ASIA PACIFIC JOURNAL of MEDICAL TOXICOLOGY
APJMT 12;1 http://apjmt.mums.ac.ir March 2023

ORIGINAL ARTICLE

Relationship between Abdominal Pain and Blood Lead Level

SAEED AFZALI [1*], RASOUL SALIMI [2], ABBAS MORADI [3], MARYAM SHIRI [4]

[1]Department of Forensic Medicine, School of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran
[2]Department of Emergency Medicine, School of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran
[3]Department of Community Medicine, School of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran
[4]Emergency medicine specialist, School of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran

Abstract

Background and Objective: Lead poisoning is a problem in Iranian society. The most common symptoms of chronic lead poisoning are abdominal pain, constipation, and dysphagia. In this study, the blood lead level (BLL) of the patients, who referred to Besat Hospital, Hamadan, Iran with non-traumatic abdominal pain was evaluated.
Materials and Methods: This is a case-control study in which 120 patients with abdominal pain, who referred to ED were divided into two groups. The first group of patients without exposure to lead (control) and the second group with exposure to lead (case), and then BLL were measured**.**
Results: Of 120 patients, 74 patients were male and 46 patients were female. The patients` mean age was 48.76 ± 17.12 years. The average BLL in the control group was 0.67 ± 1.38 µg/dL and in the case group was 1.61 ± 3.02 µg/dL ($p<0.001$). In the case group, 59 patients had a history of opium consumption and one was a building painter, whose average BLL was 1.63 ± 0.4 and 0 ± 0.3 µg/dL respectively. One patient from the control group and five patients from the case group had BLL higher than normal, but there was no statistical difference observed in both groups ($p=0.207$).
Conclusion: lead poisoning among patients with abdominal pain, especially in opium addicts, should always be considered as a differential diagnosis.

Keywords: Abdominal pain, Blood leads level, Lead poisoning, Opium

How to cite this article: Afzali S, Salimi R, Moradi A, Shiri M. Relationship between Abdominal Pain and Blood Lead Level. Asia Pac J Med Toxicol 2022; 12(1):25-28.

INTRODUCTION

Lead as a heavy metal is widely used in various industries such as battery factories, automotive industries, paint and ceramic industries, tile making, oil and refining industries, electronic engineering, and construction industries. The absorption of lead in people with long-term exposure can often cause chronic poisoning [1-6].

In countries where opium consumption is widespread, including Iran, lead is added to opium for the purpose of abuse and more profit, and its long-term use can cause lead poisoning [7].

As with other heavy metals, lead can cause disease by affecting different organs through multiple mechanisms. After binding to sulfhydryl groups, it affects various enzyme proteins and receptors. On the other hand, lead is chemically similar to the divalent cations calcium, magnesium, and zinc. It interferes with numerous metabolic pathways mediated by calcium and perhaps magnesium and zinc, particularly in mitochondria and messenger systems that regulate cellular energy metabolism. It also causes DNA methylation and mitogenic and carcinogenic effects in mammals by affecting nucleic acids through unknown mechanisms. Lead causes damage to the central and peripheral nervous system, hematological, cardiovascular, renal, reproductive system, endocrine system, digestive system, and skeletal system [8].

Acute lead poisoning due to the consumption of large amounts of inhalation, ingestion, and injection is rarely seen. It mostly occurs in adult cases, especially after chronic inhalation. Clinical symptoms of patients include colicky abdominal pain, hepatitis, pancreatitis, hemolytic anemia, and encephalopathy over days or weeks. Encephalopathy in adults is usually observed with a very high blood lead concentration, accompanied by seizures, confusion, focal movement disorders, papillary edema, headache, and optic neuritis. Peripheral neuropathy is seen in the form of wrist and foot drop. Gastrointestinal symptoms include metallic taste, abdominal pain and loss of appetite, weight loss, and constipation.

