Original Article

Association between Serum Heavy Metals Level and Cancer Incidence in Darbandikhan and Kalar Area, Kurdistan Region, Iraq

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Abstract

Background: Exposure to heavy metals is considered as the main threat to human health and biological system. Darbandikhan Lake is one of the three large lakes in Kurdistan, Northern Iraq; it is currently at a high risk of pollution by sewage and municipal wastes. The current study was designed to highlight the potential association between concentration of heavy metals and carcinogenicity in people who live in Darbandikhan and the surrounding area. **Materials and Methods:** A case–control study was carried out on 29 cancerous patients and 25 healthy individuals from Darbandikhan, Kalar, and the surrounding area; the patients were admitted to the Hiwa Oncology Center in Sulaimani City. Determination of serum concentrations of copper (Cu), iron (Fe), cadmium (Cd), arsenic (As), chromium (Cr), lead (Pb), and zinc (Zn), was performed by an inductively coupled plasma atomic absorption spectrophotometer. **Results:** Serum concentration of Pb, Fe, and Cu was higher in cancer group compared with control in nonsignificantly different ($P > 0.05$) for Pb, whereas significantly ($P < 0.05$) for Cu and Fe. Higher serum Cd concentration was detected in control group compared with the cancer group. Differences not detected in Cr and As serum concentration analysis between both groups. Serum level of Zn was nonsignificantly higher in control group compared with the cancer group ($P > 0.05$). **Conclusion:** Discrepancies in the serum level of heavy metals of cancer group might reveal the involvement of heavy metal as a contributing factor of carcinogenicity in these areas.

Keywords: *Cancer, Darbandikhan, heavy metals, Kalar, water sources*

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Introduction

Exposure to heavy metals is considered as a main threat to human health and biological system. These metals have been widely studied and their effects on human health regularly analyzed by international bodies.[1] Cadmium (Cd), mercury (Hg), lead (Pb), copper (Cu), and nickel (Ni) are among the metals that have potential adverse effects on human health,[2] and chronic exposures to them are nearly unavoidable in daily life, such as from airborne particles, soil, water, and subsequently food.[3] The general population is primarily exposed to heavy metals through food; fish being a major source of methylmercury exposure[4] These heavy metals as environmental pollutants have been recognized to have a role in induction of malignant human growths. Recently, certain heavy metals such as cadmium (Cd), mercury (Hg), lead (Pb), chromium (Cr), and arsenic (As) showed a close association to breast cancer.[5] Several epidemiological studies have demonstrated that exposure to metals has toxic and carcinogenic effects on humans and animals.[6]

Heavy metals are confirmed as human carcinogens; lead, cobalt, and iron are observed as potential carcinogens. Prostate cancer mortality was found to be strongly contributed to cadmium (Cd), followed by zinc (Zn) and

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chromium (Cr).[7] Excess occupational and environmental exposure to metals is considered to be a major cause of metal-related cancer and also associated with increased cancer risk.[8]

Darbandikhan Lake is one of the three large lakes in Kurdistan, Northern Iraq, 230 km northeast of Baghdad. Two main tributaries feed it: The Tanjero River, which flows in from the North/Northwest, and the Sirwan River, which flows in from the East (from Iran). Many people benefit from this lake and its waters as it is used as a source for drinking and irrigation water, as an important fishery, and as a beautiful site used by many for recreation. It is also an important source of electricity generated by the Darbandikhan Dam. Darbandikhan Lake is currently at a high risk due to pollution by sewage and municipal wastes. Preliminary results of tests for heavy metals in different sites performed at Darbandikhan Lake and comparing the results with other surface water references and the World Health Organization Drinking Water Standard as additional contrast indicated elevated levels of cadmium, manganese, lead, and nickel in surface waters. As well as comparing the results of test for heavy metals in sediment for different sites at this Lake with Swedish standards for contamination levels showed elevated levels of copper, lead, zinc, and nickel at some or all sites.[9]

Scanty data are available on heavy metals and its relation with carcinogenicity in this region, for that reason the current study was designed to highlight the potential association between concentration of heavy metals and carcinogenicity in people in Darbandikhan area who use Darbandikhan Lake as a source of drinking water which contain above normal limit the heavy metals.

