

Lead Poisoning: a 12-year Report from North East of Iran

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Abstract

Background: Lead poisoning is an issue of concern in developing countries and high levels of lead in blood could be resulted following occupational and environmental exposures. Several reports have raised concerns on the increasing prevalence of lead intoxication among opioid addicts. This study investigated the clinical manifestations and demographic data of subjects who were diagnosed with lead poisoning and also possible correlations of job type and opium abuse with lead poisoning.

Methods: This cross-sectional study was carried out on 82 patients admitted to Imam Reza Hospital, Mashhad, from 2004 to 2016 with the diagnosis of lead poisoning. Demographic information, clinical signs and symptoms, as well as, hematological and biochemical profiles and their possible correlations were investigated. Opium-addiction status was judged based on patient self-report.

Results: In this study, 82 patients were admitted to Toxicology Department. Patients' age ranged between 19 and 81 years old (mean \pm SD: 42.2 \pm 14.90) and 78 patients were male (95.1%). With regard to the occupational exposure, 29 individuals (35.4%) had occupational risk factors for lead poisoning; however, no significant relation was found between the type of occupation and blood lead level ($p=0.95$). Moreover, 43 individuals (52.4%) were opioid-addicted but opioid addiction was not significantly correlated with blood lead level ($p=0.91$). Among all, 70 individuals (85.4%) were anemic and with increasing blood lead level, the levels of Hb ($p=0.011$, $r=-0.279$) and Hct ($p=0.003$, $r=-0.332$) showed significant decrease.

Conclusion: Though blood lead level was not significantly correlated with opioid addiction, but most of patients were opioid addicts. Apparently, public awareness and health-care-providers' knowledge should be improved about the potential hazardous effects of using adulterated opium.

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Introduction

Lead intoxication is a typical instance of occupational toxicity which is seldom experienced in developed countries; however, sub-clinical cases are often seen (1). Besides, environmental exposures can result in lead poisoning making this type of poisoning an important “occupational and environmental health” issue (1). Thus, to diminish lead toxicity prevalence, possible sources should be identified and reduction of exposure levels must be performed (2).

Lead, due to its advantageous physicochemical characteristics (e.g. high density, low electrical conductivity and low melting point), has been extensively used over the last century in battery, gasoline, paint and ceramics production; nevertheless, its applications have been limited since the 1970s (3).

According to the WHO report, the main route of exposure to lead is via oral ingestion or inhalation. Lead can enter into human bodies via oral ingestion or inhalation of dust, automobile exhaust fumes and industrial discharges. Then, lead is absorbed into the blood and distributed in different organs such as the liver, kidney and brain. Over time, it accumulates in the teeth and bones which can be redistributed from the bones (4)

Lead exposure may cause acute and chronic poisoning. Poisoning with high levels of lead could result in colic pains in abdomen, neurological problems, seizures, encephalopathy and even death. Compared to adults, infants are at higher risk as they have higher oral intake of lead through hand-to-mouth behavior (4). According to a marked body of evidence, even low levels of lead may damage humans' health. Also, the exposure of fetus or infants to lead may impair regular development of the brain (5).

Some reports have indicated that lead toxicity could be induced even at low doses; for example, nephrotoxicity was observed at blood lead level (BLL) <5 $\mu\text{g}/\text{dl}$ (6, 7). Also, a recent report of the World Health Organization (WHO) suggested that there is no level of exposure which could be considered “safe” for this heavy metal (8).

Based on the medical literature, chronic exposure to lead (even <10 $\mu\text{g}/\text{dl}$) is associated with behavioral complications in children and long-term exposure to low-dose lead induces renal, cardiovascular, fertility and neurological disorders in adults (9). It has been reported that if blood lead level exceeds 25 $\mu\text{g}/\text{dl}$, encephalopathy and acute poisoning may occur (10).

