Lead (Pb) and cadmium (Cd) blood levels and potential hematological health risk among inhabitants of the claimed hazardous region around Qaroun Lake in Egypt

Salwa Bakr[1*], Makram Ahmed Sayed[2], Karem Mohamed Salem[3], Enas Mohamed Morsi[4], Mohamed Masoud[5] and Eman Mahmoud Ezzat[3]

Abstract

Background Lead (Pb) and cadmium (Cd) heavy metals are considered potentially hazardous toxins which cause serious health problems. Many studies reported that the water of Qaroun Lake in Fayoum, Egypt with its fish farms was contaminated with Pb and Cd above permissible levels. However, there is a lack of studies addressing levels of these toxic metals among inhabitants.

Objectives We aimed to evaluate blood levels of Pb and Cd and their potential health risk among inhabitants around Qaroun Lake.

Materials and methods This case-control study estimated Pb and Cd blood levels among 190 individuals from two destinations (near and far away) of Qaroun Lack using an atomic absorption spectrometer after full history taking and routine checkup investigations; Full blood count, serum ferritin, liver enzyme (ALT), and creatinine levels.

Results There was a significant difference between blood levels of Pb and Cd heavy metals of inhabitants from near and far away Qaroun Lake destinations (p-value < 0.001). The majority of inhabitants around Qaroun Lake had Pb and Cd blood levels above permissible levels (100% and 60% respectively). Critical levels out of them were 12.1% and 30.3% respectively. In comparison to inhabitants faraway Qaroun Lake, three individuals (2.4%) had Cd above the permissible level, while all of them (100%) had Pb level within the permissible level. There were no statistically significant differences between the two sampled populations as regards hemoglobin level, ALT, creatinine, and ferritin serum levels (p-value > 0.05). The difference between studied populations regarding types of anemia was not statistically significant. Subclinical leucopenia was higher in the population near Qaroun Lake when compare to inhabitants far from the lake (13.6% vs. 4.8%, p-value 0.032).

Conclusion Bio-monitoring of populations exposed to Pb and Cd hazardous substances could help in generating an early warning system to reduce the disease burden associated with their toxicity.

Keywords Lead, Cadmium, Wadi El-Rayan, Qaroun, Egypt

*Correspondence:
Salwa Bakr
salwabakr1@hotmail.com; Sbm00@fayoum.edu.eg
Full list of author information is available at the end of the article

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Introduction

Cadmium (Cd) and Lead (Pb) heavy metals, which are considered potentially hazardous toxins, cause serious health problems. Lead, cadmium, iron, and zinc were reported to be the commonest toxic metals that affect human health (1). Once a toxic metal enters the body, it distributes through the blood to soft tissues (e.g., liver, kidney, brain), and bones (2). Acute and chronic toxic effects of these heavy elements, as a consequence, affect different body organs causing severe complications such as; gastrointestinal disorders, kidney failure, anemia, vascular damage, birth defects, nervous system disorders, and skin lesions (3, 4).

Pb is primarily toxic to the nervous system but can also induce anemia by disturbing the heme synthesis pathway (5). Cd which has been categorized as carcinogenic for human beings by the International Agency for Research on Cancer is mainly affecting the kidney and can also cause bone demineralization (6).

Pb and Cd heavy metals enter the environment from both industry and natural resources; such as volcanic emissions and weathering of rocks, therefore, they are found in air, soil, and water and can subsequently accumulate in plants and animals (5). In addition, both Pb and Cd have been used in different industries. Although Pb has unique properties in industries, Cd has declined in the United States of America since 2001 in response to environmental pollution concerns. Lead has been used in the manufacturing of batteries, painting, plumbing, mining, pipes, and metal recycling, while Cd is used in nonferrous alloys, batteries, plastic stabilizers, pigment production, coatings, and plating (6).

According to **the Centers for Disease Control and Prevention (CDC)**, the average concentration of blood Pb among healthy unexposed adults was estimated at 0.9 ug/dL. The estimated reference values of permissible Pb blood levels are <5ug/dL in adults and <3.5 ug/dL in children, while the critical/ hazardous levels are ≥70 ug/dL in adults and ≥20 ug/dL in children (7, 8). The average range of Cd blood level of healthy unexposed adults is 0.1–4 µg/L. The estimated reference value of the permissible Cd blood level is ≤0.4 ug/L, while the critical value is >5 ug/dL (9).

Generally, the primary source of Pb and Cd exposure is contaminated food. Leafy vegetables in general including Tobacco leaves contain high levels of Cd due to bioaccumulation from the soil (9, 10, 11). However, in the United States, nonsmoker individuals who regularly consume shellfish and organ meats will have a higher Cd exposure risk (9). Because both Pb and Cd elements have no known biological role in the human body, **the Joint Expert Committee on Food Additives (JECFA)**, an international scientific committee of the Food and Agriculture Organization of the United Nations in collaboration with the World Health Organization has established the safe level of provisional tolerable monthly intake (PTMI) of Cd and Pb heavy elements of 25 µg/kg of body weight (12).

