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Determining the Relationship Between Lead Poisoning and Abdominal Pain among Opium Users Referred to the Emergency Room of Beheshti Hospital in Kashan

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Abstract

Background: Abdominal pain is one of the symptoms of lead poisoning, but due to the differential diagnosis of abdominal pain, it is often neglected and ruled out. This study aims to determine the relationship between lead poisoning and abdominal pain among opium users referred to Beheshti Hospital in Kashan.

Methods: This case-control study was conducted on 60 opium-consuming patients referred to Shahid Beheshti Hospital Gastroenterology Clinic, with ($n=30$) and without ($n=30$) abdominal pain. After obtaining consent from all patients, demographic information, the type, method, and duration of the substance consumed, clinical manifestations, and laboratory findings were recorded in the questionnaire. Blood samples were taken and analyzed for serum lead levels in the hospital laboratory.

Results: The average lead level in opium users with and without abdominal pain was 78.96 µg/dL and 11.51 µg/dL, respectively, which shows a significant relationship ($P\leq0.001$). The average blood hemoglobin in opium users with and without abdominal pain was 10.37 mg/dl and 13.5 mg/dl, respectively, and the difference was significant ($P\leq0.001$). The average lead levels were 56.5 µg/dL in opium users with nausea and 33.1 µg/dL in people without nausea. Also, there was a significant relationship between lead level and anorexia, weight loss, and constipation. The highest correlation was found between lead levels and hemoglobin ($R=0.728$) and hematocrit ($R=0.649$). Also, there was a significant correlation between ALT levels and lead ($P=0.032$).

Conclusion: This study found a strong link between lead poisoning (mean: 78.96 µg/dL) and chronic abdominal pain in opium users. The findings emphasize the need for lead screening in symptomatic opium users.

Keywords: Opium, Addiction, Lead, Poisoning, Abdominal pain, Digestive symptoms

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Introduction

Lead is one of the most commonly used metals due to its low melting point, high density, and flexibility. Decades of extensive industrial and commercial consumption of lead products, especially gasoline and paint, have led to environmental pollution and the occurrence of acute poisoning due to contact with lead. Long-time contact with lead causes gradual and progressive damage, but it does not have any apparent symptoms (1). However, acute lead poisoning presents as symptoms such as abdominal pain, constipation, neuropathy, joint pain, anorexia, nausea, and anemia (2).

The abdominal pain associated with lead poisoning, often termed "lead colic," arises from multiple pathophysiological mechanisms. Lead disrupts smooth muscle function by interfering with calcium-dependent processes, leading to uncontrolled contractions and spasms in the gastrointestinal tract. Additionally, lead induces oxidative stress and mitochondrial dysfunction in enteric neurons, impairing gut motility and causing visceral hypersensitivity. Recent studies also highlight lead's ability to disrupt the gut-brain axis by altering the levels of neurotransmitters, such as serotonin and dopamine, which regulate pain perception and gut motility. Furthermore, lead-induced anemia (due to inhibition of heme synthesis) exacerbates abdominal pain by reducing oxygen delivery to intestinal tissues. These mechanisms collectively contribute to the severe cramping abdominal pain observed in lead-poisoned individuals (3).

Many lead-poisoning prognoses are caused by the interaction of lead with vital body chemicals, such as calcium, enzymes, and other proteins (4). Lead poisoning

can occur from eating or inhaling lead components. About 90–95% of absorbed lead is stored in bones, teeth, the liver, the brain, and the kidneys. The excretion of 75% is done by the kidneys, and the remaining amounts are eliminated by the digestive system, sweat, and skin, or are accumulated in the nails and hair (5). In adults, most of the absorption of lead happens through the respiratory system, with up to 95% absorption in the lungs. The digestive system can absorb between 5 and 20% of the lead ingested orally (6).

The diagnosis of lead poisoning depends on its levels in the blood. Recently, increasing reports of lead poisoning caused by drugs such as marijuana, methamphetamine, and, especially, opioids have been published (7). In large-scale production of opium, the concentration and intensity of lead, one of its main impurities, increases (8).

