned studies, no significant correlation between BLL and serum BUN and creatinine were found in our research. There are conflicting data about the association between BLL and liver function tests. In a study by Nakhaee et al. (2019), although AST and ALT levels of patients were within the normal range, there was a significant correlation between BLL and serum levels of these enzymes. Bhagwat et al. (2008) and Dongre et al. (2010) reported similar results. In line with our study, Abbasi et al. (2009) found no correlation between BLL and liver function tests, including bilirubin, AST, ALT and ALK. Finding no correlation between BLL and kidney and liver function tests in the present study, may be attributed to the fact that BLL is not always a good predictor of body lead load (Gidlow, 2015). In acute and sub-acute toxicities, the BLL is much higher than chronic toxicity with the same amount of total body lead. It may explain fewer toxic effects on kidney and liver.

Conclusion

We found high number of cases with lead toxicity as well as higher levels of BLL in our center comparing the population-based and studies reported BLL in addicts in Iran. Lead causes severe damage in many organs in the body and its toxicity presents with various clinical and laboratory findings. Therefore, any patient with unexplained normo or hypochromic anemia with increased blood iron and decreased TIBC is better to be evaluated for BLL.

Conflicts of interest

The authors declare that they have no competing interests.

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References

Ab Latif Wani AA, Usmani JA. Lead toxicity: a review. Interdiscip Toxicol 2015; 8: 55-64. https://doi.org/10.1515/intox-2015-0009

Abbasi MM, Ansari M, Shahesmaeili A, Qaraie A. Lead serum levels in opium-dependent individuals. Addict Health 2009; 1: 106.

Ahmadinejad M, Ahmadipour M, Divsalar K. Blood lead level in opiate addicts hospitalized in the intensive care unit of a trauma referral center in Kerman, Iran. Addict Health 2019; 11: 11-17.

Alasia DD, Emem-Chioma PC, Wokoma FS. Association of lead exposure, serum uric acid and parameters of renal function in Nigerian lead-exposed workers. Int J Occup Environ Med (The IJOEM) 2010; 1.

Alinejad S, Aaseth J, Abdollahi M, Hassanian-Moghaddam H, Mehrpour O. Clinical aspects of opium adulterated with lead in Iran: a review. Basic Clin Pharmacol Toxicol 2018; 122: 56-64. https://doi.org/10.1111/bcpt.12855

Amiri M, Amini R. A comparison of blood-lead level (BLL) in opium-dependant addicts with healthy control group using the graphite furnace/atomic absorption spectroscopy (GF-AAS) followed by chemometric analysis. Iran Red Crescent Med J 2012; 14: 488-91.

Balali-Mood M, Shademanfar S, Moghadam JR, Afshari R, Ghassemi MN, Nemati HA, et al. Occupational lead poisoning in workers of traditional tile factories in Mashhad, Northeast of Iran. Int J Occup Environ Med (The IJOEM) 2010; 1.

Beigmohammadi MT, Aghdashi M, Najafi A, Mojtahedzadeh M, Karvandian K. Quadriplegia due to lead-contaminated opium--case report. Middle East J Anaesthesiol 2008; 19: 1411-6.

Bhagwat VR, Patil AJ, Patil JA, Sontakke AV. Occupational lead exposure and liver functions in battery manufacture workers around Kolhapur (Maharashtra). Al Ameen J Med Sci 2008; 1: 2-9.

Buser MC, Ingber SZ, Raines N, Fowler DA, Scinicariello F. Urinary and blood cadmium and lead and kidney function: NHANES 2007-2012. Int J Hyg Environ Health 2016; 219: 261-7. https://doi.org/10.1016/j.ijheh.2016.01.005

Carvalho FM, Silvanyneto AM, Barbosa AC, Cotrim CR, Tavares TM. Erythrocyte protoporphyrin versus blood lead: relationship with iron status among children exposed to gross environmental pollution. Environ Res 1995; 71: 11-5. https://doi.org/10.1006/enrs.1995.1061

Dadpour B, Afshari R, Mousavi SR, Kianoush S, Keramati MR, Moradi VA, et al. Clinical and laboratory findings of lead hepatotoxicity in the workers of a car battery manufacturing factory. Iranian Journal of Toxicology 2016;

10: 1-6.

