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The Association between Blood Lead Level and Cognitive Functions among the Workers of a Lead Mine in Iran

Zahra Yavar[1], Fatemeh Kargar-Shouroki[2*], Gholamhossein Halvani[2], Reyhane Sefidkar[3], Fahimeh Dehghani[4]

1. M.Sc. in Occupational Health Engineering, Industrial Diseases Research Center, Dept. of Occupational Health Engineering, School of Public Health, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.
2. Assistant Prof, Industrial Diseases Research Center, Dept. of Occupational Health Engineering, School of Public Health, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.
3. Assistant Prof, Center for Healthcare Data Modeling, Dept. of Biostatistics and Epidemiology, School of public health, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.
4. Associate Prof, Dept. of Psychology and Educational Sciences, Yazd University, Yazd, Iran

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*** Corresponding author:**
Fatemeh Kargar-Shouroki,
E-mail:
fkargar142@gmail.com

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Abstract

Background: Workers are exposed to lead in many industries and mines. The present study aimed to determine lead levels and cognitive functions among workers of a lead mine in Iran.
Materials and Methods: This cross-sectional study was conducted in Nain city in Isfahan Province, center of Iran, in 2022. The studied population consisted of 76 miners as the lead exposed group as well as a group of 76 office workers, working in the same mine, without any history of exposure to lead as the non-exposed group. Demographic information was collected using a questionnaire. The samples were analyzed using NIOSH techniques 8003 and 7082 to detect lead in the blood and breathing zone, respectively. The cognitive functions of the exposed and non-exposed groups were compared using the Wisconsin Card Sorting Test, digit span, Corsi block-tapping, Tower of London, and continuous performance tests.
Results: The mean lead levels in the breathing zone and blood were significantly higher in the exposed group (0.08 ± 0.06 mg/m^3, 37.41 ± 10.28 µg/dl, respectively), compared to the non-exposed group (0.02 ± 0.01 mg/m^3, 12.57 ± 4.27 µg/dl, respectively). The total scores for all cognitive tests in the exposed group were significantly worse than those in the non-exposed group. Even after controlling for age, work history, smoking, education, and body mass index, there were still significant correlations between blood lead levels and cognitive abilities ($p<0.05$).
Conclusion: According to the current study's findings, exposure to lead was associated with cognitive disorders.

Keywords: Lead, Cognitive Disorders, Mine Workers.

Introduction

Given its unique characteristics, lead is one of the materials most frequently employed in many different industries worldwide [1]. Human exposure to lead and its compounds occurs in factories making lead alloys, corrosion-resistant materials, gasoline additives (tetraethyl lead and tetramethyl lead), shields from radiation, construction and paper industries, pigment production, water distribution pipes, painting, welding, soldering, jewelry making, battery plants, glass production, plastic industry, automobile repair radiator, and during the production of ceramic glazes [2-5]. The extraction of lead in mines is one of the most important sites where lead exposure takes place [6].

Humans absorb lead through the gastrointestinal and respiratory tracts so that 40% of inorganic lead is absorbed through the respiratory tract while approximately 10-15% of the lead is absorbed through the gastrointestinal tract [7]. In the bloodstream, lead binds to red blood cells and is then distributed to the soft tissues (intestines, lungs, liver, spleen), and the central nervous system (CNS) and eventually accumulates in bones. The biological half-life of blood lead is 30 days; however, after distribution in soft tissues and accumulation in bones, it can remain in the body for 20-30 years. Therefore, measurement of blood lead level (BLL) is the best available method to determine recent, cumulative, and continuous lead exposures [8, 9].

Lead exposure can lead to high blood pressure, cardiovascular disease, nephrotoxicity, immunodeficiency, gastrointestinal symptoms, impaired reproductive system, and cognitive disorders including learning disabilities and memory loss [10]. Cognitive disorders are a category of mental health disorders that cause difficulties in cognitive functions so that the person needs treatment [11]. Analysis of brain volume and measurement of cognitive functions in organic lead workers revealed that lead exposure is associated with cerebral atrophy and deficits in several cognitive domains including visual structure, speed of processing, visual memory, executive function, and hand-eye coordination [12]. A systematic review of 22 studies (1976 - 2014) on 3849 people indicated that a mean BLL of 21.09 ± 6.44 μg/dL can result in cognitive impairment and sensory-motor problems including deficits in verbal ability, visuospatial ability, memory, concentration, and psychomotor functions [13].