Due to Iran's eastern border with the largest opium-producing country in the world, placing it on the opioid transmission route, the health complications caused by opium consumption in Iran are serious (9, 10). Various studies have been conducted on lead poisoning in this group of people. In a study conducted by Hayatbakhsh et al in 2017, a peak was reported in lead poisoning in people addicted to opium in Kerman. People with high lead levels had symptoms such as abdominal pain, constipation, anorexia, and vomiting (5). Another similar study in England determined that the cause of colic pain, nausea, and vomiting in an opium-addicted patient began four days before admission. This patient suffered from hemolytic anemia, and in his peripheral blood smear, basophilic stippling was observed. However, in another study in Kerman, no significant difference was found between the serum lead level in heavy opium users and the healthy control group (9).

Another study in Tehran in 2017 reported an outbreak of symptomatic lead poisoning among people who used opium and heroin in gastroenterology clinics (11). In another study in Tehran between 2014 and 2018, a peak of lead poisoning was reported in opium users, but it did not reach the baseline levels (12). A study in Kerman in 2020 on the level of lead in opium materials showed that lead is present in opium extract, methadone syrup, and opium, but it is not at a toxic level. In the ten samples taken, all the samples had serum levels ≤ 5 ppm (13).

Considering the importance of the problem of poisoning among opium users, the contradictory findings of previous studies regarding its relationship with abdominal pain in these patients, and the lack of previous similar studies in the central region of Iran, especially Kashan, the present study was designed to examine the relationship between lead poisoning and abdominal pain among opium users.

Methods

Study Design and Participants

This case-control study enrolled 60 opium-consuming patients referred to Shahid Beheshti Hospital Gastroenterology Clinic (2019–2021), divided equally into cases (with chronic abdominal pain ≥ 3 months) and controls (without abdominal pain). The cases were included if they had: (1) unexplained abdominal pain after normal endocolonoscopy/ultrasound, (2) oral opium use for ≥ 1 year, (3) ≥ 18 years of age, and (4) blood lead levels (BLL) ≥ 20 µg/dL (Qiagen kit). The controls were matched to cases by age (± 5 years), sex (29 males/1 female), duration (± 2 years), method of opium use (oral/inhalation dominant), and residential area (Kashan province) to minimize confounding. All controls lacked abdominal pain or gastrointestinal disorders and were screened for alternative lead sources. Both groups excluded patients with exposure to alternative lead sources (e.g., occupational exposure), chronic kidney disease, hemolytic anemia, or pregnancy.

Data Collection

The information of oral opium-consuming patients was collected by a questionnaire including demographic information, clinical symptoms, and the results of tests, ultrasound, and endocolonoscopy. Also, information related to opium consumption, including the history of opium addiction, the duration of addiction, and the route of administration, was recorded. Also, the patients were examined in terms of the presence of clinical manifestations related to lead poisoning. The results of tests such as CBC, liver, and kidney function tests were recorded in the patient questionnaire, and to measure the serum lead level, a 5 ml sample of venous blood was taken from the patients and sent to a central laboratory. The control group was selected from opium users without abdominal pain who provided informed consent. The information of the control group was also documented in the questionnaire. Then, 5 ml of venous blood was sent to the laboratory to measure the blood lead levels. A Qiagen kit made in Germany was used to measure lead serum levels. Serum levels above 20 µg/dL were considered higher than normal and were recorded as lead poisoning.

Statistical Analysis

Serum lead levels from both case and control groups were analyzed using SPSS (version 16). Quantitative variables were summarized using measures of central tendency and dispersion, and categorical variables were presented as absolute/relative frequencies in tables and figures. Based on data distribution characteristics, we employed either parametric tests (independent *t*-test and ANOVA) for normally distributed variables or their non-parametric equivalents (Mann-Whitney *U* and Kruskal-Wallis) when assumptions were violated, ensuring appropriate analysis of variable relationships across different classifications.

