

## CLINICAL, HAEMATOLOGICAL, AND NEUROCOGNITIVE FINDINGS IN LEAD-EXPOSED WORKERS OF A BATTERY PLANT IN IRAN

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The aim of this comparative cross-sectional study was to assess neurocognitive impairment, haematological findings, and clinical symptoms of lead exposure among 316 male battery plant workers aged between 20 and 61 years. Compared to 123 matched controls (matching in age and years of work), the exposed workers showed significantly higher mean blood lead level (BLL) and lower haematocrit, haemoglobin, and red blood cell count. Mean BLL significantly correlated with clinical symptoms such as nocturia, increased urination frequency, oedema, drop in deep tendon reflex, concentration impairment, agitation, headache, depression, abdominal pain, palpitation, fatigue, and diminished sex drive. Workers with clinical disorders had higher BLL and lower haematological parameters. These findings warn that silent toxicological problems caused by lead might go unnoticed by health professionals.

**KEY WORDS:** *haematocrit, haemoglobin, lead, RBC, toxicity*

Typically, lead enters the human body through the respiratory or gastrointestinal tract and is distributed in blood, soft tissues, and bones (1). Exposure to lead is inevitable because of its accumulation in the environment and common use in everyday life. Millions of tonnes of lead are produced or handled annually, and lead is among top metals used in lots of activities such as mining, smelting, refining, and battery manufacturing all over the world (1). Workers in these factories can be exposed to lead dusts or fumes, and if protective tools are not properly used, exposure may result in serious health disorders (2-5). Neurocognitive and neurobehavioral disorders that are associated with high blood lead level (BLL) include (6, 7) attention and intelligence impairment in children (8, 9), neurobehavioral problems (10), neurobiological defects such as schizophrenia (11), or

Alzheimer's disease (12). The aim of this study was to establish neurocognitive impairment and its association with lead-related haematological findings and clinical symptoms in workers of a battery plant in Iran.

### SUBJECTS AND METHODS

This comparative cross-sectional study included 439 men; 316 were workers from a battery plant located in Esfahan, an industrial capital of the namesake province, while 123 were control subjects matched by age and working experience with no history of job-related exposure to metals, who lived in the same city (Table 1). The plant, which has been working since 1974, currently produces three million batteries a year and employs a workforce of 600.

**Table 1** Summary of demographic data in workers and control subjects

	Subjects / N	Age / year	Years of work	Smoking / N (%)
Workers	316	33.41±6.88	8.93±5.76	87 (27.53)
Controls	123	32.40±6.47	7.40±4.26	47(38.21)
<i>P</i> value*	-	0.3	0.24	-

Data represent mean ± SD.

\*Two-sided Student's *t*-test.

All subjects were informed about the study protocol and gave their consent before entering the study. The study was approved by the Institutional Review Board.

The subjects passed complete clinical examination. The exclusion criteria were history of chronic diseases, alcohol drinking, use of any antioxidant/vitamin supplements, exposure to other toxic compounds, undergoing radiotherapy, or substance abuse. Blood samples were taken in the morning between 7 a.m. and 8 a.m. before work to determine the levels of haemoglobin, haematocrit, red blood cell (RBC) count, and lead. Blood lead was analysed using a Shimadzu GFA-4B graphite-furnace atomic absorption spectrophotometer (Kyoto, Japan). Blood cells were lysed using Triton X-100 to release lead, which in turn was chelated with ammonium pyrrolidine dithiocarbamate and extracted with methylisobutylketone. The method has been described in detail elsewhere (13). All chemicals were purchased from Sigma-Aldrich (Chemie GmbH, Munich, Germany).

Subjects with a high-risk for neurocognitive impairment were identified using the Iranian version of the Subjective Neurocognition Inventory (SNI) (14). The SNI is a self-reporting questionnaire consisting of 76 items with a focus on impairments in daily memory and deficits of attention (15). The items were scored on a five-point Likert scale (spanning from "very frequently" to "never") and included selective attention, divided attention, longstanding recall, prospective recall, and psychomotor delay (16).

#### Statistical analysis

For statistical analysis we used Stats Direct version 2.7.9 (StatsDirect Ltd., Cheshire, UK). Data were compared using the two-sample *t*-test and Mann-Whitney U test, whereas the association between variables was tested using Spearman's correlation. Data are presented as median and quartiles or

mean±SD. The *P* values lower than 0.05 were considered statistically significant.

## RESULTS AND DISCUSSION

Mean haematocrit, haemoglobin, and RBC were significantly lower in the battery plant workers than in controls ( $P<0.001$ ), whereas BLL was significantly higher ( $P<0.001$ ) (Table 2).

The workers also showed significantly lower scores for initiative/energy ( $P=0.025$ ) and divided attention ( $P=0.039$ ) than controls (Table 2).