Occupational Safety and Health Administration (OSHA) Permissible Exposure Limits (PELs) [14] and American Conference of Governmental Industrial Hygienists (ACGIH) threshold limit values (TLV) for lead is 0.05 mg/m^3 as an eight-hour time-weighted average (TWA). Additionally, the ACGIH recommended 20 μg/dl as the lead biological exposure index (BEI) [15]. The Center for Health and Environment of the Ministry of Health and Medical Education of Iran has also suggested a occupational exposure limit (OEL) of 0.05 mg/m^3 and 20 μg/dl for air-pb and blood- pb, respectively [16].

The Centers for Disease Control and Prevention (CDC) reported that cognitive impairment associated with lead exposure start at concentrations greater than 10 μg/dl. However, these effects have been observed in children and adults even at blood lead concentrations lower than 5 μg/dl [17] and 3 μg/dl [18]. Shwe et al. [19] in a study on battery manufacturing workers with a mean BLL of 4.25 ± 3.86 μg/dL reported a reduction in cognitive abilities, including attention, concentration, short-term memory, and perceptual-motor coordination. According to Lanphear et al., there is no safe threshold for the adverse effects of lead on cognitive function [17].

Heavy metal contamination in many lead and zinc mines has been reported [20] and workers are exposed to this metal in the lead mining stages including underground mining, open-pit mining, ore transportation, crushing, laboratory tests, grinding, flotation, and melting [21]. In a systematic review study, Sayehmiri et al. [22] reported a blood lead level (BLL) of 42.8 μg/dL in Iranian workers. The highest BLL was reported in zinc-lead mine workers (72.6 μg/dl). To our knowledge, frequency of neurobehavioral disorders has not been studied in lead mine workers of Iran. Thus, given the vast exposure of Iranian mine workers to lead, the current study was conducted to determine lead levels and to assess its potential effects on cognitive performance in lead mine workers in Iran.

Materials and Methods

This cross-sectional investigation was carried out to determine cognitive disorders induced by lead exposure in 76 miners in one of the lead mines in Isfahan province, Iran in 2022. A group of 76 office workers, working in same mine, without any history of exposure to lead, were selected as the non-exposed group. The following formula and statistical power analysis were used to estimate the sample size:

Formula 1.

$$n = \frac{({S_1}^2 + {S_2}^2)(Z_{1-\frac{\alpha}{2}} + Z_{1-\beta})^2}{(\bar{X}_1 - \bar{X}_2)^2}$$

Whereby power was calculated at β = 0.20 and α =0.05. According to a pilot study on 15 mine workers, the X1, X2, S1, and S2 values were determined as 7.5, 9.18, 2.81, and 4.39 respectively.

As a result, 76 participants were required for recruitment in each group. Simple random sampling was used to choose the samples.

The inclusion criteria were a work history of at least three consecutive years. Subjects with a history of occupational and non-occupational exposure to any dust and fumes (except lead) inducing cognitive disorders as well as those with a history of neuro-psychiatric disorders as well as visual and hearing problems were excluded from this study. In addition, the non-exposed group had no previous or current exposure to neurotoxic chemicals.

All participants completed written informed consent forms. Demographic data, including age, work history, level of education, height, weight, and smoking status were collected using a questionnaire.

Biological monitoring: Heparinized tubes were used for blood sample collection. The samples were kept at 4 °C for a maximum of three days until analysis. The BLLs were determined based on the NIOSH method 8003 [23].

Working standards in deionized water within the range of 10 to 150 μg/dl were prepared, and the calibration curve was made. In the next step, 0.8 ml of ammonium pyrrolidine dithiocarbamate (APDC-TX) and then 2 ml of methyl isobutyl ketone (MIBK) were added to 2 ml of the blood sample in the centrifuge tube. Then, the mixture was centrifuged at 2000 rpm for 10 minutes. Finally, the Pb-APDC solution in MIBK within 2 h of extraction was analyzed by flame atomic absorption spectrophotometry (AAS).

