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Blood Cadmium Level and Its Association with Depressive Symptoms in a Sample of Iraqi Workers

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Abstract

Background The etiologies of mental disorders involve interactions among genetic, developmental, social, and environmental risk factors. An association between blood cadmium and depression was recently reported in young adults.

Objective To determine the prevalence of elevated blood cadmium level and to evaluate its association with depressive symptoms among adult Iraqi workers.

Methods A comparative cross-sectional study that conducted in two industries in Baghdad. It included 200 young adult male and female workers in the batteries factory (100 participants) who were exposed directly or indirectly to cadmium and in the textile factory (100 participants) unrelated to direct cadmium exposure. Blood sample was taken for measurement of blood cadmium level. Patient Health Questionnaire-9 was used to measure the symptoms of depression.

Results Mean of blood cadmium level was significantly higher in participants who had depressive symptoms than that in those who didn't have; in those with moderate to severe symptoms than that in those who had mild symptoms. Blood cadmium >0.21 µg/dl is predictive for risk of development of depressive symptoms. Statistically significant weak positive correlations were detected between blood Cd with total PHQ9 score, no. of cigarettes/day, duration of work in batteries factory and in textile factory.

Conclusion Elevation of blood cadmium level among sample of adult Iraqi workers especially in batteries factory is a significant health problem. Cadmium neurotoxicity may be a contributing factor for adverse mental health outcomes, even at levels generally considered to pose low or no risk.

Keywords Depression, mental illness, health, cadmium, workers, Iraq

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List of abbreviations: Cd = Cadmium, DSM-IV-TR = Diagnostic and Statistical Manual IV Text Revision

Introduction

Cadmium (Cd) is a heavy metal that is produced during the smelting of other metals, such as zinc, lead and copper. It is most frequently used in the manufacture of nickel-cadmium rechargeable batteries found in mobile phones and cordless equipment. It is also used in metal plating, some paints, plastics and fertilizers, and is found in cigarette smoke. Exposure to Cd occurs mostly in the workplace where Cd products are made. The general population can be exposed to Cd from cigarette smoke or eating Cd-contaminated foods [(1)]. Cd disrupt mitochondrial functions through many processes leading to energy metabolism and malfunctions in mitochondrial biochemical cascade, as suggested by several

studies on the pathophysiology of bipolar disorder, major depressive disorder, and schizophrenia. There is a correlation between mitochondrial dysfunction and psychiatric disorders [2]. Depression, anxiety, and stress are now the major mental health problems that cause disability globally, and no one is immune to these problems [3].

Depression manifests as loss of interest or pleasure, sadness, feelings of guilt or low self-worth, disturbed sleep or appetite, extreme tiredness, and poor concentration [4]. Globally, depression is ranked the 11th leading cause of Disability Adjusted Life Years worldwide, but, interestingly, the 3rd in the Middle East region [5]. Depression may lead to higher risk of dementia, premature mortality [6].

The pathophysiology of neuropsychiatric disorder is poorly understood, although there is a notion that structural changes occur in the brain of patients with neuropsychiatric disorder. In the brain, Cd cause lesions including decrease in total cortical volume, white matter, enlargement of cerebroventricular system, changes in gray and white matter, and abnormal laminar organization [7]. Cd toxicity affects several organs including kidney, lung, liver, and brain; an association between blood Cd and depression was recently reported in young adults [8]. The underlying biological mechanism of how Cd may play a role in depression could potentially involve dysregulation of the hypothalamic-pituitary-adrenal axis. Cd can increase the permeability of the blood brain barrier, leading to intracellular Cd accumulation in the brain in adult rats. Furthermore, Cd may contribute by perturbing the catecholamine/serotonin system; decreased levels of serotonin, dopamine, and norepinephrine in the brain have been found in adult male rats exposed to Cd [9].

There are no prior efforts done in Iraq to determine association of depressive symptoms with environmental exposure to Cd; so the aim of this study is to determine the prevalence of elevated blood Cd level and to evaluate its association with depressive symptoms among adult Iraqi workers.