In the Middle East countries (e.g. Iran), adulteration of opium resulting in the presence of impurities, poses a marked risk to individuals with opioid addiction (11). However, it is not clear whether lead impurities found in opium are resulted from opium processing (or pollution of the soil where the poppy is grown) or adding lead to increase the weight of the final product (12). The presence of lead in opium has been previously indicated (13,14).

In a study on 22 opium-addicts (who ingested opium) and 22 non-addicts, BLL in opium-users correlated with the amount of opium intake. Also, almost half of the opium-users had a BLL >25 $\mu\text{g}/\text{dl}$ (15). In February 2016, it was reported that 18 cases were admitted to a hospital in Arak/ Iran and diagnosed with lead poisoning. These patients were all oral opium addicts and anemia was the most prevalent symptom (16). Beside opium (17), lead toxicity has been observed in subjects taking marijuana (18) or methamphetamine (19).

This article reports clinical manifestations and demographic data (including opium-addiction status, occupational exposure, etc.) of subjects who were diagnosed

with lead poisoning and hospitalized in Imam Reza hospital, Mashhad, Iran from Jan 2004 to Jan 2016; also, possible correlations of job type and opium abuse with lead poisoning were investigated.

Methods

In this cross-sectional study, medical records of 82 patients admitted to Medical Toxicology Department of Imam Reza Hospital, Mashhad, Iran from Jan. 2004 to Jan. 2016 and diagnosed with lead poisoning were reviewed for their demographic characteristics, clinical symptoms as well as the possible correlations.

Data collection

Using a checklist, demographic information (gender, age, occupation, and opium-addiction status), clinical signs and symptoms, as well as, hematological reports (including hemoglobin (Hb) and hematocrit (Hct) levels) and biochemical reports (including blood lead level measured at admission and blood levels of creatinine (mg/dl), sodium and potassium) were gathered and recorded. Adults with clinical signs of lead intoxication were included in this report and those without paraclinical confirmatory tests, were excluded. Opium-addiction status was judged based on patient self-report. Based on probable occupational exposure to lead, patients' occupations were categorized as "related" (e.g. jewelers working with gold or silver, printers, and workers of battery and tile factories and casting industries) and "unrelated".

Among these patients, 12 individuals were admitted based on a laboratory confirmation of high BLL but their

paraclinical test results were not recorded (in other words, 12 cases had missed data).

Ethical considerations

Each patient was assigned with a specific number and patients' information was kept confidential. This study was approved by the Ethics Committee of Mashhad University of Medical Sciences, Mashhad, Iran (approval No. 941750).

Statistical analysis

For data analysis, SPSS software program version 23.0 (SPSS Inc., Chicago, IL, USA) was used. Data normality was verified using the Kolmogorov-Smirnov test. Data are presented as either mean \pm SD or number (percentage). Statistical analysis was done using Student t-test where appropriate. Also, Fisher's exact test was used for qualitative variables. Moreover, the Pearson correlation test was used to determine possible relationships between BLL and blood levels of Hb and Hct. In this study, $p < 0.05$ was considered as statistically significant.

Results

In this 12-year cross-sectional study, demographic characteristics as well as occupation information and opioid dependence status of 82 patients (Figure 1) who were admitted to Medical Toxicology Department of Imam Reza Hospital, Mashhad University of Medical Sciences, Mashhad, Iran from Jan 2004 to Jan 2016 and diagnosed with lead poisoning were collected. Patients' age ranged between 19 and 81 years old (mean \pm SD: 42.2 \pm 14.90 years) and 78 patients (95.1%) were male.