Measuring BLL is one of the ways to diagnose poisoning. According to the report published by the Center for Disease Control and Prevention (CDC), BLL more than 5 micrograms per deciliter is considered toxic [9].

Considering that abdominal pain is one of the most important and common reasons for visiting medical centers and opium consumption is highly prevalent in Iran, in this

*Correspondence to: Saeed Afzali, MD, Department of Forensic Medicine, School of Medicine, Hamadan University of Medical Sciences, Hamadan, Iran.
Email: afzali691@yahoo.com, Mobile: +98 9188121542

study, the relationship between BLL and the possibility of lead poisoning in non-traumatic abdominal pain patients was investigated. It has been studied in two different groups; without exposure to lead (control) and the group with exposure to lead (case).

METHODS

In this prospective case-control study, 120 patients with non-traumatic abdominal pain referred to Besat Hospital in Hamadan, Iran during March 2018 to December 2019 were included in the study. They were divided into two groups: control group (without exposure to lead) and case group (with exposure to lead) and BLL was measured in both groups. The exposure group included all patients, who had the possibility of contact with lead due to their jobs, such as building and car painters, battery makers, soldiers, radiator makers, potters and opium users.

The sample size was obtained using the following formula at a significance level of 5%, a power of 90%, and the average data and standard deviation of the BLL in healthy people and oral opium addicts. According to the study [10], 60 patients in each group were enrolled in the study.

α.=0.05	μ2=6.05
β.=10%	S1=1.83
μ1=11.75	S2=6.06
	n.= 120

$$n = \frac{\left(Z_{1-\alpha/2} + Z_{1-\beta}\right)^2 . (S_1^2 + S_2^2)}{(U_1 - U_2)^2}$$

The inclusion criteria included obtaining informed consent, non-traumatic abdominal pain, history of occupational and non-occupational exposure to lead in the case group, and exclusion criteria included traumatic patients and lack of informed consent. Accordingly, after meeting the conditions for entering the study, the demographic data were obtained and blood samples were collected and stored for BLL measurement.

Laboratory Methods:

For each case with abdominal pain, who was exposed to lead, one patient with abdominal pain symptoms without exposure, who were matched in terms of age and gender were selected as the control group. In both groups, 1 ml of the patient's blood sample prepared with heparin was kept at minus 20 degrees Celsius until analysis. Before conducting the test, all the tools used in each step of the work were placed in 5% nitric acid for 48 hours and thoroughly washed with distilled water. Elisa method was used to determine BLL:

Wash Solution: Contains 0.0001% Triton X-100 in deionized water, filled in a sampler wash bottle.

Matrix modifier solution: prepared from 0.5% Triton X-100 and 2% ammonium dihydrogen phosphate solution in 100 ml of nitric acid with a concentration of 2% (Merck, Supra-Pure) in an LDPE bottle.

The standard sample contains 1mg/L lead stock in 1% nitric acid solution (Merck, Supra-Pure). Secondary standards included 25, 50, 100, 200, and 300 mg/L Pb from a 1 mg/L stock in 50 mL plastic flasks.

Calibration standard: 0.25, 0.5, 1, 2 and 3 ug/dl: by pipetting 100 uL of each of the secondary solutions in a 1/2 plastic sampler and diluting them all by adding 900uL of the matrix solution adjusted and mixing them with a micropipette tip. Calibrate the blank in the same way using 1% HNO3 solution.

Sample solution: taking 100uL of each of the blood samples in a 1.2 mL plastic container and diluting it with 900uL of the adjusted matrix solution and then mixing it.

Analysis was performed using atomic absorption spectrophotometry with a PinAAcle TM 900T device using automatic color spectrum and furnace technique with THGA graphite tubes [11].

Statistical Analysis:

After collecting data, they were analyzed with SPSS-16 software. In order to compare the mean BLL in both control and case groups by non-parametric Mann-Whitney test, comparing BLL and abdominal pain between two groups by Fisher's exact test, correlation between BLL and age by Spearman's correlation coefficient and comparing BLL Kruskal-Wallis test for blood in opium addicts was performed based on the method of consumption. All analyses were performed at the 95% confidence level and a significance level of less than 0.05 was considered.

