Available online at www.garmian.edu.krd

Passer Journal of Basic and Applied Sciences

Passer 7 (Issue 2) (2025) 635-640

Original Article

Determination of heavy metal levels in blood serum and urine of lung cancer patients at Babylon Cancer Center, Iraq

Ashraf H. Kadhem*[1], Mohammed Abdul Ammar [1], Mohsin Kadhim [1]

[1] *Department of Physics, College of Science, University of Babylon, Iraq.*

Received 11 January 2025; revised 07 March 2025;
accepted 09 June 2025; available online 13 June 2025

DOI: 10.24271/psr.2025.499366.1895

ABSTRACT

Lung cancer development may be impacted by certain trace element concentrations. The purpose of this study was to detect certain trace elements in the serum and urine of lung cancer patients from Iraq. A total of 89 patients were involved in this study: 25 individuals who were healthy and 64 individuals who had lung cancer. A spectrophotometer for atomic absorption used to measure the levels of zinc and cadmium. Through independent T, the data examined using SPSS 23. Lung cancer patients and healthy people did not significantly differ in their serum amounts of Cd or Zn ($p \geq 0.05$); nevertheless, there was a significant difference in urine between the two groups ($p \geq 0.05$). Lung cancer patients showed higher amounts of zinc and cadmium in their urine and lower levels in their serum compared to healthy volunteers.

Keywords: Trace element, Lung cancer, Atomic Absorption Spectrophotometer, RAD 7, CR-32.

1 Introduction

Lung cancer remains the most common malignant neoplasm worldwide and is the leading cause of cancer-related mortality, accounting for 1.8 million deaths (18%) annually, as reported by Thun (2010)[1]. The dismal 5-year survival rate of approximately 20% results from to the fact that the disease often remains asymptomatic until it reaches an advanced, incurable stage, as described by pervious studies in [2], [3]. According to early diagnosis is critical to improving patient outcomes[4].

Several risk factors have been established in previous studies, including tobacco smoking [4], exposure to radon[5], and asbestos [6]. Many researchers also suggested other potential contributors such as HIV infection, a history of asthma[7], pneumonia[8], and tuberculosis[9].

Conversely, it has been found that imbalanced levels of trace elements, such as zinc [10], copper[11], and others, are strongly associated with lung cancer risk[12]. Detecting trace elements in the human body plays a crucial role in the early diagnosis of lung cancer[13].

Zinc, in particular, is essential for numerous physiological functions including cellular metabolism, thyroid regulation, blood coagulation, immune function, wound healing, and enzymatic activity. Naja and her co-workers stated that zinc deficiency can lead to immunodeficiencies, inflammatory disorders, dermatological diseases, developmental complications, neurological issues, oxidative stress, and hormonal imbalances[14].

Over time, even with brief exposure, the very toxic metal cadmium (Cd) builds up in the body and stays there for an extended period of time[14]. Inhalation, diet, cigarette smoke, and drinking water tainted with lead are some of the ways it can enter the body. About 5% of Cd enters the body through nutrition and is mostly absorbed in the lungs. The primary method by which lead enters the lungs is through cigarette smoking. The lungs can be harmed or even killed by breathing in excessive amounts of mercury. Plus, eating too much CD that contains nutrients can make you throw up and have diarrhea. Low-level mercury (Hg) absorbed through the air, water, and nourishment over an extended period of time builds up in the kidneys and can be lethal because it damages the renal arterioles and glomeruli (Satarug et al., 2011)[15].

According to Satarug et al. (2011), cadmium exposure has been linked to higher rates of human mortality; it has also been detected in the composition of kidney stones and urine that has been released with glomerular protein. The purpose of this study was to examine the levels of zinc and cadmium in urine and blood across groups of healthy individuals and patients.

* Corresponding author
E-mail address wellmsc@gmail.com (Instructor).
Peer-reviewed under the responsibility of the University of Garmian.

2 Materials and methods

2. 1 Study Participants

Serum and urine samples collected from participants at Marjan Hospital. The study group consisted of 64 lung cancer patients (13 males and 16 females), with ages ranging from 33 to 89 years. The second group included 25 healthy individuals, comprising 8 women and 17 men.