Many studies reported that contamination of freshwater with heavy metals with subsequent contamination of aquatic organisms, particularly fish, has become a matter of critical concern (13, 14). Previous studies that evaluated the level of heavy metal in Lake Qaroun in El-Fayoum Governorate and its fish farms found that some toxic heavy metals, particularly lead, iron, zinc, and cadmium were higher than the permissible level (15, 16, 17, 18). However, there is a lack of studies that evaluated these toxic heavy metals among inhabitants around the tourist Qaroun Lake. Hence, the present study is aiming to evaluate the level of lead and cadmium metals in the blood of inhabitants of the region around Qaroun Lake of Fayoum Governorate in Egypt and to assess their potential health risks.

Materials and methods

Study design and sample population

This case-control study, which was carried out in Fayoum Governorate of Egypt during the period from October to December 2022 from two destinations (near and far away) of Qaroun Lack as per the Declaration of Helsinki ethical standards and after taking the approval of the ethical committee of Faculty of Medicine Fayoum University (Fig. 1). The sample size was calculated using (G power version 3.1.9.4) to get a power level of 0.90, an alpha level of 0.05, and a medium effect size of 0.5 for Pb and Cd blood levels between the two study areas. We assumed 1:2 as a ratio between the two destinations, so the sample size was estimated to be 64 and 128 in the areas near and far away from Qaroun Lake, respectively. The final study sample was 190 participants including 66 and 124 inhabitants from areas near and far away from Qaroun Lake, respectively.

Full history taking and clinical examination that addressed the risk of exposure to Pb and Cd either environmental or occupational risk, as well as, any expected medical outcomes manifestation. Peripheral venous blood samples withdrew from each participant with informed consent into serum and ethylene diamine tetra acetic acid (EDTA) Becton Dickinson vacutainer tubes (BD, Franklin Lakes, NJ, USA). Routine checkup investigations including Full blood count (CBC), serum ferritin, ALT liver enzyme, and serum creatinine levels were performed for the study population. Pb and Cd heavy metals were analyzed in serum samples of the participants using an atomic absorption spectrometer after sample separation and digestion using the ISO standard methods for determination of Pb and Cd levels.
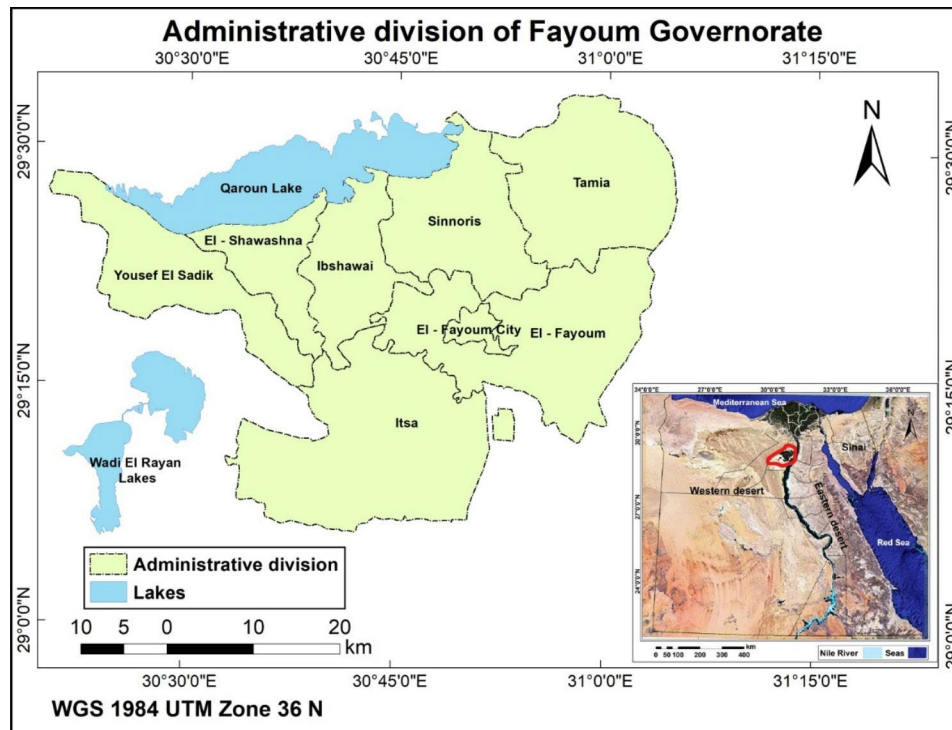
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Fig. 1 Ibshwai and Tamia Districts located around Qaroun Lake in Fayoum Governorate in Egypt

Metal analysis in blood samples

Sample digestion

The sample digestion occurred depending on the ISO standard methods for wet digestion samples DIN EN 13805 (19). A weight in the range of 0.25 g of the sample was placed in the digestion vessel (DAP 60), then 1.25 ml of concentrated nitric acid (Merck, Germany) was added to it. After fumes volatilization under the fume hood, the digestion vessels are sealed and placed in the microwave (Berghof, Germany). The digestion program starts by raising the temperature to 160°C at a rate of 5°C / minute, then increasing to 190°C at a rate of 1°C/minute. At the end of the digestion cycle, the temperature is reduced to 75°C at the rate of 1°C/minute.