Materials and Methods

This study was a case–control study that was carried out on 29 newly diagnosed cancer patients (cases) and 25 healthy individuals (control). The newly diagnosed patients who enrolled in the current study were residents from Darbandikhan and Kalar area who are using well and tap water as a main source of drinking water and they were admitted to the Hiwa Oncology Center in Sulaimani City. Controls were healthy individuals also selected from the same area; they were matched for both age and gender. The inclusion criteria for the present study includes patients with different types of cancers including breast cancer, prostate cancer, nonsmall cell lung cancer, and gallbladder carcinoma admitted to the hospital during the period from October 2015 to March 2016. Relevant information including occupational history, smoking habits, and reproductive history was obtained from each patient by face-to-face interview using a questionnaire, which was designed for this study. Patients with positive family history of cancer were excluded from the study. Individuals using supplementation with trace elements and metals during the last 3 months before the study were excluded. The study approved by the Research Ethics Committee of the College of Medicine, University of Sulaimani (No. 21 in 07/07/2015) in accordance with the Declaration of Helsinki and its amendments,[10] and each patient signed informed consent before enrollment. Venous blood samples (5 ml) of newly diagnosed cancerous patients and control group were obtained from the antecubital fossa veins in accordance with the guidelines set out in the Declaration of Helsinki. Serum was separated by centrifugation immediately. The serum samples were placed in plain tubes and kept at −80°C (without thawing) until samples were analyzed. Determination of serum concentrations of Cu, Fe, Cd, As, Cr, Pb, and Zn were performed by an inductively coupled plasma atomic absorption spectrophotometer. Statistical analyses of results were performed using GraphPad Prism software.

Results

The mean age for the cancer group was 54.3 ± 14.8 years, whereas for the control group, it was 51.1 ± 22.8 years. Other demographic data for the participants including age, gender, resident area, education level, types of cancer, and sources of drinking water of both cancer and control groups are shown in Table 1.

The results of serum concentration of metals in the current study show differences between both cancer patient group and control group. Serum concentration of lead (Pb) was higher in cancer group compared with control but nonsignificantly different ($P > 0.05$) was detected.

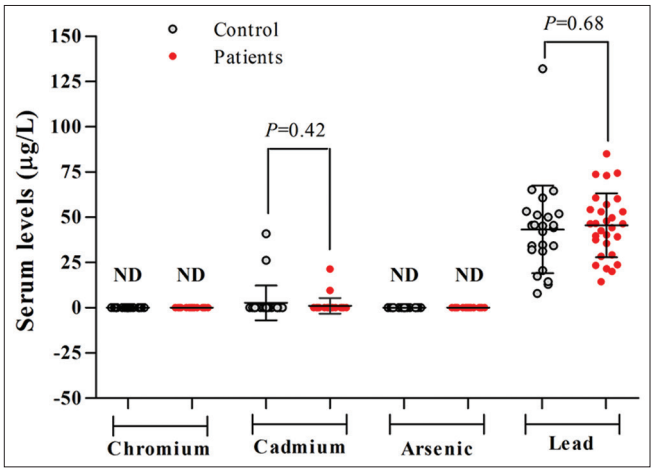

Figure 1: Serum levels of chromium, cadmium, arsenic, and lead in healthy participants and cancer patients from Kalar and Darbandikhan areas. Values are presented as mean ± Standard deviation; ND: Nondetectable; $P > 0.05$: Nonsignificant difference compared with control

Table 1: Demographic characteristics of included participants

Parameter	Control (*n*=25)	Cancer patients (*n*=29)
Age, year (mean±SD)	51.1±22.8	54.3±14.8
Gender, *n* (%)		
Female	15 (60)	17 (58.6)
Male	10 (40)	12 (41.4)
Residence, *n* (%)		
Kalar	17 (68)	25 (86.2)
Darbandikhan	8 (32)	4 (13.8)
Education level, *n* (%)		
Illiterate	14 (56)	24 (82.8)
Secondary school	1 (4)	4 (13.7)
High school	10 (40)	1 (3.5)
Cancer type, *n* (%)		
Breast	-	6 (20.7)
Brain	-	2 (6.9)
Lung	-	3 (10.3)
GIT	-	6 (20.7)
Leukemia	-	3 (10.3)
Miscellaneous	-	9 (31.1)
Source of drinking water, *n* (%)		
Well	9 (36)	13 (44.8)
Tap water	6 (24)	5 (17.2)
Well and tap water	10 (40)	11 (38)