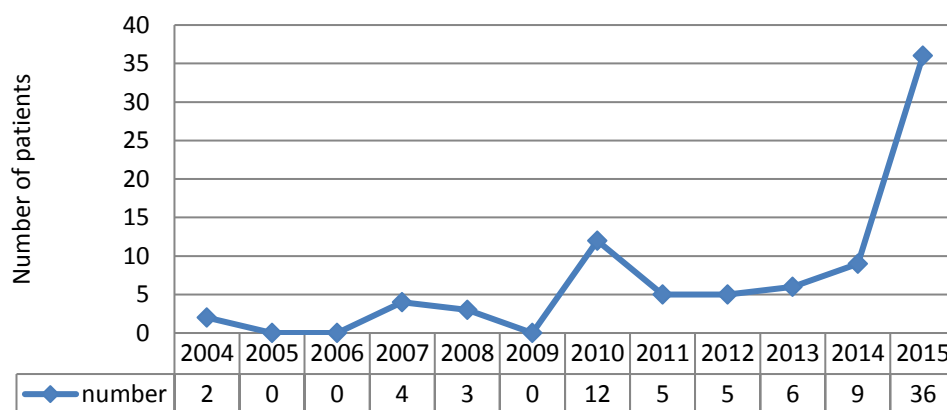


Figure 1. Number of patients admitted to Medical Toxicology Department of Imam Reza Hospital, Mashhad University of Medical Sciences, Mashhad, Iran from Jan 2004 to Jan 2016 with the diagnosis of lead poisoning

As shown in Figure 2A, based on the type of job that may cause lead exposure, patients' jobs were categorized as related and unrelated to this type of intoxication. Among these

patients, in 29 individuals (35.4%), occupational risk factors might have contributed to lead poisoning. The frequency of related occupations is shown in Table 1.

Table 1. Number of lead-poisoned patients with related occupations

Related occupations	Number of lead-poisoned patients
Jewelers (Working with gold or silver)	2
Printers	1
Workers of battery-producing factories	6
Workers of tile factories	1
Workers of casting industries	13
Workers with unspecified jobs, but having lead exposure in their workplace	6
total	29

Comparison between individuals with occupational risk factors and those who had no occupational lead exposure, showed no statistical significant difference in terms of blood lead level (69.20 ± 36.3 vs. 69.9 ± 57.8 ; $P = 0.95$). In terms of opioid-dependence, 43 individuals (52.4%) were addicted, 26.8% were not addicted to opioids and opioid-dependence status for 20.7% of the patients was unknown (Figure 2B). BLL was not statistically different between opioid addicts and

those who were not addicted to opioids (68.29 ± 59.9 , vs. 69.85 ± 33.3 ; $P = 0.91$).

As it is seen in figure 3, the most common signs and symptoms were anorexia (11%), vertigo (9.8%), vomiting (8.5%) and constipation (7.3%). Vertigo (50% and 7.7% in women and men, respectively; $p = 0.046$) and vomiting (50% and 6.4% in women and men, respectively; $p = 0.035$) were significantly more frequent in women as compared to men.

Other symptoms did not show statistically significant difference between the two genders.

As shown in Table 2, biochemical analysis showed that among these patients, 70 individuals (85.4%) were anemic. Overall, in our patients, with increasing BLL, significant

decreases were observed in the levels of Hb ($p= 0.011$, $r= - 0.279$) and Hct ($p=0.003$, $r= - 0.332$) (Figure 4). However, MCH, MCHC and MCV levels were not correlated with BLL ($p>0.05$).