RESULTS

In this study, 120 patients, who referred to the hospital with non-traumatic abdominal pain, were divided into two groups of 60 patients. The first group (control) included patients, who had no history of exposure to lead compounds, and the second group (case) included patients, who had a history of possible exposure to lead. The demographic data of the patients is shown in Table. 1.

The average total BLL in male and female of both groups was 1.36 ± 2.24 and 1.36 ± 2.61 μg/dL, respectively. According to the Mann-Whitney test, there was no statistically significant difference between the BLL and gender (p=0.787).

Table 1. Demographic data of patients in both groups

Total	Control group N (%)	Case group N (%)	N (%)
Sex			
Male	28(23.3)	46(38.3)	74(61.7)
Female	32(26.7)	14(11.7)	46(38.3)
Symptoms			
Nausea &Vomiting	42(35)	42(35)	84(70)
Constipation	8(6.7)	34(28.3)	42(35)
Frequency	12(10)	8(6.7)	20(16.7)
Weakness	3(2.5)	4(3.3)	7(5.8)
Fever	2(1.6)	3(2.5)	5(4.1)

The average age of the patients in the two groups was 48.76 ± 17.12 years and the minimum age was 14 and the maximum was 80 years. BLL was higher in the elderly than in the young. Based on Spearman's correlation coefficient, there was no statistically significant relationship between age and BLL between the two groups (p=0.450).

Of the 60 patients in the case group, 59 patients had a history of opium use and one was a building painter, whose average BLL was 1.63 ± 0.4 and 0.3 ± 0 µg/dL, respectively. Methods of exposure to lead in the case group are shown in Table 2.

Table 2. **Routes of lead consumption in case group**

Routes	N (%)	BLL(µg/dL)	Pvalue
Inhalation	31(51.7)	1.25 ±2.46	0.298
Oral	15(25)	2.44 ± 3.65	
Inhalation+Oral	14(23.3)	1.50 ± 3.44	

Table 3. **Frequency distribution of BLL in both groups**

	Control group N (%)	Case group N (%)	Pvalue
Normal	59(49.2)	55(45.8)	0.207
Abnormal	1(0.8)	5(4.2)	

Based on the findings of Table 2 and using the Kruskal-Wallis statistical test, no statistically significant difference was observed between BLL and the method of exposure to lead in the case group (p=0.298).

The minimum BLL was 1 µg/dL and the maximum was 13.90 µg/dL. The average BLL in the control group was 0.67 ± 1.38 µg/dL and in the case group was 1.61 ± 3.02 µg/dL, which was statistically different between the two groups (p<0.001).

One patient from the control group and five patients from the case group had BLL higher than normal. According to Fisher's exact test, there was no statistically significant difference between abdominal pain and BLL in two groups (p = 207) (Table 3).

DISCUSSION

Among the clinical symptoms, abdominal pain is almost the most common symptom that causes patients to refer to medical centers. Several reasons, whether medical or surgical, can cause abdominal pain. One of the causes for this can be lead poisoning.

Considering the high prevalence of opium consumption in Iran and the possibility of adding impurities such as lead to gain more profit, the possibility of lead poisoning, especially in people with a history of opium addiction, should always be considered [12].

Based on the analyses performed on opium samples, different amounts of lead have been observed in them. The long-term consumption of which can cause lead poisoning and complications [7, 13, 14]. According to the Center for Disease Control and Prevention (CDC), there is no safe level of lead in the blood, so the presence of any level of lead in the blood can cause various harms [15].

In lead poisoning, various gastrointestinal symptoms, anemia, and neuropathy occur, which are sometimes non-specific and may lead to a lot of overlap in diagnosis. Failure to diagnose and treat on time can cause irreparable and irreversible injuries. In patients with a history of opium addiction, who present with abdominal pain, failure to diagnose lead poisoning may lead to unnecessary medical procedures and even surgery.