Results

Thirty people addicted to opioids with abdominal pain

Table 1. Frequency distribution of background variables according to the presence or absence of abdominal pain in opium users

Variables		Stomach ache		*P* value*
		Yes	No	
Sex	Male	30 (100%)	29 (96.7%)	NS
	Female	0 (0%)	1 (3.3%)	
Type of addiction	Opium	24 (80%)	22 (73%)	0.774
	Heroin	1 (3.3%)	2 (6.7%)	
	Juice	5 (16.7%)	6 (20%)	
	Edible	28 (93.3%)	23 (76.7%)	
Consumption rout	Inhalation	1 (3.3%)	7 (23.3%)	0.05
	Injectable	1 (3.3%)	0 (0%)	
Age		52.2 ± 11.3	54.03 ± 14.56	0.588
Duration of addiction		17.97 ± 9.49	16.27 ± 10.47	0.513

NS: not significant; $P > 0.05$
*Tests: chi-square for categorical variables; independent *t*-test for continuous variables; $\alpha = 0.05$

and 30 people without abdominal pain participated in this study. All people with abdominal pain were men, and there were 29 men and one woman without abdominal pain. The mean and standard deviation of the age were 52.2 ± 11.3 years in the group with abdominal pain and 54.03 ± 14.56 years in the group without abdominal pain. No significant associations were found between abdominal pain and gender ($P = 0.32$), type of opium use ($P = 0.77$), age ($P = 0.59$), or duration of addiction ($P = 0.51$). A significant relationship was seen between drug use and abdominal pain ($P = 0.05$) (Table 1). The multivariable linear regression analysis (Table 2), adjusted for age, sex, and duration of addiction, confirmed that abdominal pain was the strongest independent predictor of elevated blood lead levels ($\beta = 62.4$ µg/dL, 95% CI: 54.1–70.7, $P < 0.001$). Duration of opium use showed a marginal association with lead levels ($\beta = 0.8$ µg/dL per year, $P = 0.06$), while age and sex were not significantly associated ($P > 0.2$).

In opium users with abdominal pain, the frequency of nausea was 66.7% and in the group without abdominal pain, it was 33.3%. Statistically, there was a significant relationship between abdominal pain and nausea. Also, a statistically significant relationship was seen with vomiting, anorexia, weight loss, and constipation. The highest frequency of pain was in the epigastrium with 51.7%, followed by the umbilical area with 20.7%. Also, in terms of pain quality, 53.8% had constant pain (Table 3).

The average blood hemoglobin was 10.37 mg/dL in opium users with abdominal pain, and 13.5 mg/dL in people without abdominal pain, with a statistically significant difference between them. Also, a significant relationship was seen in terms of liver enzyme levels and abdominal pain. The highest correlation was seen between lead levels and hemoglobin (R = 0.728) and hematocrit (R = 0.649). Also, there was a significant correlation between ALT and lead levels (Table 4).

In opium users with nausea, the average lead level was 56.5 µg/dL, and in people without nausea, it was 33.1 µg/dL, with a statistically significant difference. Also, there was a significant relationship between lead levels and anorexia, weight loss, and constipation. However, there was no statistically significant relationship between lead levels and vomiting and high blood pressure. The average level of lead was 78.9 µg/dL in opium users with abdominal pain and 11.51 µg/dL in people without abdominal pain, with a statistically significant difference (Figure 1). The average level of lead at the site of pain in different parts of the abdomen was almost the same. Also, in continuous pain, the average level of lead was 83.1 µg/dL. The average levels of lead in people consuming opium, opium juice, and heroin were 46.7, 1.49, and 11.8, respectively. However, no significant relationship was seen between the consumption of these three substances and lead levels (Table 5).