Determination of lead and cadmium concentration

Agilent atomic absorption spectrometer equipped by graphite furnace unit model 240ZAA (Agilent Technologies, Germany) was used to determine cadmium (Cd) and lead (Pb) concentrations according to EN 14084:2003 (20). The temperature program used for these elements is as fellow:

step	Cadmium (Cd)			Lead (Pb)		
	Temp. (°C)	Time (sec)	Flow (L/min)	Temp. (°C)	Time (sec)	Flow (L/min)
1	85	5	0.3	85	5	0.3
2	95	40	0.3	95	40	0.3
3	120	10	0.3	120	10	0.3

step	Cadmium (Cd)			Lead (Pb)		
	Temp. (°C)	Time (sec)	Flow (L/min)	Temp. (°C)	Time (sec)	Flow (L/min)
4	250	5	0.3	400	5	0.3
5	250	1	0.3	400	1	0.3
6	250	2	0	4000	2	0
7	1800	0.8	0	2100	0.9	0
8	1800	2	0	2100	2	0
9	1800	2	0.3	2100	2	0.3

The used method was validated using the average percent recovery and standard deviation plotted into a quality control chart. The quality control sample was carried out with every set of samples by spiking the sample with known concentrations of lead and cadmium. The data of the quality control samples was used to calculate recovery percent, which was determined as an average of 95% and to ensure the accuracy and the precision of the method used.

Statistical data analysis

Statistical Package for Social Sciences (SPSS 22) was used for data statistical analysis. For lead and cadmium levels, median and interquartile range (IQR) were estimated. In comparing the two studied inhabitants, the Mann-Whitney U test was used. Categorical data were presented as frequencies and percentages. For comparing categorical data, the $\chi 2$ test or Fischer exact test was performed. P values less than 0.05 was considered to be statistically significant.

Results

The present study enrolled 190 residents aged (3–80 years) from two different districts located around Qaroun Lake in Fayoum Governorate in Egypt, where Ibshwai province located nearby the lake and Tamia province located far away from the lake were selected (Fig. 1). Only (10%) of the total population practiced risky occupations relevant to Pb and Cd heavy metal toxicity. There were no significant differences between the two studied populations as regards age, sex, house, and occupation. There were statistically significant differences between the two studied groups as regards working in farming, smoking, and consumption of fish being higher in inhabitants of regions far from Qaroun Lake (p-value: 0.037, 0.001, 0.029 respectively) (Table 1). The prevalence of abortion and birth defects was higher in areas far from the lake as compared to those near the lake. The sociodemographic

and clinical characteristics of the two groups of the study population are presented in Table (1).

Although more than one-third of the study population (74/190, 38.9%) was anemic, only less than one-fifth of them (14.3%) had chronic diseases with no statistically significant differences between the two studied populations (p-value 0.594 and 0.547 respectively) (Table 1).

Regarding hematological lab findings, out of a total of 66 inhabitants with microcytic hypochromic anemia, only 24 (12.63%) were iron deficiency anemia (IDA) confirmed with serum ferritin levels below normal cutoff value for gender and age. Additionally, subclinical leucopenia was higher in the population near Qaroun Lake when compare to those far from the lake (13.6% vs. 4.8% with a p-value of 0.032) (Table 2). Regarding liver and renal function tests, there were no statistically significant differences between the two sampled populations

Table 1 Sociodemographic and Clinical Characteristics among Sample Population:

Variables		Population Near Qaroun Lake (n = 66)	Population Distant Qaroun Lake (n = 124)	P-value
		No. (%)	No. (%)	
Age (years)	3–17	15 (22.7%)	23 (18.5%)	0.546
	18–39	27 (40.9%)	50 (40.3%)	
	40–59	23 (34.8%)	44 (35.5%)	
	60–80	1 (1.5%)	7 (5.6%)	
Sex	Male	21 (31.8%)	46 (37.1%)	0.468
	Female	45 (68.2%)	78 (62.9%)	
Occupation	Not working	56 (84.8%)	85 (68.5%)	0.051
	Risky**	4 (6.1%)	15 (12.1%)	
	Not risky	6 (9.1%)	24 (19.4%)	
Previous working in farming	Yes	1 (1.5%)	13 (10.5%)	**0.037***
	No	65 (98.5%)	111 (89.5%)	
Previous work in painting	yes	0 (0%)	1 (0.8%)	1.000
	No	66 (100%)	123 (99.2%)	
Smoking	Smoker	0 (0%)	18 (14.5%)	**0.001***
	Non-smoker	65 (98.5%)	98 (79.0%)	
	Ex-smoker	1 (1.5%)	8 (6.5%)	
House	Old	33 (50%)	72 (58.1%)	0.287
	New	33 (50%)	52 (41.9%)	
Eating fish	Once/ week	5 (7.6%)	11 (8.9%)	**0.029***
	3 times/ month	7 (10.6%)	25 (20.2%)	
	2 times /month	33 (50%)	70 (56.5%)	
	Never	21 (31.8%)	18 (14.5%)	
Abortion	Yes	6 (13.3%)	25 (32.1%)	**0.021***
	No	39 (86.7%)	53 (67.9%)	
Birth defects	Yes	2 (4.4%)	23 (29.5%)	**0.001***
	No	43 (95.6%)	55 (70.5%)	
Chronic diseases	Diseased	8 (12.1%)	19 (15.3%)	0.547
	Non-diseased	58 (87.9%)	105 (84.7%)	
HTN	Hypertensive	1 (1.5%)	14 (11.3%)	**0.017***
	Non-hypertensive	65 (98.5%)	110 (88.7%)	
DM	Diabetic	1 (1.5%)	7 (5.6%)	0.177
	Non-diabetic	65 (98.5%)	117 (94.4%)	