Correlations between BLL and clinical symptoms were significant for nocturia, urinary frequency, oedema, low deep tendon reflex (DTR), low concentration, agitation, headache, depression, abdominal pain, palpitation, fatigue, and diminished sex drive, whereas correlations with other symptoms were not statistically significant.

The first thing that stands out are the results of our control population. Firstly, this group had a much larger percentage of smokers (Table 1) and secondly, their BLL was higher than in other control populations around the world or the same province in Iran (3), reaching in fact moderate-to-high lead-exposure characteristic for lead workers (17, 18). Blood lead level this high may partly be explained by the high percentage of smokers among controls, but not entirely. A more likely contributing factor, however, is the industrial pollution of the city of Esfahan, which is notorious as the second most polluted city in Iran (3, 19). To make the problem even worse, the city is surrounded by mountains that entrap the polluted air. In addition to air pollution, several reports of high heavy metal content in soils (20), raw milk (21), and the hair (22) of people who live in this city point to lead exposure through food and water.

Even with elevated BLL in controls, our workers showed significantly higher exposure and accumulation of lead in the body. Our findings support many reports

**Table 2** Neurocognitive impairment scores in battery plant workers and controls

Group	PS	SA	DA	VM	NVM	PM	SF	IE	TOTAL
Workers	33(28 to 37)	41(32 to 48)	17(14 to 19)	27(23 to 31)	16(13 to 18)	27(23 to 31)	23(19 to 25)	37(29 to 43)	298(252 to 336)
Controls	33(30 to 37)	42(34 to 48)	18(16 to 19)	28(23 to 31)	17(14 to 19)	28(24 to 32)	23(20 to 25)	41(30.5 to 44.5)	302(269.5 to 340.5)
<i>P</i> value *	0.217	0.131	0.039	0.431	0.177	0.095	0.105	0.025	0.038

PS: psychomotor speed; SA: selective attention; DA: divided attention; VM: verbal memory; NVM: nonverbal memory; PM: prospective memory; SF: spatial functioning; and I/E: initiative/energy

Data represent the median and quartiles (Q1 to Q3).

\*Two-sided Mann-Whitney U test

**Table 3** Haematological parameters in battery plant workers and controls

	Pb / $\mu\text{g dL}^{-1}$	Haematocrit / %	Haemoglobin / $\text{g dL}^{-1}$	Red blood cells / $\times 10^6 \mu\text{L}^{-1}$
Controls	37.57 (28.33 to 67.92)	47 (45 to 49)	15.9 (15 to 16.3)	5.36 (5 to 5.745)
Workers	52 (37 to 70)	43.1 (40.8 to 45.7)	14.7 (13.9 to 15.6)	5.22 (4.93 to 5.48)
<i>P</i> value*	<0.001	<0.001	<0.001	0.001

Data represent the median and quartiles (Q1 to Q3).

\*Two-sided Mann-Whitney U test

**Table 4** The relationship (*r*) between blood lead level and clinical symptoms

Clinical symptom	Ratio BLL/Clinical symptom
History of urinary infection	0.068
Nocturia	0.380**
Urinary Frequency	0.483**
Oedema	0.095*
Green line	0.029
Tingling	0.032
Foot Drop	0.069
Wrist drop	0.087
DTR decrease	0.098*
Memory impairment	0.086
Less concentration	0.087*
Agitation	0.11*
Insomnia	0.059
Hypersomnia	0.034
Headache	0.094*
Depression	0.131**
Anorexia	0.083
Abdominal pain	0.132**
Palpitation	0.13**
Diarrhea	0.027
Constipation	0.066
Fatigue	0.088*
Sweat taste	0.075
Limping	0.070
Tremor	0.086
Diminished sex drive	0.094*
Intercourse satisfaction	0.085
Erectile function	0.08

\*\* $P < 0.01$ ; \* $P < 0.05$ ; BLL: blood lead level

on higher BLL in workers than controls. Were et al. (23) reported mean BLL  $\pm$ SD of  $(427 \pm 124) \mu\text{g m}^{-3}$  in lead battery recycling workers vs.  $(59.2 \pm 22.7) \mu\text{g m}^{-3}$  in office workers from the same plant. Similar was found by Raafat et al. (24), who studied elevated BLL as a risk factor for osteoporosis in Egyptian lead battery workers of either sex and by Kašuba et al. (25), who investigated genotoxic effects of lead in battery workers in Croatia. In India, Ravichandran et al. (26) found much higher mean air lead concentrations in buffing ( $1444.45 \mu\text{g m}^{-3}$ ), plate cutting ( $430.14 \mu\text{g m}^{-3}$ ), and pasting ( $277.48 \mu\text{g m}^{-3}$ ) sections of a battery plant than prescribed by regulatory agencies.