Measurement of lead levels in the breathing zone: Lead levels in the worker's breathing zone were measured using NIOSH method 7082 [24]. Using this technique, a personal sampling pump (SKC cat. no. 226-81A) equipped with a 37 mm cellulose ester membrane filter (pore size 0.8-μm) at a flow rate of 2 l/min was used to collect an 8-hour sample of the workers' breathing zone.

Working standards with concentrations range of 0.25 to 20 µg/ml were prepared for the calibration curve.

For sample preparation, 3 ml of nitric acid and 1 ml 30% H_2O_2 were added to the filters, and heated at 140°C until only 0.5 ml of nitric acid remained. This stage was repeated twice using 2 ml HNO_3 and 1 ml 30% H_2O_2. The walls of the beaker were washed using 3-5 cc of 10% nitric acid. When the samples were dried at room temperature, the residues were dissolved in 1 ml of nitric acid. The solution was transferred to a volumetric flask and diluted to 10 ml with distilled water. The lead concentrations were measured using an atomic absorption spectrophotometer at a wavelength of 283.3 nm.

Wisconsin Card Sorting Test (WCST): Executive functions such as concept formulation and planning skills are evaluated using the Wisconsin Card Sorting Test [25]. Cards can be sorted on the basis of figures (circle, triangle, cross, and star), color (yellow, green, red, and blue), and number (from one to four). Sixty-four cards were displayed at the bottom of the screen but only the deck's up-card was visible. Once the participant made six consecutive correct choices, the sorting principle was changed and the participant had to switch from the previous rule to a new rule [25]. The WCST was scored for the number of categories completed, the total number of errors, the number of perseverative, and the number of times the sorting principle was lost.

Continuous Performance Test (CPT): Attention and impulsivity were evaluated using the Continuous Performance Test. In this test, the participant was required to detect a particular target stimulus presented among a sequence of stimuli on the monitor at regular intervals. The errors of commission and omission were measured on this test [26].

The Tower of London Test: Planning skills were assessed using the Tower of London test. Subjects were asked to achieve the solution by moving the colored balls (green, blue, and red) to match a target display (problem-solving block) with the least number of possible moves [27]. The measured variables on this test were delay period, test period, total period, total errors, and total score.

Corsi block-tapping test: The Corsi block-tapping test was employed to evaluate visuospatial working memory [28]. This test is based on the digit span task, though instead of the verbal form of the digit span, it requires the use of visuospatial memory. In each trial, nine blocks are presented on the screen, and then, a certain number of the squares sequentially light up in yellow and the participant is required to recall the block sequence. When the sequence is finished, the participant has to click on each square in the same order as shown before. This test starts with a sequence of 2 blocks and continues up to nine blocks; the test is finished when the participant is not able to remember the sequence for two consecutive trials, whereby the longest remembered sequence is noted [29]. In a second round, the participant points to the blocks in the inverse order from that demonstrated. The scores of forward and backward span, as well as the score for visuospatial memory (total score of forward and backward span), are obtained in this test.

Digit span Test: The Digit Span Test is used to assess short-term memory and verbal working memory.

While Digit Span Backwards concentrates on working memory and mental manipulation, Digit Span Forward assesses memory, attention, and encoding [13].

The participants are read a random series of digits and must repeat them in the same or in reverse order. Beginning with three digits, the number of digits to be recalled is progressively increased; the inability to recall two successive sequences ends the task. The participant receives no feedback throughout the test. The outcome is a maximum number of correctly repeated numbers in the forward and backward modalities [13].

Data management and analysis were performed using SPSS 24.0. Continuous variables with normal and non-normal distribution were presented as mean±SD and median (first quartile, third quartile), respectively. The chi-square test was used to assess the distribution of smoking and level of education between the groups.

For continuous variables, the means of two groups were compared using the Independent Sample T test (normal distribution) and the Mann-Whitney U test (non-normal distribution). For three or more groups, the means were compared using the one-way ANOVA (normal distribution) and the Kruskal-Wallis test (non-normal distribution).