In the present study, which evaluated patients with abdominal pain, despite the fact that the average BLL in the exposed group with lead was significantly higher than that in the non-exposed group, a small number of patients had BLL higher than normal range. In the exposed and non-exposed groups, there was no significant relationship between age and BLL, but in both groups, the total correlation between BLL and age was significant and also the BLL increased with age. There was no statistically significant relationship between BLL and gender and the method of lead exposure. Considering the obtained results, lead poisoning should always be considered as a differential diagnosis in patients with abdominal pain.

The average age and male to female ratio in this study was similar to the other studies [16, 17]. Due to the tendency of most Iranians to consume traditional drugs, opium consumption is more common and is widely seen, especially in men and middle-aged people.

Based on the findings of this research, in the case group, BLL was higher in elderly patients than in young patients, so the possibility of lead poisoning is higher in this group. Despite the higher consumption of opium among the elderly [18, 19], currently young people are more inclined to use industrial drugs such as amphetamine compounds and its derivatives and marijuana [20].

The average BLL in the present study in both groups was lower than the findings of the other studies that specifically examined the BLL of opium addicts [21, 22]. However, it was consistent with other studies [10, 23].

In the present study, as in other studies conducted on opium users, the most common symptoms were abdominal pain, nausea, and constipation [21, 23, 24]. Considering that in lead poisoning, in addition to abdominal pain, there are other accompanying symptoms, including the mentioned symptoms, while investigating other causes of abdominal pain; lead poisoning should always be considered, especially in patients with lead exposure.

As in other studies, in the patients, who were likely to be exposed to lead (case group), most of them were opium users and the most common method of consumption was inhalation. The BLL in oral opium users was higher than inhalers [10, 22].

CONCLUSION

The results of this study showed that although statistically significant difference was not observed between BLL and

abdominal pain, due to the high prevalence of opium consumption in Iran and the possibility of lead poisoning, emergency physicians should be aware of this complication and consider lead poisoning, especially in opium users presenting with abdominal pain.

LIMITATION

In the current study, the final causes of abdominal pain were not determined. Therefore, to investigate the relationship between abdominal pain and lead poisoning, this issue should be considered in future studies.

ACKNOWLEDGMENT

This article is taken from the doctoral dissertation on emergency medicine. It was carried out with the permission of the ethics committee of Hamadan University of Medical Sciences under the number IR.UMSHA.REC.1397.63.

In addition, the authors sincerely appreciate the Day laboratory personnel, who cooperated in this research study.

Conflict of interest: None to be declared.
Funding and support: None.