Deldar K, Nazemi E, Mood MB, Emami SA, MohammadPour AH, Tafaghodi M, et al. Effect of Coriandrum sativum L. extract on lead excretion in 3-7 year old children. J Birjand Univ Med Sci 2008; 15: 11-19.

Domeneh BH, Tavakoli N, Jafari N. Blood lead level in opium dependents and its association with anemia: a cross-sectional study from the capital of Iran. J Res Med Sci 2014; 19: 939-43.

Dongre NN, Suryakar A, Patil AJ, Rathi D. Occupational lead exposure in automobile workers in North Karnataka (India): effect on liver and kidney functions. Al Ameen J Med Sci 2010; 3: 284-92.

Fakoor M, Akhgari M, Shafaroodi H. Lead poisoning in opium-addicted subjects, its correlation with pyrimidine 5′-nucleotidase activity and liver function tests. Int J Prev Med 2019; 10. https://doi.org/10.4103/ijpvm.IJPVM_490_18

Farhat ASH, Parizadeh SMJ, Balali M, Khademi GR. The serum lead level of children in emergency ward. Med J Mashad Univ Med Sci 2006; 48: 405-8.

Farzin L, Amiri M, Shams H, Ahmadi Faghih MA, Moassesi ME. Blood levels of lead, cadmium, and mercury in residents of Tehran. Biol Trace Elem Res 2008; 123: 14-26. https://doi.org/10.1007/s12011-008-8106-y

Fatemi R, Jafarzadeh F, Moosavi S, Afshar Amin F. Acute lead poisoning in an opium user: a case report. Gastroenterol Hepatol From Bed Bench 2008; 1: 139-42.

Froutan H, Kashefi ZA, Kalani M, Andrabi Y. Lead toxicity: a probable cause of abdominal pain in drug abusers. Med j Islam Repub Iran 2011; 25: 16-20.

Gerhardsson L, Chettle DR, Englyst V, Nordberg GF, Nyhlin H, Scott MC, et al. Kidney effects in long term exposed lead smelter workers. Occup Environ Med 1992; 49: 186-92. https://doi.org/10.1136/oem.49.3.186

Ghane T, Zamani N, Hassanian-Moghaddam H, Beyrami A, Noroozi A. Lead poisoning outbreak among opium users in the Islamic Republic of Iran, 2016-2017. Bull World Health Organ 2018; 96: 165-72. https://doi.org/10.2471/BLT.17.196287

Gidlow DA. Lead toxicity. Occup Med 2015; 65: 345-56. https://doi.org/10.1093/occmed/kqv018

Halmo L, Nappe TM. Lead Toxicity. Treasure Island (FL): StatPearls Publishing 2021.

Hassanian-Moghaddam H, Zamani N, Hamidi F, Farnaghi F, Gachkar L. Blood lead levels in pregnant women referring to midwifery clinic in a referral center in Tehran. J Res Med Sci 2018; 23: 88. https://doi.org/10.4103/jrms.JRMS_72_18

Hayatbakhsh MM, Oghabian Z, Conlon E, Nakhaee S, Amirabadizadeh AR, Zahedi MJ, et al. Lead poisoning among opium users in Iran: an emerging health hazard. Subst Abuse Treat Prev Policy 2017; 12: 1-8. https://doi.org/10.1186/s13011-017-0127-0

Jalili M, Azizkhani R. Lead toxicity resulting from chronic ingestion of opium. West J Emerg Med 2009; 10: 244-6.

Karrari P, Mehrpour O, Abdollahi M. A systematic review on status of lead pollution and toxicity in Iran; Guidance for preventive measures. DARU J Pharm Sci 2012; 20: 1-7. https://doi.org/10.1186/1560-8115-20-2

Keramati MR, Sadeghian MH, Mahdi M. Correlation between iron deficiency and lead intoxication in the workers of a car battery plant. Int J Hematol Oncol Stem Cell Res 2010; 30: 169-74.

Kianoush S, Balali-Mood M, Mousavi SR, Shakeri MT, Dadpour B, Moradi V, et al. Clinical, toxicological, biochemical, and hematologic parameters in lead exposed workers of a car battery industry. Iran J Med Sci 2013; 38: 30.