2. 2 Sample Collection and Storage

Urine samples collected from patients after they fasted for eight hours before surgery, as diet can influence the trace-element content. Control participants asked to fast overnight, and their urine samples collected the following morning, which is typically the best time for urinalysis due to concentrated urine. To prevent degradation and contamination of the trace elements, all urine samples were stored in high-density polyethylene containers and kept at -20°C until analysis. Upon arrival at the hospital, all patients were diagnosed with primary superficial lung cancer, except for those with metastatic tumors, other malignancies, renal disease, or malnutrition, who excluded from the study.
Approximately 10 ml of venous blood collected from each participant. After the blood transferred into gel tubes, it was centrifuged for 10 minutes at 3000 rpm to extract the serum. The blood allowed to coagulate, and once the copper and zinc concentrations were determined, the serum transferred into labeled Eppendorf tubes and stored at -80°C for further analysis.

2.3 Determining Trace Elements (Atomic Absorption Spectrophotometer)

One technique to measure a variety of heavy metal concentrations in liquid samples is the Atomic Absorption Spectrophotometer (AAS). Fascinatingly, this technique can analyze and pinpoint the concentration of more than 62 distinct metals in a given mixture. Copper, cadmium, and lead are among them. To measure the concentration of the chemical element of interest, the AAS technique measures the amount of radiation that the element absorbs. This technique often involves irradiating a sample. Because of their absorption of visible or ultraviolet light during the radiation, the sample atoms reach a higher energy level. According to (Rashed 2011)[16]. according to AAS is fitted with a detector that can contrast the wavelengths of light passing through it with the wavelengths of light transmitted by the sample. An energy absorption peak at a particular wavelength is produced by a signal processor upon detecting the variations in light wavelength. It is helpful to know that the ionization energy—a distinct quantity for every chemical element—is the amount of energy required by an atom in a mole to lose one electron. Physically, as an electron moves within an atom, a photon with a specific amount of energy E is released. A characteristic pattern of wavelengths at which an atom may absorb energy is derived from its individual electron configuration. The ability to assess a sample's concentration through a qualitative examination made possible by this characteristic. The Beer- Lambert law serves as the basis for calculating saturation. A group of Australian chemists led by Alan Walsh significantly improved the present form of the AAS technology in the 1950s, despite the fact that it was created in the nineteenth century [17].

Statistical analysis

To assess the results, Student's t-tests were used. Set at $P < 0.05$, statistical significance considered.

4 Result and Discussions

Forty-eight males and sixteen females, ages ranging from 34 to 89, made up the first group of sixty-four patients (thirty-two urine samples and thirty-two serum samples). In addition, there were also 25 healthy people in the second group—17 men and 8 women—with normal lung tissue and no prior history of lung systemic illnesses. According to the ages individuals categorized into, 22% were between the ages of 50 and 65, and 31% were between the ages of 34 and 49. Among the sample, 47% of participants were aged 66-89. Of the gender divisions, 75% of men and 25% of women , 62% were smoked, and 38% of people did not smoke (table 1, figure 1, 2, 3).

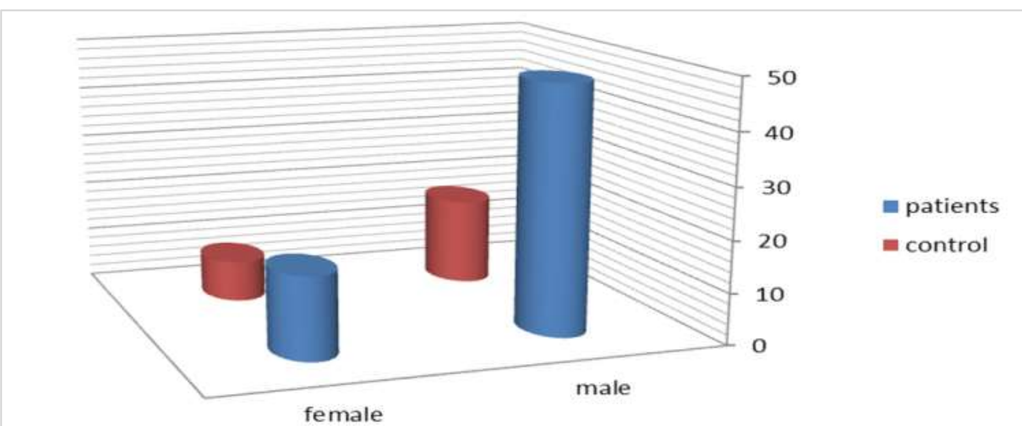

Figure 1: Distribution of patients according to sex.