REFERENCES

1. Abdollahi M, Ebrahini-Mehr M, Nikfar S, Jalali N. Monitoring of lead poisoning in simple workers of a copying center by flame atomic absorption spectroscopy. MJIRI. 1996; 10(1):69-72.
2. Abdollahi M, Sadeghi Mojarad A, Jalali N. Lead toxicity in employees of a paint factory. MJIRI 1996; 10(3):203-6.
3. Abdollahi M, Shohrati M, Nikfar S, Jalali N. Monitoring of lead poisoning in bus drivers of Tehran. Irn J Med Sci. 1995; 20:29-33.
4. 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. International Journal of Occupational & Environmental Medicine. 2010; 1(1). PMID: 23022779
5. Malekirad AA, Oryan S, Fani A, Babapor V, Hashemi M, Baeeri M, et al. Study on clinical and biochemical toxicity biomarkers in a zinc-lead mine workers. Toxicology and industrial health. 2010; 26(6):331-7. PMID: 20371635 DOI: 10.1177/0748233710365697
6. Mehrpour O, Karrari P, Abdollahi M. Chronic lead poisoning in Iran; a silent disease. DARU Journal of pharmaceutical Sciences. 2012; 20(1):8. PMID: 23351197 DOI: 10.1186/2008-2231-20-8
7. 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. Bulletin of the World Health Organization. 2018; 96(3):165. PMID: 29531415 DOI: 10.2471/BLT.17.196287
8. Calello DP, Henretig FM. Goldfrank's toxicologic emergencies.11th ed New York: McGraw-Hill, 2019.
9. Control CDC, Prevention. Blood lead levels in children aged 1-5 years-United States, 1999-2010. MMWR Morbidity and mortality weekly report. 2013; 62(13):245.
10. 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. Journal of research in medical sciences: the official journal of Isfahan University of Medical Sciences. 2014; 19(10):939. PMID: 25538776
11. 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. PMID: 23105986
12. Masoodi M, Zali MR, Ehsani-Ardakani MJ, Alizadeh AH, Aiassofi K, Aghazadeh R. Abdominal pain due to lead-contaminated opium: a new source of inorganic lead poisoning in Iran Arch Iran Med 2006 Jan;9(1):72-5. PMID: 16649384
13. Soltaninejad K, Faryadi M, Akhgari M. Determination of lead in opium by flame atomic absorption spectrometry method. Sci J Forensic Med 2003; 9:176-9.
14. Aghaee Afshar M, Khazaeli P, Behnam B, Rezazadehkermani M, Ashraf-Ganjooei N. Presence of Lead in Opium. Arch Iran Med 2008; 11:553–4.
15. Control CFD, Prevention. Blood lead levels in children aged 1-5 years-United States, 1999-2010. MMWR Morbidity and mortality weekly report. 2013; 62(13):245.
16. Shabani M, Hadeiy S.K, Parhizgar P, Zamani N, Mehrad H, Hassanian-Moghaddam H, et al. Lead poisoning; a neglected potential diagnosis in abdominal pain. *BMC* Gastroenterol 2020; 20, 134. DOI: 10.1186/s12876-020-01284-1
17. Neghabi Z, Amiri H, Aghabiklooei A, Saburi Shekofte H. Relationship of serum lead level in patients consuming oral opium with abdominal pain. J Prev Epidemiol. 2019; 4(2):e10.
18. Froutan H, Kashefi Zadeh A, Kalani M, Andrabi Y. Lead toxicity: a probable cause of abdominal pain in drug abusers. Med J Islam Repub Iran 2011; 25 (1):16-20.
19. Amin-Esmaeili M, Rahimi-Movaghar A, Sharifi V, Hajebi A, Radgoodarzi R, Mojtabai R, et al. Epidemiology of illicit drug use disorders in Iran: prevalence, correlates, comorbidity and service utilization results from the Iranian Mental Health Survey. Addiction. 2016 Oct; 111(10):1836–47. PMID: 27177849 DOI: 10.1111/add.13453
20. Moghimi Sarani E, Ahmadi J , Oji B , Mahi-Birjand M, Bagheri N, etal. Investigating the sequential patterns of methamphetamine use initiation in Iran. Subst Abuse Treat Prev Policy.2020 Jul 29; 15(1):52.Doi: 10.1186/s13011-020-00297-z
21. 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. Substance abuse treatment, prevention, and policy. 2017; 12(1):43.
22. Afzali S, Torabian S, Taheri SK. Do Opium Abusers Develop Lead Toxicity? A Study on Opium Abusers in Hamadan, Iran. Asia Pacific Journal of Medical Toxicology. 2017; 6(2):55-8. DOI:10.22038/apjmt.2017.8951
23. Nemati A, Jafari S, Afshari M, Dahmardeh S, Tabrizian K. Comparing Blood Lead Level among Oral/inhaled Opium Addicts with a Non-addict Control Group in the Southeast of Iran. Addiction & health. 2016; 8(4):235.
24. Farzaneh E, Habibzadeh A, Mehrpour O. Lead Toxicity among Oral Opium Addicts with Abdominal Pain: A Case Series of 17 Cases. Indian Journal of Forensic Medicine & Toxicology. 2017; 11(2). DOI: 10.5958/0973-9130.2017.00057.3