*Significant at p < 0.050, ** Occupations related to exposure to heavy metals, ***IDA: Iron deficiency anemia

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Table 2 Comparison between Hematological and Routine Laboratory Checkup Parameters of Sample Population:

Laboratory Investigations	Population Around Qaroun Lake (n = 66)	Population Distant Qaroun Lake (n = 124)	P- value
	No. (%)	No. (%)	
White Blood Cell Count	57 (86.4%)	118 (95.2%)	**0.032******
- Normal count (4–11 10⁹/L)	9 (13.6%)	6 (4.8%)	
- Leucopenia			
Hemoglobin Conc.	42 (63.6%)	74 (59.7%)	0.594
- Normal conc. (11.5–17.5 g/dL)	24 (36.4%)	50 (40.3%)	
- Anemic level			
Subclinical MHA*:	23 (34.8%)	43 (34.7%)	0.981
- Anemic	43 (65.2%)	81 (65.3%)	
- Non-anemic			
Subclinical IDA**	5 (21.7%)	19 (44.2%)	0.071
- Iron deficiency	18 (78.3%)	24 (55.8%)	
- Non-iron deficiency			
Mentzer screening index (< 14) *	1 (4.4%)	7 (16.3%)	0.179
- Positive	22 (95.6%)	36 (83.7%)	
- Negative			
MHA with uncertain etiology#	17 (73.9%)	17 (39.5%)	**0.039******
Serum Ferritin	49 (74.2%)	90 (72.6%)	0.970
- Normal range (Male: up to 300 – Female: up to 200 ug/L)	16 (24.2%)	32 (25.8%)	
- Low level	1 (1.5%)	2 (1.6%)	
- High level			
ALT	62 (93.9%)	118 (95.2%)	0.719
- Normal range (Up to 40 IU/L)	4 (6.1%)	6 (4.8%)	
- High serum level			
Serum Creatinine	65 (98.5%)	116 (93.5%)	0.127
- Normal range (Male: 1.1–1.4 mg/dl; Female: 0.6–1.1 mg/dl)	1 (1.5%)	8 (6.5%)	
- High serum level			

*MHA: Microcytic Hypochromic Anemia among the anemic study population. **IDA: Iron deficiency anemia. ***Mentzer index (MCV/ RBCs) calculated among individuals with microcytic hypochromic anemia < 14 suggestive of thalassemia trait. ****Significant at p < 0.050. # MHA after exclusion of those cases due to IDA and positive Mentzer with suspicious thalassemia trait

as regards ALT, creatinine, and ferritin (p-value > 0.05) (Table 2).

There was a significant difference between blood levels of Pb and Cd elements of inhabitants from near and far away Quaron Lake destinations (p-value < 0.001). The majority of inhabitants around Qaroun Lake had Pb and Cd blood levels much above permissible levels established by the CDC (100% and 60.6% respectively). Critical levels out of them were 12.1% and 30.3% respectively. In comparison to inhabitants faraway Qaroun Lake, three individuals (2.4%) had Cd above the permissible level, while all of them (100%) had Pb level within the permissible level (Table 3). The median (IQR) blood concentration for Pb and Cd among our study population near Qaroun Lake was 36.25 (26.20–48.78) ug/dL and 1.45 (0–7.90) ug/dL, respectively. Whereas, their median (IQR) values among those who live far away from the lake were 0 (0–1.7) ug/L and 0 (0–0) ug/L, respectively (Fig. 2).

In inhabitants around Qaroun Lake, our results found that the critical Pb levels were detected more among younger age groups rather than other age categories (p-value 0.036) (Table 4), however, there were no statistically significant differences between the studied heavy metals (Pb and Cd) blood levels and occurrence of noteworthy clinical/ subclinical manifestations (p-value > 0.05) (Table 5). Though the most obvious clinical/ subclinical manifestation among them was microcytic hypochromic anemia, the majority (17 out of 66 individuals, 73.91%) of them were diagnosed without a clear conclusive underlying etiology (Table 2). Out of a total of 23 inhabitants with microcytic anemia, only 5 (21.7%) had iron deficiency and another had suspicious thalassemia traits by using the Mentzer screening index [21].