GIT=Gastrointestinal tract; SD=Standard deviation

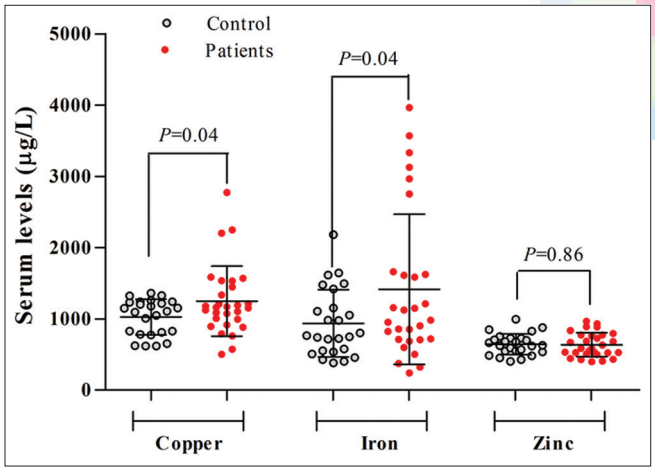

Figure 2: Serum levels of copper, iron, and zinc in healthy participants and cancer patients from Kalar and Darbandikhan areas. Values are presented as mean ± Standard deviation; $P < 0.05$: Significant difference compared with control

Meanwhile, higher serum cadmium (Cd) concentration was detected in control group compared with the cancer group. Differences were not detected in chromium (Cr) and arsenic (As) serum concentration analysis between both control and cancer group as shown in Figure 1.

High concentrations of copper (Cu) and iron (Fe) were found in the blood samples of the cancer patients from Kalar and Darbandikhan areas compared with the healthy participants in the areas. The concentration of Cu and Fe was significantly higher in cancer patient group compared with control group ($P < 0.05$) as shown in Figure 2. Meanwhile, serum level of zinc was nonsignificantly higher in control group compared with the cancer group ($P > 0.05$).

Discussion

Despite new advances and efforts in cancer research, the etiology of many types of cancer is still unknown. Although the risk factors do not fully clarify variations in the incidence of complex disorders such as cancers.[11] Many epidemiological studies reported the involvement of the trace elements in the etiology of many diseases including cancer, and indicate a close association between metals like copper (Cu), cadmium (Cd), arsenic (As), lead (Pb), zinc (Zn), and nickel (Ni), which are found naturally in the environment and the development of breast and prostate cancers.[12,13]

Heavy metals are basically defined as those trace elements that have ≥5 g/cm^3 densities and may cause harmful biological and environmental effects,[14] usually biological organisms need trace amounts of some heavy metals, including cobalt, copper, iron, molybdenum, vanadium, strontium, and zinc.[15] Analysis of heavy metals and trace elements in human tissues also shows a significant role both in human health and diseases states. They are of significant importance in different cellular metabolic pathways, and each of the essential and nonessential trace elements may be harmful if present in high cellular levels; trace element deficiency or excess was implicated in the development or progression of some cancers.[16] It is apparent that some trace metals are claimed to be carcinogenic and capable of inducing a toxic effect through the formation of reactive oxygen species (ROS) and acting as cofactors in the oxidative damage of biological macromolecules and deoxyribonucleic acid (DNA).[17]

Excessive exposure to lead has many negative impacts on human health. Evidences suggest that lead exposure increases susceptibility to cancer and may exert diverse toxic effects through interference with the repair mechanism of DNA after genotoxic insult, impede the ability of cells to develop appropriate and precise responses to environmental genotoxins.[18,19]

In the present study, high level of lead concentration has been detected remarkably in the cancer patients as compared with the control group; this shows consistency with the finding of Blaurock-Busch *et al*. who detected in the hair samples of cancer patients a significantly higher levels of lead when compared to a control group,

suggesting a probable relationship between lead exposure and the disease.[20] In the present study, increased levels of serum iron were also detected in cancer patients compared with controls, and this finding was in tune with that reported by da Silva *et al*.[21] Iron was involved in many tumorigenesis including breast cancer, and the suggested role of iron in tumor development could be related to its action as enzymatic cofactor involved in carcinogenesis.[22]