The Poisson log-linear, linear regression, and ordinal logistic models were employed to identify the association between BLL and cognitive consequences after controlling for the effect of confounding variables such as age, work history, smoking, body mass index, and education level. To determine the association between BLL and cognitive test results, Pearson's correlation coefficient was used.

Results

Table 1 reports the demographic information for both exposed and non-exposed groups. The mean age, job history, and smoking status of the two groups did not differ significantly (Table 1). BLL in the exposed group was significantly higher than that of the non-exposed group (37.41±10.28 µg/dl vs. 12.57±4.27 µg/dl).
The exposed group's mean breathing zone lead levels were 0.08 ± 0.06 mg/m^3, while the non-exposed group's were 0.02 ± 0.01 mg/m^3.

Table 1. Comparison of demographic data in the exposed and non-exposed groups

Variable		Exposed group	Non-exposed group	P-value
		Mean ± SD	**Mean ± SD**	
Age (year)		34.19±6.85	34.93±7.31	0.52[a]
Work history (year)		4.30±1.43	4.37±1.77	0.60[a]
Body mass index (kg/m^2)		23.40±3.48	26.07±4.36	<0.001[a]
		Number (percentage)	Number (percentage)	
Smoking status	**Smoker**	26 (34.20)	16 (21.10)	0.07[b]
	Non-smoker	50 (65.80)	60 (78.90)	
Level of education	**Diploma**	46 (60.50)	19 (25)	<0.001[b]
	postgraduate diploma	21 (27.60)	23 (30.30)	
	Masters level	9 (11.80)	34 (44.70)	

[a] Independent Sample T-Test
[b] Chi-square test

Comparison of BLL in the exposed and non-exposed groups according to demographic information: As observed in Table 2, the non-exposed smokers had significantly higher BLL when compared with non-smokers (p=0.003). Also, BLL in subjects with lower levels of education was significantly higher than that of the subjects with higher levels of education. The difference in BLL was not statistically significant for other variables.

Table 2. Comparison of blood lead levels of the exposed and non-exposed groups in terms of demographic information

Variable		Number	Exposed group: Mean ± SD / Median (1st quartile, 3rd quartile)	Number	Non-exposed group: Mean ± SD / Median (1st quartile, 3rd quartile)
Age(year)	22-30	26	36.44±10.86	25	11.44±4.74
	31-35	22	38.18±9.70	20	12.12±4.49
	36-52	28	37.71±10.46	31	13.78±3.48
	P-value		0.83[c]		0.10[c]
Work history (year)	1-3	25	30.11 (25.03, 43.84)	42	11.83±4.26
	3.01-6	51	40.93 (30.94, 46.32)	34	13.49±4.16
	P-value		0.06[b]		0.09[a]
Body mass index (kg/m^2)	<18.49	5	42.71 (26.81, 49.96)	4	12.88 (8.76, 17.77)
	18.5-25	45	40.02 (28.13, 45.87)	26	12.9 (7.69, 15.68)
	>25.01	26	37.51 (27.71, 44.89)	46	13.77 (9.85, 15.75)
	P-value		0.87[d]		0.60[d]
Smoking status	smoker	26	37.01±10.02	16	14.94±3.01
	Non-smoker	50	37.62±10.51	60	11.94±4.35
	P-value		0.80[a]		0.003[a]
Level of education	Diploma	46	41.49 (30.89, 46.24)	19	13.76±3.73
	Postgraduate diploma	21	33.31 (28.02, 47.91)	23	14.38±3.74
	Masters level	9	22.23 (21.76, 39.73)	34	10.69±4.22
	P-value		0.01[d]		0.002[c]

[a] Independent Sample T-Test
[b] Mann-Whitney U test
[c] one-way ANOVA
[d] Kruskal-Wallis

Cognitive outcomes in the exposed and non-exposed groups: Table 3 compares the cognitive outcomes in the exposed and non-exposed groups. According to this Table, number of losing the sorting principle (p=0.003), number of total errors (p=0.003), number of perseverative errors (p=0.008), errors of commission (p<0.001) and omission (p=0.01), delay period (p=0.01), test period (p<0.001), total period (p<0.001), and number of total errors (the Tower of London result) (p<0.001) were significantly higher, while other parameters were significantly lower in the exposed group than in the non-exposed group. Generally, the total scores for all cognitive tests in the exposed group were significantly worse than those in the non-exposed group.