Methods

Study design, setting, and time

This was a comparative cross-sectional study with analytic component that conducted in two industries in Baghdad (Batteries factory in Al-Waziriya and textile factory in Al-Kadhimiya) during a period of 18 months from 1st of Apr. 2020 to 1st of Oct. 2021.

Study population and sample size

The study population included 200 young adult male and female workers in the batteries factory (100 participants) who were exposed directly or indirectly to Cd according to their duties and in the textile factory (100 participants) unrelated to direct Cd exposure. They informed about the purpose of the study and those who agreed to participate were given an informed consent and enrolled in the study. Exclusion criteria included participants who had a recent history of psychological trauma ((Diagnostic and Statistical Manual IV Text Revision (DSM-IV-TR) that defines trauma as a direct personal experience of an event that involves actual or threatened death or serious injury) [10].

Data collection tools

Two different types of questionnaires were applied to all enrolled participants to collect needed information. First questionnaire was included questions to gather the following information: Age and gender, marital status, no. of children and family number, residence, educational level, type of job in the factory (manufacturing or office job), duration and weekly hours of working, smoking (cigarettes and shisha), alcohol drinking, and Blood Cd level: From each participant, blood sample, which was obtained from the antecubital area was sent to the Toxicology Center in Baghdad / Medical City for measurement of blood Cd level (normal value of Blood Cd is ≤0.3 µg/dl). The second questionnaire was a Patient Health Questionnaire-9 (PHQ-9), which is a validated depression screening tool to measure the

symptoms of depression including nine items. Each question would be pointed from 0 to 3, and the total score would be ranged from 0 to 27. Depression severity was characterized as none (0–4), mild (5–9), moderate (10–14), moderately severe (15–19), and severe (≥ 20) [11].

Statistical analysis

The data analyzed using Statistical Package for Social Sciences version 26. The data presented as mean, standard deviation and ranges. Categorical data presented by frequencies and percentages. Normality of data was tested by skewness value and showed that it is normally distributed. Independent t-test (two tailed) was used to compare blood Cd level accordingly. Receiver operating characteristic curve analysis was constructed for blood Cd as a predictor for risk of development of depressive symptoms. Pearson's correlation test was used to assess correlation between blood Cd level and certain variables. A level of P-value <0.05 was considered significant.

Results

In this study, mean of age was 31.58±6.42 years; 62.5% were males; 51.5% were married, 43% were finished higher education, 39% were current smokers, 53.8% were smoking ≤20 cigarettes/day, 45.5% were working in the selected factories for period <5 years and 61% of batteries factory workers were working in production sector. Regarding depressive symptoms, 35% of study participants showed features of moderate level of depressive symptoms; while 29% of them didn't show significant features of depressive symptoms. Cd level was high in 35.5% of study participants (Table 1).

Mean of blood Cd level was significantly higher (P <0.05) in participants who had depressive symptoms than that in those who didn't have; in those with moderate to severe symptoms than that in those who had mild symptoms; in participants who are working in batteries factory than that who are working in textile factory, in those who are working in production sector than that in those who are working in administration, and in smokers than that in nonsmokers as shown in table (2).

Receiver operating characteristic (ROC) curve analysis was constructed for blood Cd as a predictor for risk of development of depressive symptoms. The cut point of blood Cd was 0.21 µg/dl. So, blood Cd >0.21 µg/dl is predictive for risk of development of depressive symptoms, as a large significant area under the curve (AUC=60%) indicating significant association between higher level of blood Cd with risk of development of depressive symptoms. Blood Cd level was 66.2% sensitive, 56.9% specific, and 63.5% accurate in predicting risk of development of depressive symptoms (Table 3) and (Figure 1).

Statistically significant weak positive correlations were detected between blood Cd with total PHQ9 score (r=0.335, P=0.001), no. of cigarettes/day (r=0.301, P=0.007), duration of work in batteries factory (r=0.357, P=0.001) and in textile factory (r= 0.214, P= 0.032) (Table 4).