Regarding those inhabitants having microcytic hypochromic anemia with uncertain etiology, there was a statistically significant difference between them being higher among those living near Qaroun Lake with a p-value of 0.039 (Table 2). Out of those 17 individuals with microcytic hypochromic anemia with inconclusive

Table 3 Prevalence of Pb and Cd in Blood of Sample Population

| Blood/ Serum Level		Population Around Qaroun Lake (n = 66)	Population Distant Qaroun Lake (n = 124)	P-value
		No. (%)	No. (%)	
Lead (Pb)	Permissible blood level (Children < 3.5 ug/dl; Adult < 5 ug/dl)	0 (0%)	124 (100%)	< 0.001*
	Above permissible level	58 (87.9%)	0 (0%)	
	Critical/ Hazardous level (Children ≥ 20 ug/dl; Adult ≥ 70 ug/dl)	8 (12.1%)	0 (0%)	
Cadmium (Cd)	Permissible blood level (≤ 0.4 ug/L)	26 (39.4%)	121 (97.6%)	< 0.001*
	Above permissible level	20 (30.3%)	3 (2.4%)	
	Critical/ Hazardous level (≥ 5 ug/L)	20 (30.3%)	0 (0%)	

*Significant at p < 0.050
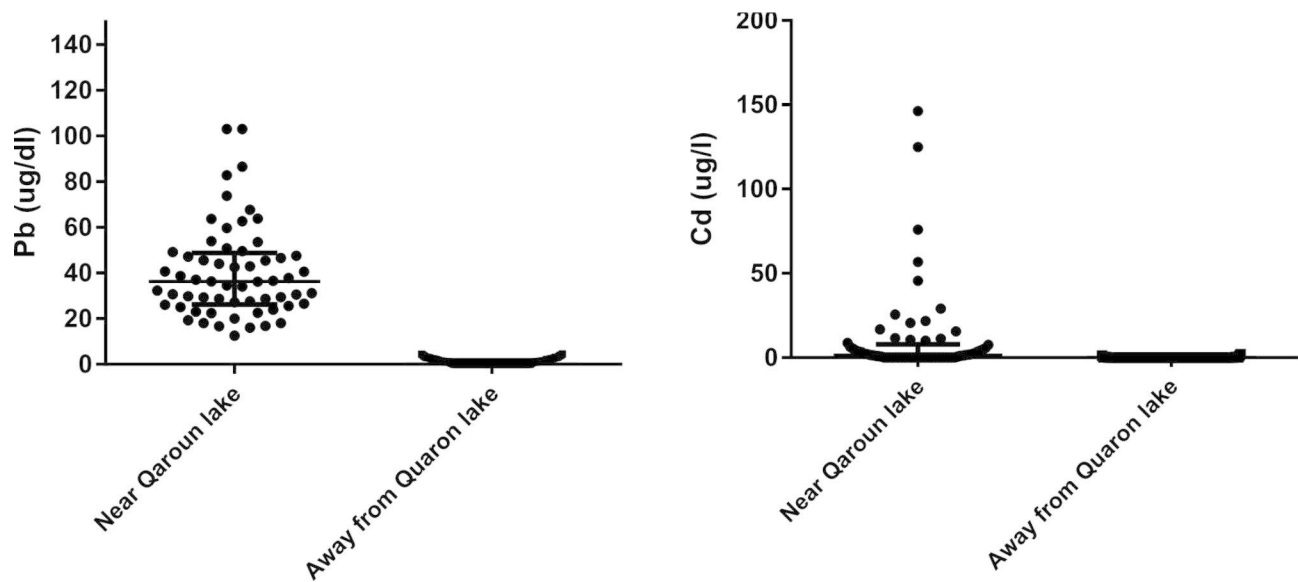
Fig. 2 Jitter plot with median (IQR) for blood Pb and Cd levels in both study population

etiology lived near the lake, 17 (100%) had Pb and 5 (29.41%) had Cd above the permissible level.

Discussion

There is no data in the literature on the potential health risks of Pb and Cd heavy metals in the Egyptian population particularly in the region claimed to be potentially polluted, around Qaroun Lake in Egypt. Nevertheless, the previously published studies on the pollution of Lake Qaroun with heavy metals particularly Pb and Cd have been noted [15–18, 22]. Hence, in this study, we aimed to evaluate the most hazardous of these claimed elements (Pb and Cd) in the blood of 190 inhabitants in Fayoum Governorate from different regions using an atomic absorption spectrometer after sample digestion. This study will be considered a preliminary study to assess the commonest hazardous heavy metals of Lack Qaroun of Fayoum Governorates in Egypt.