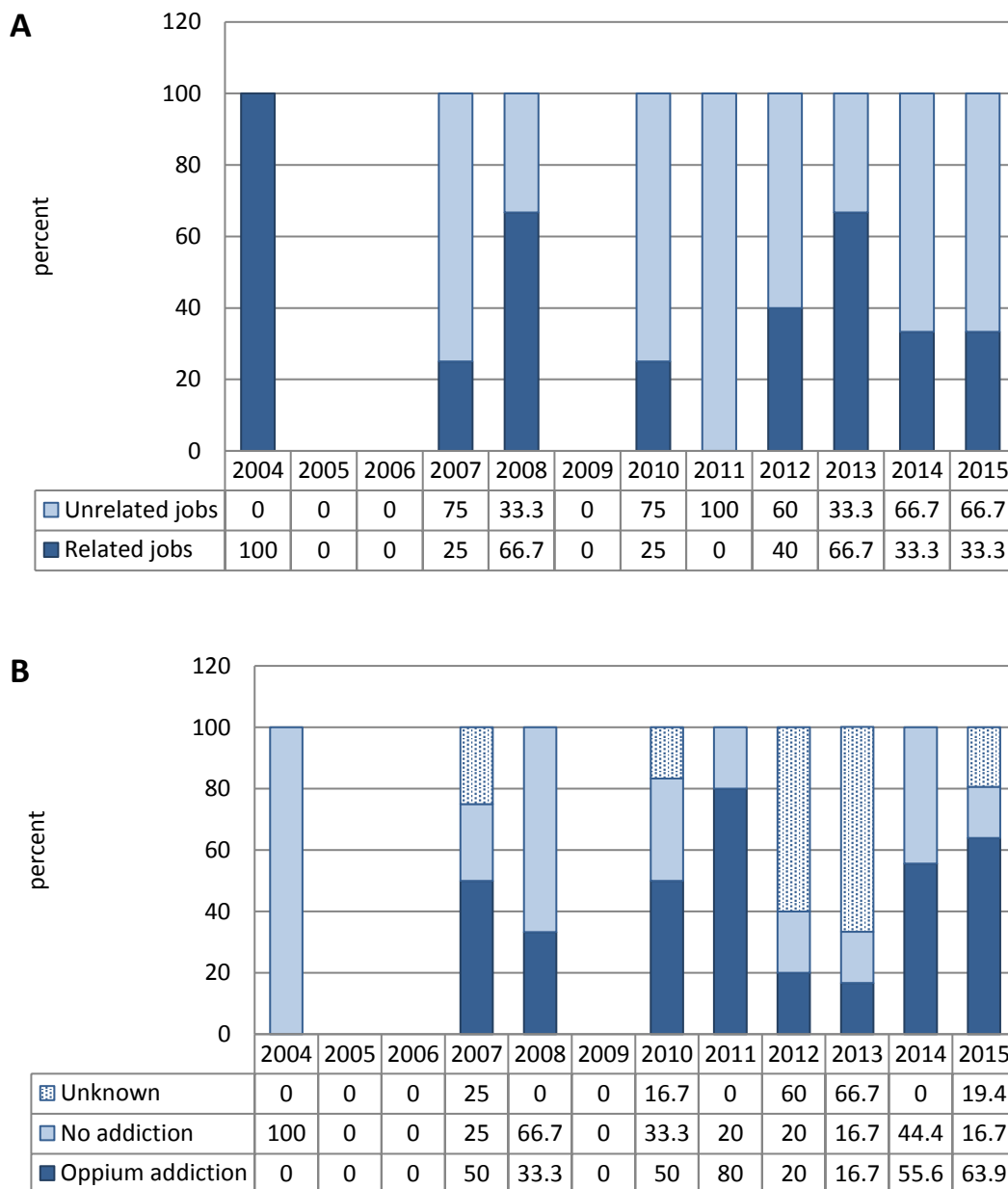


Figure 2. A) Percentages of lead-poisoning related jobs and unrelated jobs, B) Percentages of opioid-addict, opium non-addict and unknown cases among patients admitted to Medical Toxicology Department of Imam Reza Hospital, Mashhad University of Medical Sciences, Mashhad, Iran and diagnosed with lead poisoning from January 2004 to January 2016