Table 1. Distribution of study participants by certain characteristics

Variable		No. (n= 200)	Percentage (%)
Age (Year)	<30	82	41.0
	≥30	118	59.0
Gender	Male	125	62.5
	Female	75	37.5
Marital status	Single	52	26
	Married	103	51.5
	Divorced	21	10.5
	Widowed	24	12.0
Educational level	Illiterate	14	7.0
	Primary school	45	22.5
	Secondary school	55	27.5
	Higher education	86	43.0
Smoking Status	Current smoker	78	39.0
	Ex-smoker	9	4.5
	Nonsmoker	113	56.5
Number of cigarette smoking/day; n=78	≤ 20	42	53.8
	> 20	36	46.2
Type of job (Batteries **factory);** n=100	Production sector	61	61.0
	Administration job	39	39.0
Duration of work (Year)	< 5	91	45.5
	5 - 9	62	31.0
	≥ 10	47	43.5
Depressive symptoms	No	58	29.0
	Mild	64	32.0
	Moderate	70	35.0
	Severe	8	4.0
Cd level	High	71	35.5
	Normal	129	64.5

Table 2. Comparison in blood Cd level by certain characteristics

Variable		Blood Cd (µg/dl)	P - value
Depressive symptoms	Yes	0.272 ± 0.1	0.038
	No	0.237 ± 0.1	
Severity of depressive symptoms	Mild	0.22 ± 0.08	0.001
	Moderate to severe	0.3 ± 0.1	
Factory type	Batteries	0.32 ± 0.08	0.001
	Textile	0.2 ± 0.08	
Type of job in batteries	Production sector	0.34 ± 0.07	0.001
	Administration job	0.28 ± 0.09	
Smoking Status	Current smoker	0.29 ± 0.11	0.004
	Nonsmoker	0.24 ± 0.09	

Table 3. Diagnostic accuracy of blood cadmium for prediction of risk for development of depressive symptoms

Cd (µg/dl)	Cut-off value	Sensitivity	Specificity	PPV	NPV	Accuracy
	0.21	66.2%	56.9%	79%	40.7%	63.5%

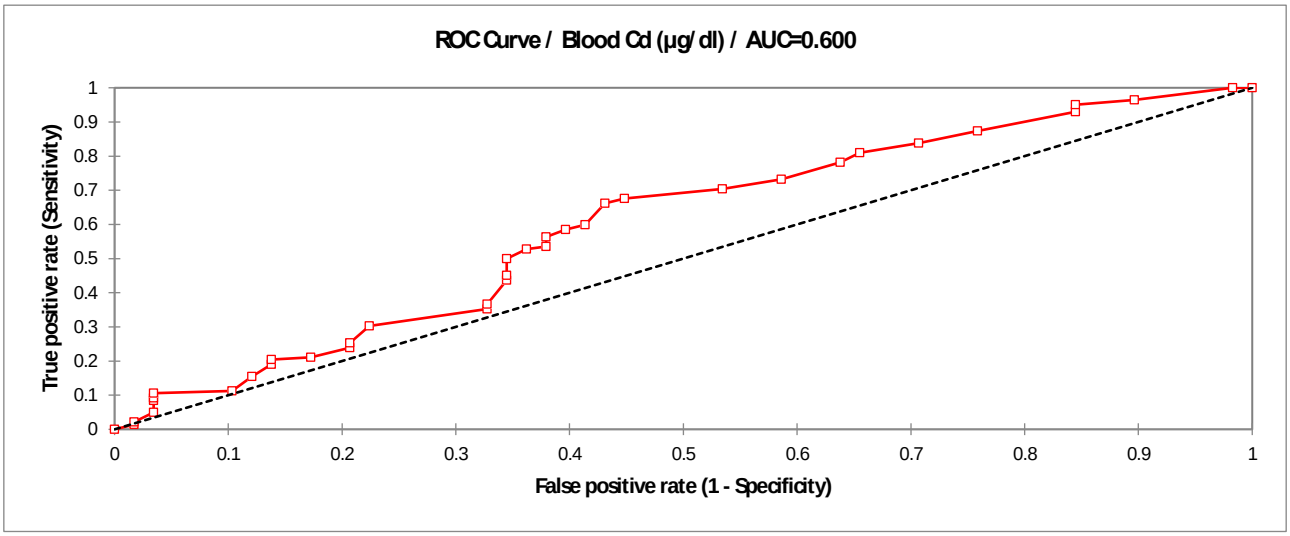

Figure 1: ROC curve for blood cadmium level in predicting risk of development of depressive symptoms