Table 3. Comparison of the results of cognitive tests in the exposed and non-exposed groups

Type of cognitive test		Exposed group Mean ± SD	Non-exposed group Mean ± SD	P-value *
Wisconsin card sorting test	Number of categories completed	5.30±1.23	5.84±0.46	0.001
	Number of losing the sorting principle	11.41±6.84	8.54±4.37	0.003
	Number of total errors	11.40±6.84	8.53±4.37	0.003
	Number of perseverative errors	5.1±2.27	4.81±2.19	0.008
Continuous performance test	Errors of commission	1.21±1.04	0.47±0.37	<0.001
	Errors of omission	1.76±4.39	0.40±0.83	0.01
Tower of london test	Delay period	187.43±108.45	148.36±87.83	0.01
	Test period	294.68±163.28	202.09±129.78	<0.001
	Total period	484.97±232.92	338.52±170.45	<0.001
	Number of total errors	12.05±8.32	7.02±4.63	<0.001
	Total score	29.98±4.50	32.92±2.03	<0.001
Corsi block-tapping test	Forward span score	46.95±21.77	67.42±19.92	<0.001
	Backward span score	36.92±19.41	61.23±17.71	<0.001
	Visuospatial memory score	82.22±35.06	128.65±32.30	<0.001
Digit span memory test	Forward digit span	4.97±0.85	5.94±0.83	<0.001
	Backward digit span	4.49±0.89	5.51±0.84	<0.001

* Independent Sample T-Test

The Poisson log-linear and linear regression models were used for modeling the effect of BLL on cognitive performance after adjustments for confounding variables (age, work history, smoking, body mass index, and education level). Poisson log-linear analysis revealed that a one-unit increase in BLL elevated the number of losing the sorting principle, number of perseverative errors, number of total errors, errors of omission and commission, and number of total errors (Tower of London result) by 3%, 0.3%, 1%, 5%, 3%, and 2%, respectively (Table 4).

linear regression analysis indicated that a one-unit increase in mean BLL resulted in 1.74, 4.47, and 6.26 second increments in delay period, test period, and total period, respectively plus 0.10, 0.85, 0.78, and 1.66 unit reductions in total score, forward and backward span scores, and visuospatial memory score, respectively (Table 4).

Table 4. The association between the blood lead level and cognitive performance

Cognitive test		Non-standard coefficients B	Non-standard coefficients SE	P-value
Wisconsin card sorting test	Number of losing the sorting principle	0.03	0.01	0.02*
	Number of perseverative errors	0.003	0.000	0.001*
	Number of total errors	0.01	0.002	0.001*
Continuous performance test	Errors of omission	0.05	0.00	<0.001*
	Errors of commission	0.03	0.00	<0.001*
Tower of london test	Number of total errors	0.02	0.002	<0.001*
	Delay period	1.74	0.63	0.007+
	Test period	4.47	0.92	<0.001+
	Total period	6.26	1.28	<0.001+
	Total score	-0.10	0.02	<0.001+
Corsi block-tapping test	Forward span score	-0.85	0.12	<0.001+
	Backward span score	-0.78	0.11	<0.001+
	Visuospatial memory score	-1.66	0.20	<0.001+

* Poisson log-linear model
+ linear regression model

An ordinal logistic regression model was used to determine the effect of BLL on the results of the digit span memory test and the number of categories completed after adjustments for confounding variables (Table 5). Based on Table 5, a one-unit increase in mean BLL augmented the probability of having a smaller number of categories completed and lower scores of forward and backward digit spans by 6%, 8%, and 10%, respectively (p<0.001) (Table 5).