Table 2. Multivariable linear regression analysis of factors associated with blood lead levels in opium users

Variable	β coefficient (µg/dL)	95% CI	*P* value*
Abdominal pain (yes/no)	62.4	54.1–70.7	<0.001
Age (per year)	0.2	–0.1–0.5	0.22
Sex (male/female)	1.8	–4.2–7.8	0.55
Duration of addiction (per year)	0.8	–0.04–1.6	0.06

*Test: linear regression; $\alpha = 0.05$

Discussion

Our study demonstrates a significant association between lead poisoning and chronic abdominal pain among opium users, corroborating and expanding upon previous research in this field. The findings align with the work of Hayatbakhsh et al who reported elevated lead levels (mean: 52 µg/dL) in symptomatic opium users in Kerman, Iran (5). However, our observed levels (mean: 78.96 µg/dL) were notably higher, likely reflecting regional variations in opium contamination patterns. In contrast, Hashemi Domeneh et al documented lower lead concentrations

Table 3. Frequency distribution of clinical symptoms, location, and quality of abdominal pain, based on the presence or absence of abdominal pain in opium users

		Stomach ache		*P* value*
		Yes	No	
Clinical signs	Nausea	21 (66.7%)	10 (33.3%)	0.009
	Vomiting	14 (46.7%)	6 (20%)	0.054
	Anorexia	15 (50%)	5 (17.2%)	0.013
	Weight loss	9 (30%)	1 (3.4%)	0.012
	Constipation	25 (83.3%)	12 (40%)	0.001
	High blood pressure	3 (10%)	2 (6.7%)	NS
Abdominal pain	Epigastrium	15 (51.7%)	--	
	RUQ	1 (3.4%)	--	
	Umbilical lobe	6 (20.7%)	--	
	Hypogaster	2 (6.9%)	--	
	Generalized	5 (17.2%)	--	
Quality of pain	Colic	12 (46.2%)	--	
	Ongoing	14 (53.8%)	--	
All people		30	30	

NS: not significant, $P>0.05$; RUQ: right upper quadrant
*Tests: chi-square for symptoms; $\alpha=0.05$

Table 4. The mean and standard deviation of test results based on the presence or absence of abdominal pain, and their linear correlation coefficient with lead levels in opium users

Laboratory factors	Stomach ache			Lead level	
	Yes	No	*P*-value*	Linear correlation coefficient	*P* value*
Hb	10.37±1.94	13.5±1.78	<0.001	−0.728	<0.001
Hct	31.8±5.89	39.5±5.17	<0.001	−0.649	<0.001
AST	55.3±46.7	25.9±10.9	0.003	0.265	0.056
ALT	80.9±67.2	20.1±7.5	0.006	0.295	0.032
ALP	174.3±270.9	187.9±47.6	0.026	0.258	0.065
PT	27.5±3.43	26.04±2.39	0.107	0.078	0.0616
INR	1.12±0.13	1.19±0.24	0.242	−0.134	0.379
BUN	16.2±7.2	15.2±19.1	0.387	−0.119	0.393
Cr	1.09±0.2	1.13±0.67	0.798	0.051	0.713
Alb	4.17±0.56	3.93±0.55	0.329	0.055	0.771

Hb: hemoglobin (g/dL); Hct: hematocrit (%); AST: aspartate aminotransferase (U/L); ALT: alanine aminotransferase (U/L); ALP: alkaline phosphatase (U/L); PT: prothrombin time (seconds); INR: international normalized ratio; BUN: blood urea nitrogen (mg/dL); Cr: creatinine (mg/dL); Alb: albumin (g/dL)
*Tests: independent *t*-test for group comparisons; Pearson correlation for associations; $\alpha=0.05$

(mean: 11.73 µg/dL) in Tehran, possibly due to their inclusion of asymptomatic individuals in their cohort (14). The high prevalence of abdominal pain (96.3%) among users with blood lead levels > 40 µg/dL strongly supports earlier clinical observations by Masoodi et al (15), while providing more robust evidence through our controlled study design. The inverse correlation between lead levels and hemoglobin (R = −0.728) confirms Ghane et al's (11) outbreak investigation findings and offers a more precise quantification of this hematological effect. Similarly, our observed association between lead exposure and ALT elevation reinforces Shabani et al's (16) report of liver function abnormalities, though the stronger correlation in our study may reflect stricter case definitions (pain duration ≥ 3 months).