Moreover, iron can also promote tissue damage – carcinogenesis through its action as a catalyst in the conversion of hydrogen peroxide to free radicals that attack cellular membranes, breaks DNA strands, inactivate enzymes and initiate lipid peroxidation then accelerate tumor initiation.[23]

Cadmium, the nonessential heavy metal, represents a potential environmental and human hazards, and it is established as toxic and carcinogenic metal, and can induce elevated ROS formation, which in turn induces DNA damage, in addition to its ability to interfere with cell signaling.[24] Based on epidemiological studies, Cd seems to be associated with overall cancer mortality in men and women including lung cancer, pancreatic cancer, non-Hodgkin lymphoma, and leukemia, ovarian and uterine cancer.[25] Surprisingly, in the present study, serum level of cadmium in the control group was higher than that in cancer patients, the current result was inconsistent with the results reported by Czerny *et al*.[26] This may be attributed to analytical errors or inconsistent selection of the control group. Copper has been suggested to play an important role in normal immune function and several health disorders.[27] In the present study, serum copper level was increased significantly in the cancer patients compared with the control group. This finding is comparable with the study performed by Baharvand *et al*. who found that serum level of copper was increased significantly in the cancer patients compared to controls.[28] Although we cannot establish a clear link between copper and cancer, our data are consistent with those studies which also found higher level of copper in cancer patients.[13] The role of zinc in causation of cancer is ambiguous because both its deficiency and excess has been implicated in cancer[29] Zinc is essential for cell growth and proliferation and may be accumulated in tumor sites to supports tumor growth, it may also play a crucial role in cancer etiology and outcome.[30] Siddiqui *et al*. showed that blood zinc was significantly higher in malignant cases than in those of benign and control.[31] In the present study, nonstatistically significant decrease was reported in serum level of zinc in the cancer group compared with the control group, the obtained result is comparable with that reported in some studies on cancer cases such as lung, breast, head and neck, liver, stomach, and prostate cancer,[29,32] which might explain a possible link between zinc deficiency and occurrence of cancer, as reported in some case-control studies.[13,33]

The common type of malignancies in Sulaymaniyah province, Kurdistan, Iraq was determined by a hospital-based, retrospective study. This study shows the results of 8 years cancer registration of the province including patients of Darbandikhan and Kalar area, and the common types by primary site were leukemia, lymphoma, brain, kidney, and bone. In males, they were lung, leukemia, lymphoma, colorectal, prostate, bladder, brain, stomach, carcinoma of unknown primary and skin, whereas in females, they were breast, leukemia, lymphoma, colorectal, ovary, lung, brain, carcinoma of unknown primary, and stomach.[34] Although the serum level of the studied metals in the present study did not provide a sufficient evidence for supporting the hypothesis that metals are a major contributing factor for developing cancer but the vast majority of researches are consider metals as a risk factor for initiation the cancer.[35] Obviously, there is a strong correlation between cancer rate and metal exposure, lung cancer is associated with the occupational exposure to metals including cadmium, chromium, nickel, copper, cobalt, lead, and mercury. Occupational exposure to cadmium and nickel are linked to renal and prostate cancer and copper exposure is linked to non-Hodgkin's lymphoma and skin cancer. Exposure to chromium is also connected to an increased risk of liver, larynx, esophagus, and gastrointestinal cancer. Lead is associated with glioma and stomach cancers while mercury exposures are associated with prostate and bladder cancers. Metalloestrogens such as cadmium, calcium, cobalt, copper, nickel, chromium, lead, mercury, and tin activate the estrogen receptor, and exposure to these metals may increase the risk of developing breast cancer.[36-38]

Conclusion

Discrepancies in the serum level of trace element and heavy metals of cancer patients in comparison of noncancerous patients of the Darbandikhan and Kalar region might reveal involvement of heavy metal as a contributing factor of carcinogenicity in these areas.

Acknowledgment

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Declaration of patient consent

The author clarifies that she has obtained all appropriate patient consent forms. In the form, the patient has given their consent for their images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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