Table 4. Correlation between blood cadmium and certain parameters

Variable		Blood Cd level (µg/ml)	
		r	P - value
Total PHQ9 score		0.335	0.001
No. of cigarettes/day		0.301	0.007
Duration of work (Year)	Batteries factory	0.357	0.001
	Textile factory	0.214	0.032

Discussion

Improving mental health contributes to promoting healthy development and achieving educational, social, and economic goals, and avoiding communicable and non-communicable conditions [12]. In the current study, a high level of Cd was significantly observed in workers of batteries factory more than in those of textile factory. This finding is in accordance with a study conducted by Baloch et al. in Pakistan 2020 when they noticed that mean value of Cd concentration in blood samples of workers of both workshops (batteries recycling factoring and welding workers) were five to eight folds elevated as observed for referent adolescents [13]. This study also revealed that depressive symptoms were more obvious in those had a significantly higher means of blood Cd levels than those who didn't have. Agreements observed in studies conducted by Buser et al. in 2017 [9], by Kostrubiak et al. in 2017 [14], and by Berk et al. in 2014 [15].

The biological plausibility of Cd effect on depression is unclear because of the scarcity of studies pertaining to Cd exposure and neurobehavioral outcomes. Studies in animals have shown that Cd can increase the permeability of the blood brain barrier, which can cause an intracellular Cd accumulation in the brain and cell dysfunction in adult rats [16]. Impairment in the mono-aminergic neurotransmission system is associated with the depression and anxiety disorder, and Cd may contribute to the etiology of depression through perturbation of the catecholamine/serotonin system. Adult male rats exposed to Cd show a decreased content of serotonin, dopamine and norepinephrine in all brain regions [17]. Other experimental studies on rats indicate that early exposure to Cd can induce behavioral and neurotoxic effects, including a decrease of locomotor activity or an increase of anxiety-like behavior, which reported an impaired cognition and enhanced anxiety-like behavior related to high acetylcholinesterase activity and a decrease of Na^+, K^+-ATPase activity in pubertal male rats treated with cadmium in the diet [18]. Moreover, present study showed a significantly higher mean of blood Cd in current smokers than that in nonsmokers. Smoking is an exogenous source of metals contamination in human body; a single cigarette contains 1.0-4.5 µg Cd and at least one tenth of the metal content of a cigarette is inhaled [19].

Cadmium toxicity affects several organs including kidney, lung, liver, and brain; an association between blood Cd and depressive symptoms was recently reported in young adults [8]. Results observed in Kostrubiak et al. study in 2017 agreed to the current one in that exposure in patients with depressive symptom were predominately current smokers [14]. Another similar result was published in Scinicariello et al. study in 2015, in which claimed that smoking status was significantly associated with depressive symptoms in those exposed to Cd [8]. Since Cd exposure is associated with depression, continued efforts at reducing Cd population exposures mainly via tobacco smoking cessation programs, which have the added benefit of decreased Cd exposure through second- and third-hand smoke, may help decrease the population incidence of depression [20]. There is a strong association between smoking and depression; however, this link may be bidirectional, depression increases the risks of smoking, and smoking increases the risks of depression [21].

In conclusion, elevation of blood Cd level among adult Iraqi workers especially in batteries factory is significant health problem and rises in production sites with increased duration of work that disrupts individuals' well-being, have predictive effects on the development of depressive symptoms and can affect the severity of these symptoms. These findings suggest that Cd neurotoxicity may be a contributing factor for adverse mental health outcomes, even at levels generally considered to pose low or no risk.

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Author contribution

Dr. Al-Samaraee: Designing the work, collecting part of data, analysis and interpretation of data, and drafting the work. Took public responsibility for suitable portions of the content after participating sufficiently in the work. Dr. Sahib: Designing the work, collecting part of data, interpretation of data, and final approval of the version. Took public responsibility for suitable portions of the content after participating sufficiently in the task.

Conflict of interest

None.

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