Table 5. The association between the blood lead level and cognitive performance

Type of cognitive test		Odds ratio	95% Confidence interval		P-value*
			Upper	Lower	
Wisconsin card sorting test	Number of categories completed	1.06	1.02	1.09	<0.001
Digit span memory test	Forward digit span	1.08	1.05	1.11	<0.001
	Backward digit span	1.10	1.06	1.12	<0.001

* Ordinal logistic regression model

The correlations of BLLs with the results of cognitive tests in the studied groups are outlined in Table 6. There was a significant negative correlation between BLLs and number of categories completed, total score, forward and backward span scores, visuospatial memory, plus forward and backward digit span. However, BLL was positively and significantly associated with other variables.

Table 6. The association between blood lead level and the results of cognitive tests

Test name	Test variable	r	P-value*
Wisconsin card sorting test	Number of total errors	0.38	<0.001
	Number of perseverative errors	0.36	<0.001
	Number of categories completed	-0.34	<0.001
	Number of losing the sorting principle	0.22	0.006
Continuous performance test	errors of commission	0.28	<0.001
	errors of omission	0.22	0.005
Tower of london test	Delay period	0.23	0.003
	Test period	0.39	<0.001
	Total period	0.41	<0.001
	Total number of errors	0.47	<0.001
	Total score	-0.46	<0.001
Corsi block-tapping test	Forward span score	-0.54	<0.001
	backward span score	-0.56	<0.001
	Visuospatial memory score	-0.63	<0.001
digit span memory test	Forward digit span	-0.59	<0.001
	backward digit span	-0.58	<0.001

* Pearson Correlation

Discussion

The present study aimed to evaluate cognitive disorders caused by lead exposure in some mine workers. The mean lead content in the exposed workers' breathing zone in this study was 0.08 ± 0.06 mg/m^3, which is higher than the OEL and TLV of 0.05 mg/m^3 suggested by the Center for Health and Environment of Iran [16] and ACGIH [15], respectively. This is in line with the findings of other studies in different industries. For example, the mean lead concentration in the breathing zone of 40 female soldiers, working at two electrical equipment manufacturing factories in Neyshabur, Iran was 0.09± 0.01 mg/m^3 (0.08± 0.02 mg/m^3 and 0.10± 0.04 mg/m^3) [30]. Further, Kargar et al. [31] reported a mean lead concentration of 0.62 mg/m^3 in the breathing zone of 78 battery workers. Also, Were et al. [32] in the battery manufacturing and battery recycling workers reported mean lead concentrations of 0.427±0.124 and 0.349±0.107 mg/m^3, respectively. Similarly, Xiao Qing et al. [33] reported lead levels of 0.89 mg/m^3 in 108 battery workers.

The effectiveness of ventilation systems, old or new machines, duration of daily exposure, and maintenance of the machines might explain the reasons of these discrepant results [31].

In this study, mean BLLs were 37.41±10.20 µg/dl and 12.57±4.27 µg/dl in the exposed and non-exposed groups, respectively. These values in the exposed group were higher than the BEI of 20 µg/dl recommended by ACGIH [15]. These results are consistent with the findings of other Iranian studies conducted on lead mine workers. For instance, Malekirad et al. [34], Mirsalimi et al. [35], Rahimpour et al. [36], and Firouzi et al. [37] reported mean BLL of 96.40±32.80, 24.5±5.43, 25.88, and 24.16±8.36 µg/dl, respectively. In other countries for example, Akhtar Ahmad et al. [38] reported a mean BLL of 65.25±26.66 µg/dl in the battery manufacturing industry in Bangladesh. Fenga et al. [39] from Italy, reported a mean BLL of 56.4 µg/dl in 40 battery recycling workers compared with 15.4 µg/dl in 40 non-exposed subjects. Elsewhere, Batra et al. [40] reported a mean BLL of 38.02± 19.92 µg/dl in 80 granite workers, painters, motor garages, gear, and color workers in comparison to 2.33±1.21 µg/dl in 80 non-exposed subjects. In addition, Rathi et al. [41] found mean BLL of 39.5±31.9 µg/dl and 10.5 ± 12.2 µg/dl in 100 Indian battery workers and 100 non-exposed subjects, respectively.