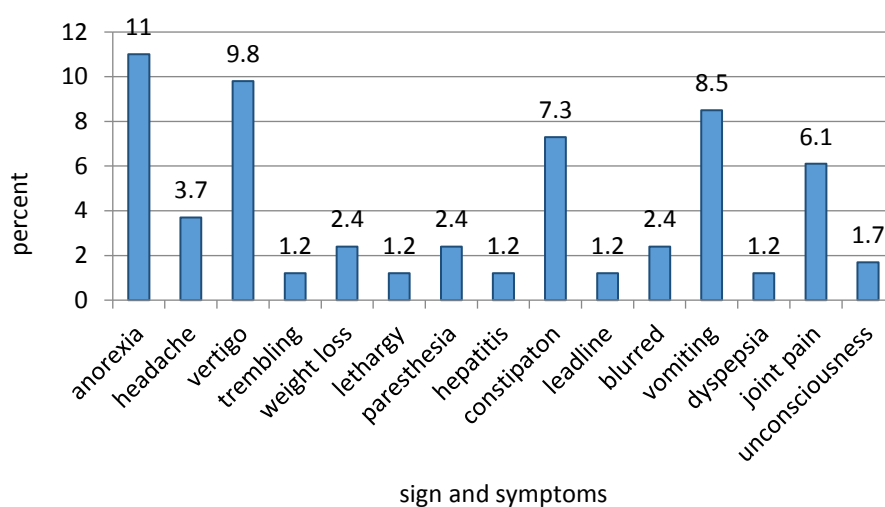


Figure 3. Percentage of main signs and symptoms observed in patients admitted to Medical Toxicology Department of Imam Reza Hospital, Mashhad University of Medical Sciences, Mashhad, Iran and diagnosed with lead poisoning from Jan 2004 to Jan 2016

Table 2. The results of serum biochemical analysis of studied cases

Biochemical parameters	Level	Frequency No (%)
	test result not available	12 (14.6)
Blood lead level (BLL; $\mu\text{g}/\text{dl}$)	20-69	36 (43.9)
	70-100	18 (22)
	>100	16 (19.5)
Anemia (Hb; g/dl)	Male <13.5	67 (85.9)
	Female <12	3 (75.0)
Creatinine (mg/dl)	<1	28 (37.8)
Creatinine (mg/dl)	1-3	46 (62.2)
Creatinine (mg/dl)	>3	0
Hyponatremia (mmol/L)	<135	7 (9.9)
Hypernatremia (mmol/L)	>145	6 (8.5)
Hypokalemia (mmol/L)	<3.6	5 (7.0)
Hyperkalemia (mmol/L)	>5.2	4 (4.9)