The historically renowned Qaroun Lake, a close eco-system in nature, is located in the north of Fayoum Governorate in Egypt (Fig. 1), where contaminants from El-Bats and El-Wadi drains discharge along with agriculture drainage water of Fayoum province [17]. It was reported that such anthropogenic inputs and/ or geological sources contribute to the biodiversity of the water lake, where its original freshwater turned into the currently brackish one. Additionally, the evaporation of water due to the hot climate of the region augments the intensification of heavy metals, salts, and pesticide concentrations in the lake [15]. Accordingly, such heavy metals contaminations in Qaroun Lake may have devastating effects on the ecological balance of the aquatic environment, hence on the environmental media such as dust, air, soil, and others [14, 23].

Our study results coincide with previous studies in which Pb and Cd concentrations in water samples collected from Wadi EL-Rayan Lakes were higher than the maximum permissible level recommended by Egyptian Environmental law, (48) decision 1992/2013, in the spring/ hot season, but within permissible levels in cold one [15, 16, 22]. Furthermore, in correlation, they found that urea and creatinine serum levels in Tilapia fish showed a significant increase. On the other hand, **George and his colleagues (2013)** reported that Cd concentration in the water samples collected from Wadi El-Rayan Lakes was within the recommended permissible limits (100 µg/L) of the National Environmental Law [24], where it ranged from (12 to 16.8 µg/L) in the cold season and from (15.7 to 30.7 µg/L) in the hot one [16].

In our study, the median (IQR) blood concentration for Pb among our study population lived near Qaroun Lake was 36.25 (26.20–48.78) ug/dL, while it was 0 (0–1.7) ug/ dL among those who lived far away the lake. Although various studies disclosed that the normal value for blood Pb concentration was 42.6 µg/L, different values were also reported for other countries. The mean Pb level in an Amazonian district was 32.77 µg/L, while it was 14.5 µg/L in Australia, 21.3 µg/L in Canada, 12.3 µg/L in the Americas, 65.4 µg/L in Brazil, 33.4 µg/L in Italy, and 19.1 µg/L in Korea [11]. In conclusion, our results showed in agreement with previous studies that the level of blood Pb concentration might be influenced by numerous epidemiological and environmental variables such as diet, age, and gender [25]. Regarding the median (IQR) of Cd blood level, the value was 1.45 (0–7.90) µg/L among those who lived nearby the lake, but an undetectable level was noted among those who lived far away from the claimed destination of the Qaroun Lake region.

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Table 4 Association between Impermissible Blood Levels of Pb and Cd and Basic Characteristics of Inhabitant near Qaroun Lake in Fayoum Governorate:

Variables		Lead (Pb) (n=66)		Cadmium (Cd) (n=66)	
		Critical (n=8)	Under-critical/ Impermissible (n=58)	Critical/ Impermissible (n=40)	Permissible (n=26)
		No. (%)	No. (%)	No. (%)	No. (%)
Age (years)	3–17	5 (62.5%)	10 (17.2%)	10 (25.0%)	5 (19.2%)
	18–39	1 (12.5%)	26 (44.8%)	15 (37.5%)	12 (46.2%)
	40–59	2 (25.0%)	21 (36.2%)	15 (37.5%)	8 (30.8%)
	60–80	0 (0.0%)	1 (1.7%)	0 (0.0%)	1 (3.8%)
P-value		0.036*		0.520	
Sex	Male	4 (50.0%)	17 (29.3%)	13 (32.5%)	8 (30.8%)
	Female	4 (50.0%)	41 (70.7%)	27 (67.5%)	18 (69.2%)
P-value		0.253		0.883	
Occupation	Not working	8 (100%)	48 (82.8%	33 (82.5%)	23 (88.5%)
	Risky occupation	0 (0.0%)	4 (6.9%)	3 (7.5%)	1 (3.8%)
	Non-Risky occupation	0 (0.0%)	6 (10.3%)	4 (10.0%)	2 (7.7%)
P-value		0.444		0.777	
House	Old	3 (37.5%)	30 (51.7%)	21 (52.5%)	12 (46.2%)
	New	5 (62.5%)	28 (48.3%)	19 (47.5%)	14 (53.8%)
P-value		0.708		0.614	
Eating fish	One/week	0 (0.0%)	5 (8.6%)	1 (2.5%)	4 (15.4%)
	Three/month	1 (12.5%)	6 (10.3%)	2 (5.0%)	5 (19.2%)
	Two/month	5 (62.5%)	28 (48.3%)	24 (60.0%)	9 (34.6%)
	Never	2 (25.0%)	19 (32.8%)	13 (32.5%)	8 (30.8%)
P-value		0.768		0.037*	
Abortion	Yes	0 (0.0%)	6 (15.0%)	4 (15.4%)	2 (11.1%)
	No	4 (100.0%)	34 (85.0%)	22 (84.6%)	16 (88.9%)
P-value		1.000		1.000	
Birth defects	yes	0 (0.0%)	2 (5.0%)	1 (3.8%)	1 (5.6%)
	No	4 (100.0%)	38 (95.0%)	25 (96.2%)	17 (94.4%)
P-value		1.000		1.000	