Lead exposure was high in all studies. Poor hygiene and a lack of proper personal protection equipment could be the cause of these findings. As another explanation, employees did not wash their hands before eating in the workplace since they were not aware of the dangers of lead [31].

In the present study, the BLL of the non-exposed smokers was significantly higher than that of non-smokers (p=0.003). Similarly, Akhtar Ahmad (2014) performed a study on 118 battery workers in Bangladesh and found that the BLL of smokers (71.5 µg/dl) was significantly higher than that of the non-smokers (59.35 µg/dl) [38]. Similar findings have been reported by others [42, 43]. A possible explanation for these results may be the lead in cigarettes and smoking with lead-contaminated hands [44].

In the present study, BLL was inversely associated with education. Similarly, Rodrigues et al. (2009) [44] in a study on 84 Bridge painters in New Zealand reported that low levels of education are a predictor of high BLL in the workers. The authors suggested that unhealthy behaviors such as eating or smoking with contaminated hands in the workplace, and less use of personnel protective equipment might explain the reasons for this result. In contrast, some studies have failed to find such an association [30, 43, 45].

Long-term exposure to lead can cause cognitive disorders such as impaired memory, attention, visuospatial function, verbal learning and memory, and executive function deficits [46].

One important tool for assessing executive dysfunction is the Wisconsin Card Sorting Task (WCST) [46, 47]. The WCST revealed that the mean of categories completed was significantly lower (p=0.001), while number of losing the sorting principle (p=0.003), the number of total errors (p=0.003), and number of perseverative errors (p=0.008) were significantly higher in the exposed group than in the non-exposed group, indicating the impairment of cognitive flexibility, problem–solving, and decision-making in the exposed group. Similarly, Winker et al. [48] reported increased errors, perseverations, and loss of sorting principle in 47 lead-exposed subjects (30.80±11.20 µg/dl) in comparison to a non-exposed control group (5.40±2.70 µg/dl) [49]. Similar results were reported by Chiodo et al. [50] and Barth et al. [25], who demonstrated poorer performance in WCST in the lead-exposed workers in comparison to the control group.

The results of the present study revealed that BLL was positively and significantly associated with the number of total errors (p< 0.001), number of perseverative errors (p< 0.001), and number of losing the sorting principle (p=0.006). There was a significant inverse association between BLL and the number of categories completed (p<0.001).

Lead exposure causes attention deficit hyperactivity disorder (ADHD), a neurodevelopmental disorder, which is characterized by inattention and hyperactivity [26]. Continuous performance tests (CPTs) are widely used in the assessment of ADHD and measure both selective and sustained attention [51]. The present study results revealed more commission and omission errors in lead exposed group in comparison to the non-exposed group. Commission errors show inappropriate responses to non-targets, a measure of impulsivity, while omission errors indicate inability to respond to targets, a measure of inattention [52]. BLL was positively and significantly associated with the number of omission errors (p=0.005), and commission errors (p<0.001). This result is in agreement with the findings of other studies [50, 52, 53]. But, chuang et al. [54] in a four-year-follow up found no significant difference in the mean score for the continuous performance test between the non-exposed and exposed groups in the final year. The decrease of BLL in the workers from 26.3 µg/dl to 8.3 µg/dl might explain the reasons for these results. Thus, the authors suggested that the neurotoxic effects of lead exposure may be reversible in some cases.

The Tower of London also measures planning ability, inhibitory control, problem-solving performance, and general executive functioning [50, 55] and is sensitive to dorsolateral prefrontal cortex (DLPFC) damage [27]. Larger DLPFC is associated with better performance on tests of executive functions [56].

In the present study, Tower of London results revealed that BLL was positively and significantly associated with delay period (p=0.003), test period (p< 0.001), total period (p<0.001), and number of total errors (p<0.001). Further, BLL was negatively and significantly associated with the total score (p<0.001), indicating diminished activation in DLPFC followed by planning dysfunction and working memory deficits [45, 57].

The Corsi block-tapping test evaluates working memory and short-term visuospatial memory. In this study, BLL was negatively and significantly associated with mean scores of forward and backward span scores, as well as visuospatial memory score (p<0.001). Consistent with the findings of the present study, Chiodo et al. [50] reported a negative significant association between the backward span score and lead exposure (p≤0.05).