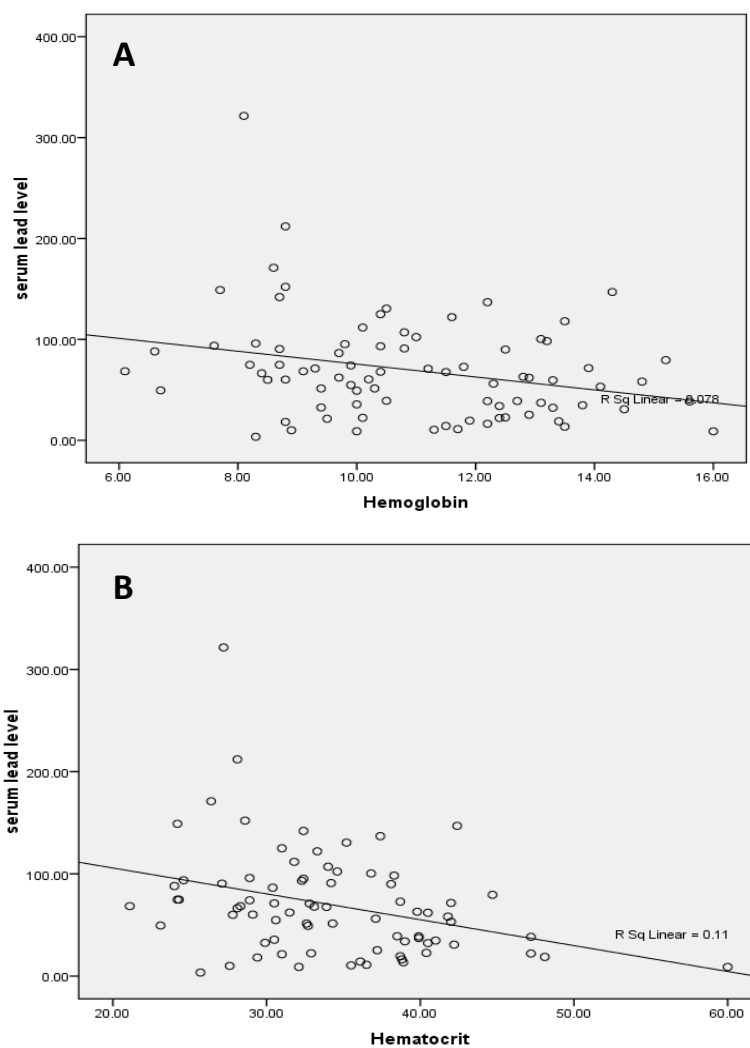


Figure 4. The correlation between A: BLL and Hb and B: BLL and Hct in patients admitted to Medical Toxicology Department of Imam Reza Hospital, Mashhad University of Medical Sciences, Mashhad, Iran and diagnosed with lead poisoning from Jan 2004 to Jan 2016

Discussion

In this study, we reported serum biochemical analyses and major clinical symptoms of patients admitted to Medical Toxicology Department of Imam Reza Hospital, Mashhad University of Medical Sciences, Mashhad, Iran and diagnosed with lead poisoning from Jan 2004 to Jan 2016; also, we investigated possible associations between their demographic characteristics (including type of occupation and opioid addiction) and lead poisoning.

In Iran, opium and its derivatives are among the most commonly abused drugs (20). This could lead to more complicated situations if addicts use opium adulterated with other substances; for instance, lead-contaminated opium is regarded as a serious health threat for opioid-dependent individuals (11, 21, 22). It should be noted that it is not yet clear whether lead-contamination occurs during the production process or is added to manipulate its weight (15, 23). Based on the WHO report, tolerable daily intake (TDI)

for a 68-kg adult is 240 µg/day. If adulterated opium is consumed, intake of 30g of opium/day accounts for at least 20% of TDI which will cause deleterious effects upon long-term consumption (14, 24).

Besides environmental exposure to lead, occupational toxicity may result in lead poisoning particularly in under-developed countries; however, while decreases have been reported in occupational lead poisoning, other non-occupational toxicities have emerged (25-27). Based on the findings of the present study, almost one-third of lead-poisoned cases had jobs with possible contributing risk factors in terms of lead exposure; however, BLL did not show statistically significant differences between the two groups of related and unrelated jobs.

According to a recently published review article concerning clinical aspects of lead poisoning in opium-addicts in Iran, the most-common characteristics of these patients were abdominal pain, nausea, constipation and hematological changes, most of which could be attributed to both lead toxicity and opium dependence (12). Thus, it was suggested that due to non-specific symptoms of lead poisoning, BLL should be checked in patients with abdominal pain, constipation, irritability and anaemia (12). These non-specific manifestations (e.g. abdominal pain (lead colic), constipation, irritability, myalgia, muscle pain, headache, anorexia, decreased libido, and anemia) may result in misdiagnosis and mismanagement. For instance, lead colic might be misinterpreted as acute cholecystitis or pancreatitis (15).

Consistently, anorexia, vertigo, vomiting and constipation were the most common symptoms observed in the present study; notably, vertigo and vomiting were significantly more prevalent among women compared to men. Also, most of the patients were opium-addicts, which it raises concerns about adulterations of opium by producers/suppliers with lead and is in line with previously published reports (12, 28, 29). However, our data showed no significant differences in BLL when comparing opium-addicts with non-addicts.

Previous reports have warned about raises in lead toxicity among opium addicts. Though, based on the present findings (Figure 2), we cannot concretely conclude that there is an increasing trend in the percentage of opium-addicts among lead-poisoned cases. It seems necessary to improve public awareness and knowledge about this health issue; also, continuous education of health-care-professionals is of crucial importance (28, 29).

Incompleteness of patients' records (or missed data) was the main limitation of this report.

Conclusion

Though BLL was not significantly correlated with opioid addiction, but most of these patients were opioid addicts. This confirms previously reported evidence showing possible adulterations of opium with other chemicals such as lead or arsenic. Apparently, public awareness and health-care-providers' knowledge should be improved about the potential hazardous effects of using adulterated opium.

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