Kim HS, Lee SS, Hwangbo Y, Ahn KD, Lee BK. Cross-sectional study of blood lead effects on iron status in Korean lead workers. Nutrition 2003; 19: 571-6. https://doi.org/10.1016/S0899-9007(03)00035-2

Kshirsagar M, Patil J, Patil A, Ghanwat G, Sontakke A, Ayachit RK. Biochemical effects of lead exposure and toxicity on battery manufacturing workers of Western Maharashtra (India): with respect to liver and kidney function tests. Al Ameen J Med Sci 2015; 8: 107-14.

Kuhlmann WD. Romanowsky-Giemsa staining. MVZ für Laboratoriumsmedizin Koblenz-Mittelrhein Viktoriastrasse 2018; 39: 56068.

Leikin S, Eng G. Erythrokinetic studies of the anemia of lead poisoning. Pediatrics 1963; 31: 996-1002.

Lilis R, Eisinger J, Blumberg W, Fischbein A, Selikoff IJ. Hemoglobin, serum iron, and zinc protoporphyrin in lead-exposed workers. Environ Health Perspect 1978; 25: 97-102. https://doi.org/10.1289/ehp.782597

Mansoori M, Shah Farhat A, Mohammadzadeh A. The evaluation of the effect of maternal blood lead concentration on the incidence of delivery of low birth weight neonates. J Kurdistan Uni Med Sci 2009; 14: 41-46.

Masoodi M, Zali MR, Ehsani-Ardakani M, Mohammad-Alizadeh AH, Aiassofi K, Aghazadeh R, et al. Abdominal pain due to lead-contaminated opium: a new source of inorganic lead poisoning in Iran. Arch Iran Med 2006; 9: 72-75.

McPherson RA. Henry's clinical diagnosis and management by laboratory methods: First South Asia Edition_e-Book: Elsevier India, 2017.

Meybodi FA, Eslick GD, Sasani S, Abdolhoseyni M, Sazegar S, Ebrahimi F. Oral opium: an unusual cause of lead poisoning. Singapore Med J 2012; 53: 395-7.

Moharari RS, Khajavi MR, Panahkhahi M, Mojtahedzadeh M, Najafi A. Loss of consciousness secondary to lead poisoning--case reports. Middle East J Anaesthesiol 2009; 20: 453-5.

Nakhaee S, Amirabadizadeh A, Brent J, Mehrpour O. Impact of chronic lead exposure on liver and kidney function and haematologic parameters. Basic Clin Pharmacol Toxicol 2019; 124: 621-28. https://doi.org/10.1111/bcpt.13179

Palmer L, Briggs C, McFadden S, Zini G, Burthem J, Rozenberg G, et al. ICSH recommendations for the standardization of nomenclature and grading of peripheral blood cell morphological features. Int J Lab Hematol 2015; 37: 287-303. https://doi.org/10.1111/ijlh.12327

Patil AJ, Bhagwat VR, Patil JA, Dongre NN, Ambekar JG, Das KK. Biochemical aspects of lead exposure in silver jewelry workers in western Maharastra (India). J Basic Clin Physiol Pharmacol 2006; 17: 213-30. https://doi.org/10.1515/JBCPP.2006.17.4.213

Salman-Roghani H, Foroozan A. Lead poisoning, report of an interesting case. Govaresh J 2009; 14: 39-45.

Soltaninejad K, Flückiger A, Shadnia S. Opium addiction and lead poisoning. J Subst Use 2011; 16: 208-12. https://doi.org/10.3109/14659891.2010.545860

Soltaninejad K, Shadnia S. Lead poisoning in opium abuser in Iran: a systematic review. Int J Prev Med 2018; 9. https://doi.org/10.4103/ijpvm.IJPVM_22_17

Verheij J, Voortman J, van Nieuwkerk CM, Jarbandhan SV, Mulder CJ, Bloemena E. Hepatic morphopathologic findings of lead poisoning in a drug addict: a case report. J Gastrointestin Liver Dis 2009; 18: 225-7.

Wang VS, Lee MT, Chiou JY, Guu C-F, Wu CC, Wu TN, et al. Relationship between blood lead levels and renal function in lead battery workers. Int Arch Occup Environ Health 2002; 75: 569-75. https://doi.org/10.1007/s00420-002-0362-0

Wibowo AA, Del Castilho P, Herber R, Zielhuis R. Blood lead and serum iron levels in non-occupationally exposed males and females. Int Arch Occup Environ Health 1977; 39: 113-20. https://doi.org/10.1007/BF00380891