Ho et al. (27) suggested that high BLL detected in their workers was related to extensive contact with lead and use of unwashed hands while eating. Gottesfeld et al. (28) reported that BLL and air lead levels in battery workers were higher in developing nations, probably as a consequence of quick development in lead acid battery trade and recycling in these countries.

Given the absence of monitoring and regulation in some countries, third-party certification programs may be the only viable option to improve working conditions. Our earlier study (29) indicated that the key reason for increased BLL in lead/zinc mine workers is inappropriate use of safety equipment. The workers did use masks, but failed to use protective clothing or take regular showers, even though suitable facilities were available. The same goes for using gloves and shoes. Battery recycling and manufacturing involves manual use of metallic lead for making grids, bearings, and solder. In the process, lead particles and vapours are released that can contaminate the environment.

Our analysis showed a significant positive correlation between BLL and some clinical symptoms. Supporting these data, our previous study (29) in lead/zinc mine workers showed clinical symptoms such as memory loss, diminished concentration, sleeplessness, headache, limping, epigastric pain, lack of appetite, anxiety, tremor, low DTR, deafness, and fatigue. Lead exposure can also end up with abdominal cramps, peripheral and central neuropathy, anaemia, or with vague symptoms such as myalgia, tiredness, bad temper, and headache, or with no symptoms at all (29). In another study, by Zhang et al. (30), petrol workers exposed to tetraethyl lead had a significantly higher incidence of tremor and sinus bradycardia than controls, which is similar to our findings. In a study by Schwartz et al. (31), former lead workers performed

worse than controls in visuo-constructive ability, verbal memory, and learning. Their peak tibia lead predicted decline in verbal memory, learning, visual memory, executive ability, and manual dexterity (31).

Besides, in human adults, encephalopathy resulting from lead poisoning is often characterised by sleeplessness, poor attention span, vomiting, convulsions, and coma (32). Also, lead is known to produce oxidative stress, disrupt the blood-brain barrier and alter several  $\text{Ca}(2+)$ -dependent processes, including physiological processes that involve nitric oxide synthesis in the central nervous system (32). Lead also interferes with nitric oxide-related physiological mechanisms, and lead neurotoxicity may affect processes involved in learning and memory (32). Hirata et al. (33) suggest that lead exposure affects high cerebral functions of cognition and attention, but its adverse effects on movement are still unclear.

In contrast to our findings, Kianoush et al. (34) found no correlation between clinical manifestations of lead poisoning and BLL among car battery workers. Osterberg et al. (35) reported no sign of behavioural deterioration in lead-exposed individuals, either in objective cognitive tests or in subjective symptom/mood self-rating scales. Similarly, Winker et al. (36) found no significant differences in cognitive parameters between lead-exposed and control subjects.

Policy makers should be aware of health risks involved in lead exposure and increase in the global burden of disease. Fortunately, many countries have recognised this issue and taken necessary measures. To us, it seems that many other factors such as workers' lifestyle are involved in neurocognitive impairment and its correlation with BLL. However, the key to minimising lead exposure and chronic poisoning in the industries is in the proper use of protective equipment and regular and thorough hygiene. Our findings warn about silent toxicological problems related to lead that are not easily recognised by health professionals (37).

#### *Conflict of interests*

We declare that no relationship or circumstance presents a conflict of interest in conducting this study or reporting about it.

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**Sažetak**

**KLINIČKI, HEMATOLOŠKI I NEUROKOGNITIVNI NALAZI U RADNIKA IZ IRANSKE TVORNICE AKUMULATORA IZLOŽENIH OLOVU**

Cilj je ovog usporednog, presječnog ispitivanja bio ocijeniti oštećenje neurokognitivne funkcije, hematološke nalaze i kliničke simptome izloženosti olovu u 316 radnika u dobi od 20 do 61 godine uposlenih u tvornici akumulatora. U odnosu na odgovarajuću kontrolnu skupinu (po dobi i stažu) od 123 ispitanika, izloženi su radnici iskazali značajno više razine olova u krvi te niže razine hematokrita, hemoglobina i eritrocita. Srednja razina olova u krvi značajno je kolerilala s kliničkim simptomima poput nokturije, učestalog mokrenja, edema, slabijeg dubokog tetivnog refleksa, smanjenom koncentracijom, psihomotoričkom uzbuđenosti, glavoboljom, depresijom, bolom u trbuhu, palpitacijama, zamorom i smanjenim spolnim nagonom. Radnici s kliničkim poremećajima imali su više razine olova u krvi i slabiju krvnu sliku. Ovi nalazi upozoravaju na to da toksikološki poremećaji uzrokovani olovom mogu promaknuti zdravstvenim radnicima.

**KLJUČNE RIJEČI:** *eritrociti, hematokrit, hemoglobin, olovo, toksičnost*

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