*Significant at p<0.050

Furthermore, our results found that there were no significant differences between the population who lived nearby Qaroun Lake compared to those who lived far away the lack as regards age, gender, house, and occupation. However, we found that there was a significant difference between blood levels of Pb and Cd heavy elements of inhabitants from the two destinations around Quaron Lake (p-value<0.001). Inconsistent with previous studies described from Bangladesh (26), Mexico (27), and Russia (28), our results showed that the majority of inhabitants nearby Quaron Lake who had Pb and Cd blood levels much above permissible levels established by the CDC were among the younger age group (p-value 0.036). Although the developing biological systems of the human body particularly the nervous system in children is most sensitive to the effects of Pb blood level (9), previous studies similarly revealed that the mean blood lead level was higher in children aged from 6 to 11 years than other age categories (29). There is no acknowledged safe blood Pb concentration in children, where cognitive, behavioral, and learning difficulties were reported with low blood Pb concentration even as low as 5ug/dL, the CDC (2021) updated the blood lead reference value in children to 3.5 μg/dL instead of 5 μg/dL for avoiding the serious consequence of lead exposure on children's health (7).

Table 5 Association between Pb and Cd Blood Levels and Clinical/ Subclinical Manifestation of Inhabitants near Qaroun Lake in Fayoum Governorate:

Clinical/ Subclinical Manifestation		Lead (Pb) (n = 66)		Cadmium (Cd) (n = 66)	
		Critical (n = 8)	Under-critical/ Impermissible* (n = 58)	Critical/ Impermissible (n = 40)	Permissible (n = 26)
		No. (%)	No. (%)	No. (%)	No. (%)
History of any Chronic diseases	Yes	1 (12.5%)	7 (12.1%)	3 (7.5%)	5 (19.2%)
	No	7 (87.5%)	51 (87.9%)	37 (92.5%)	21 (80.8%)
P-value		1.000		0.247	
History of HTN	Yes	0 (0.0%)	1 (1.7%)	1 (2.5%)	0 (0.0%)
	No	8 (100.0%)	57 (98.3%)	39 (97.5%)	26 (100.0%)
P-value		1.000		1.000	
History of DM	Yes	0 (0.0%)	1 (1.7%)	1 (2.5%)	0 (0.0%)
	No	8 (100.0%)	57 (98.3%)	39 (97.5%)	26 (100.0%)
P-value		1.000		1.000	
Microcytic Hypochromic Anemia	Present	3 (37.5%)	20 (36.2%)	12 (30.0%)	11 (42.3%)
	Absent	5 (62.5%)	38 (63.8%)	28 (70.0%)	15 (57.7%)
P-value		1.000		0.305	
Subclinical IDA	Present	1 (33.3%)	4 (20.0%)	1 (8.3%)	4 (36.4%)
	Absent	2 (66.7%)	16 (80.0%)	11 (91.7%)	7 (63.6%)
P-value		0.539		0.155	
Subclinical Leucopenia	Present	0 (0.0%)	9 (15.5%)	7 (17.5%)	2 (7.7%)
	Absent	8 (100.0%)	49 (84.5%)	33 (82.5%)	24 (92.3%)
P-value		0.586		0.465	
ALT Liver Enzyme	High	0 (0.0%)	4 (6.9%)	3 (7.5%)	1 (3.8%)
	Normal	8 (100.0%)	54 (93.1%)	37 (92.5%)	25 (96.2%)
P-value		1.000		1.000	
Serum Creatinine	High	0 (0.0%)	1 (1.7%)	0 (0.0%)	1 (3.8%)
	Normal	8 (100.0%)	57 (98.3%)	40 (100.0%)	25 (96.2%)
P-value		1.000		0.394	
Serum Ferritin	Normal	4 (50.0%)	45 (77.6%)	30 (75.0%)	19 (38.8%)
	Low	4 (50.0%)	12 (20.7%)	9 (22.5%)	7 (26.9%)
	High	0 (0.0%)	1 (1.7%)	1 (2.5%)	0 (0.0%)
P-value		0.187		0.675	

*None of the inhabitants had lead levels within the permissible level

On the contrary, **Queiroz and his colleagues (2019)** reported that blood Pb levels show trends with age and gender being higher in adults and the elderly (11, 30–32). This point out that the duration of exposure to lead in a residential area is consistently found to be a strong predictor of high blood Pb level (33–35). Regarding gender variant in this study, though the mean blood Pb and Cd critical levels were not statistically different between males and females, the prevalence was almost the same regarding the critical level of blood Pb level being equal (50%) in both gender but and the prevalence of elevated blood Cd level in females was higher than males. This might be explained by the higher number of females who participated in this study in comparison to males. Controversial results were noted in previous studies conducted in Egypt (29, 36), Bangladesh (37), Thailand (38), and Pakistan (33), where the incidence of elevated blood lead concentration was higher in males than females. This

might be explained by the different traditional roles of male and female in these societies, where increased outdoor activities and occupational risk for males appears to be involved in this sex-related difference (29).