This study advances current knowledge in several important ways. First, it establishes a clear dose-response relationship not previously quantified in this population. Second, it provides controlled comparisons between symptomatic and asymptomatic users. Third, it identifies specific clinical thresholds (40 µg/dL) that may guide therapeutic interventions. These findings suggest that lead screening should become routine for opium users presenting with abdominal pain and that the 40 µg/dL threshold warrants consideration for chelation therapy initiation.

While the single-center design may limit generalizability, our careful matching of controls strengthens the study's internal validity. Future multicenter studies should investigate geographic variations in opium contamination

Table 5. Mean and standard deviation of lead levels based on the presence or absence of clinical complaints, abdominal pain, location and quality of pain, type and method of consumption in opium users

Symptom		Yes	No	*P* value*
Clinical complaints	Nausea	48±56.5	35.9±33.1	0.037
	Vomiting	55.9±48.5	40.9±39.9	0.186
	Anorexia	62.4±47.6	40.2±37.1	0.036
	Weight loss	84.7±40.9	40.7±37.7	0.002
	Constipation	59.9±45.6	21.7±28.6	0.001
	High blood pressure	33.5±47.9	44.9±45	0.888
Stomach ache		78.9±37.9	11.2±11.51	<0.001
Location of pain	Epigastrium	37.9±78.5	--	<0.001
	RUQ	12.27	--	
	Umbilical lobe	86.8±19.2	--	
	Hypogaster	79±2.82	--	
	Generalized	67.9±43.7	--	
Quality of pain	Ongoing	83.1±31.7	--	<0.001
	Colic	32±73	--	
Type of opium	Opium	46.72±45.47	--	0.324
	Juice	40.1±49.13	--	
	Heroin	8.11±3.85	--	
Consumption rout	Inhalation	7.44±2.61	--	<0.001
	Edible	51.8±44.4	--	
	Injectable	0±12.3	--	

RUQ: right upper quadrant
*Tests: independent *t*-test/Mann-Whitney *U* for symptoms; ANOVA/Kruskal-Wallis for multi-group comparisons; $\alpha = 0.05$*

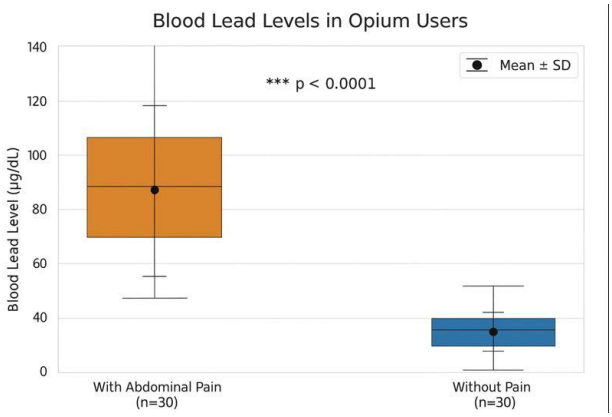

Figure 1. Comparison of blood lead levels (µg/dL) between opium users with abdominal pain (cases) and without abdominal pain (controls)

patterns, evaluate long-term outcomes following chelation therapy, and assess the cost-effectiveness of systematic screening programs.

In conclusion, our findings both confirm and extend previous research by Hayatbakhsh, Ghane, and others, while providing novel quantitative evidence to inform clinical practice. The results underscore lead poisoning as a critical consideration in the evaluation of opium users with chronic abdominal pain, particularly in endemic regions. These insights should guide the development of more targeted screening protocols and treatment algorithms for this vulnerable population.

Conclusion

This study found a strong link between lead poisoning (mean: 78.96 µg/dL) and chronic abdominal pain in opium users and digestive symptoms. However, the small sample size ($n = 60$) and observational design limit broader generalizations. Despite potential confounders like opium source variability, the findings emphasize the need for lead screening in symptomatic opium users. Future multicenter studies should confirm these results and explore long-term effects. Clinicians in high-risk regions should consider lead toxicity in differential diagnoses. This research provides critical evidence for a growing public health concern.

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Competing Interests
The authors declare that they do not have any conflict of interest.

Ethical Approval
This study was approved by the Ethics Committee of Kashan University of Medical Sciences (approval code: IR.KAUMS.MEDNT.REC.1399.132)

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