The results of this study indicated that mean scores for forward and backward digit span tests were significantly lower in the exposed group compared to those in the non-exposed group (p<0.001). Similar findings have been previously documented by Kumar et al. [58], Lindgren et al. [59], and Fenga et al. [39]. Thazin Shwe et al. [19] indicated that even exposure to low BLLs of 2.25 µg/dl can result in low score for the digit span. Indeed, the digit span test was used to measure the reproduction and storage capacity. The forward digit span assesses encoding, memory, and attention. In contrast, backward digit span emphasizes mental manipulation and working memory [13].

Lead exposure causes diminished activation in the ventrolateral prefrontal cortex (VLPFC). This area is critical for the recall or retrieval of data. Therefore, lead-induced damage in the prefrontal cerebral cortex results in the inability to maintain and manipulate the information held in the working memory.

The present study found that BLL was negatively and significantly associated with mean scores for forward and backward digit span tests (p<0.001). Similarly, Counter et al. [60] reported a negative significant association between BLL and mean scores for forward plus backward digit span tests (p<0.006). The authors suggested the lead-induced impairment of auditory working memory. In contrast, Baker et al. [61] found no significant association between BLL and the score of the digit span test.

Given the results of the present study, after controlling for the effects of confounding variables, the association between BLL and cognitive problems remained significant. In line with this result, Yuan et al. [62] and Seo et al. [46] reported less activation in DLPFC in the lead-exposed group in comparison with the non-exposed group after controlling for age, educational level, smoking amount, BMI, and hemoglobin level.

Chiodo et al. in 2004 and 2007 [50, 53] observed a negative association between BLL and the continuous performance test after controlling for the effects of confounding variables. The authors suggested that the incidence of attention deficit even at BLLs below 5 μg/dl shows that there is no safe blood lead threshold.

Similarly, Fenga et al. [39], Counter et al. [60], and Chiodo et al. [50] reported that the association between BLL and the mean score for the digit span test remained significant (p<0.05) after controlling for the effects of confounding variables.

In contrast, Baker et al. [61] reported no significant association between BLL and mean scores for digit span and continuous performance tests after controlling for the effects of confounding variables. Likewise, chiodo et al. [50] reported no significant association between BLL and mean scores for the Tower of London and Corsi block–tapping tests. The exact reasons for these conflicting results are not known. However, these might be related to differences in study populations, concentration of lead, sample sizes, confounder variables, and statistical analyses [63].

A limitation of this study was that the health habits of the workers were not investigated. Therefore, further studies are warranted on the role of healthy behaviors and education level in high BLL.

Conclusion

The findings revealed that exposure to airborne lead at levels above permissible exposure limits can raise BLL, which in turn can result in cognitive disorders such as disability in using problem-solving and decision-making skills as well as planning and organizing skills, impaired inhibitory control, plus impaired verbal memory and visuospatial memory functions. The occurrence of cognitive disorders can be attributed to the BLL since no statistically significant difference was observed in demographic variables (such as age, work history, and smoking status between the exposed and non-exposed groups). Also, the association between BLL and cognitive disorders remained significant after adjustments for the effects of the confounders. According to the results, to prevent cognitive disorders in lead-exposed workers, technical practices such as improved ventilation as well as management strategies including a reduction of exposure time, rotating shift work, high-quality respiratory protective equipment, and training workers are necessary.

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Conflict of interest

None declared.

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Ethical Considerations

This study has been in agreement with the Helsinki Declaration and Iranian national guidelines for ethics in research.

Code of Ethics

The research Ethics Committee of Shahid Sadoughi University of Medical Sciences approved this research (IR.SSU.SPH.REC.1400.225).

Authors' Contributions

Zahra Yavar: Helped in the data collection. Fatemeh Kargar-Shouroki: Participated in designing of the study. Gholamhossein Halvani: Participated in designing of the study. Reyhane Sefidkar: Analysed the data. Fahimeh Dehghani: Participated in designing of cognitive tests. All authors have read, reviewed, edited and approved the final manuscript.

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