Independent of the level of lead heavy metal intoxication in human body fluids, it was reported that the appearance of clinical manifestations varies from one individual to another depending on the surrounding environmental differences [31]. Though the most obvious clinical/ subclinical manifestation among inhabitants living near Qaroun Lake was microcytic hypochromic anemia, the majority (73.91%) of them were diagnosed without a clear conclusive underlying etiology. Regarding those inhabitants having microcytic hypochromic anemia with uncertain etiology, there was a statistically significant difference between them being higher among those living near Qaroun Lake with a p-value of 0.039. Out of those 17 individuals with microcytic hypochromic

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anemia with inconclusive etiology lived near the lake, had 17 (100%) Pb and 5 (29.41%) Cd above the permissible levels. Additionally, subclinical leucopenia was noted higher in inhabitants of the region nearby Qaroun Lake compared to those far away from the lake (13.6% vs. 4.8% with a p-value of 0.032). Similarly, several published studies have noted that cumulative Pb poisoning is associated with increased potential health risks for hematological disorders particularly anemia [36, 39, 40]. However, others reported a non-significant association between the presence of anemia and elevated blood Pb level [36, 41].

Though there is no safe level of Pb blood level, previous studies have shown that lead-induced anemia microcytic hypochromic can be easily diagnosed at Pb blood levels higher than 50 μg/dL in adults [42]. It was reported that anemia-associated chronic exposure to Pb is the result of both interfering with heme biosynthesis and shortening of red blood cell lifespan [43]. The critical effect of Pb in the human body is mainly attributed to cellular enzymatic disruption of δ-aminolevulinic acid dehydratase (ALAD) that is essential in heme biosynthesis with a consequent decrease in various red blood cell hematological parameters (RDW-CV, MCV, MCH, and hematocrit) and potential risk of anemia [9, 44, 45].

For the well-known Pb and Cd biogeochemical cycle, these heavy metals are usually absorbed from regional background levels and might be present in drinking water, household dust, and food in which environmental media such as dust, air, soil, and others may have an excess of these toxic heavy elements. According to a study carried out in the region around Qaroun Lake in Fayoum Governorate a region with a characteristic ecosystem, geology, and residency might contribute to overt circulating Pb and Cd levels in the region [11]. This might explain the statistically significant differences between the two studied groups as regards working in farming, consumption of fish, smoking, and hypertension despite being higher in inhabitants of the region far from Qaroun Lake.

Though there were no statistically significant difference significant differences between the studied heavy metals (Pb and Cd) blood levels and occurrence of noteworthy clinical/ subclinical manifestations in both kidney and liver functions when ALT, creatinine, and ferritin serum levels have been estimated in all the study population (p-value>0.05). The present study results, in agreement with previous studies, are considered an alarm to the toxic effect of environmental changes in Qaroun Lack ecosystem for being the final reservoir for most of such heavy metals, where it receives heavy loads of organic and inorganic pollutants via several agricultural drains and huge amounts of raw sewage, agricultural and industrial wastewater discharged into the lake [46, 47].

Bio-monitoring of populations exposed to Pb and Cd hazardous substances could help in generating an early warning system to reduce the disease burden associated with their toxicity. However, a mass screening program for both inhabitants and environmental media of the regions nearby Qaroun Lake and Wadi El-Rayan in Fayoum Governorate is mandatory to validate such heavy metals' hazardous impact.

Conclusion

This study could be a preliminary study for bio-monitoring of the Fayoum population who are exposed to the hazardous effect of heavy metals in Lake Qarun water and its farm fish. Hence, to generate an early warning system to reduce the disease burden associated with their increased level and lethal toxicity; such as Alzheimer, kidney failure, and anemia for unknown causes, that are otherwise easily preventable.

Authors' contributions
S.B: The concept of the study development, clinical laboratory work, and corresponding author to the journal. M.S and E.M: contributed to laboratory work of heavy metal estimation. E.E, and K.S contributed scientifically to data and sample collection. M.M: Data analysis. All authors contributed in design study questionnaire, writing the original draft of the manuscript, critical revision of the manuscript, and approved its final version.

Data Availability
All relevant data are within the paper.

Declarations

Ethical approval and consent to participate
The study was approved by the ethical committee of the Faculty of Medicine, Fayoum University. Written informed consent was obtained from the participants. All study procedures were following the ethical standards of the institutional/ and or national research committee and with the 1964 Declaration of Helsinki.

Consent for publication
Not applicable.

Competing interests
All authors declare there is no conflict of interest.

Author details
[1]Department of Clinical Pathology/ Hematology & Transfusion Medicine, Faculty of Medicine, Fayoum University, P.O Box: 63514, Fayoum, Egypt [2]Head of Environmental and Food Pollutants Analysis Lab, Faculty of Agriculture, Fayoum University, Fayoum, Egypt [3]Department of Internal Medicine, Faculty of Medicine, Fayoum University, Fayoum, Egypt

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[4]Department of Forensic Medicine and Clinical Toxicology, Faculty of Medicine, Fayoum University, Fayoum, Egypt
[5] Department of Public Health and Community Medicine, Faculty of Medicine, Fayoum University, Fayoum, Egypt

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