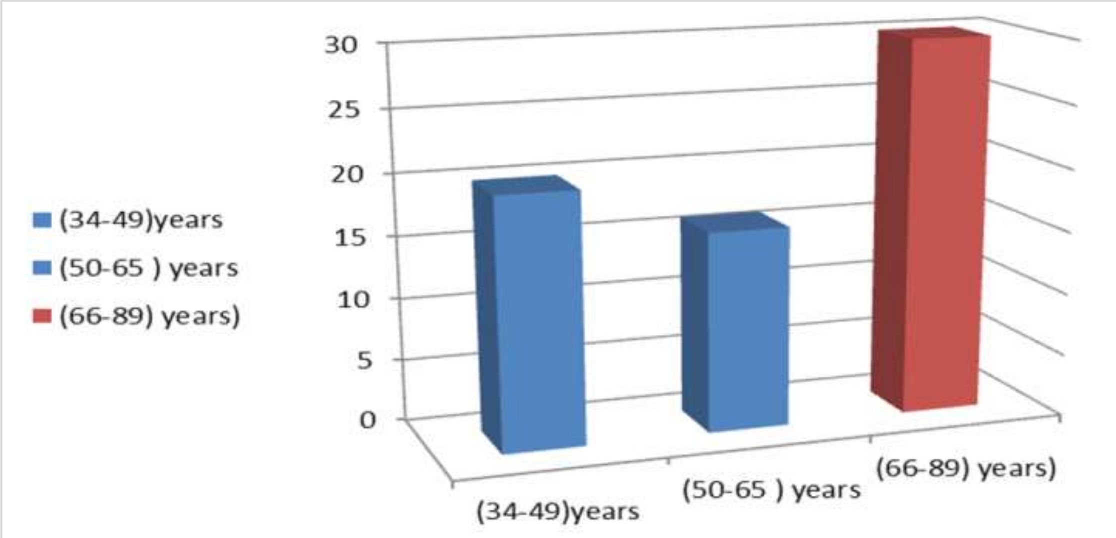

Figure 2: Distribution of patients according to age groups.

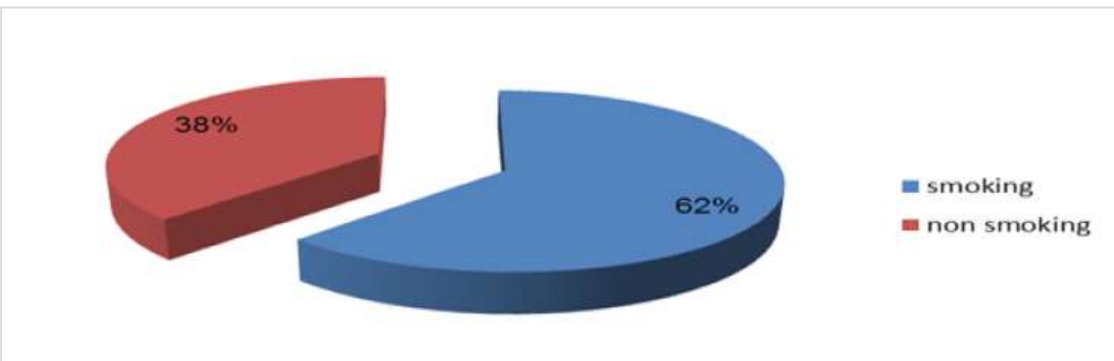

Figure 3: Distribution of patients according to smoker.

Table 1: Relation between demographic data and studied groups.

Information	Groups			
	Patients	No. (%)	Healthy	No. (%)
Gender	Male	48 (75%)	Male	17 (68%)
	Female	16(25%)	Female	8(32%)
Age groups	(34-49)	20 (31%)	(34-49)	7(28%)
	(50-65)	14(22%)	(50-65)	5(20%)
	(66-89)	30(47%)	(66-89)	13(52%)
Smoking	Smoker	40 (62%)		
	Non smoker	24 (38%)		

Zinc and cadmium mean and standard division values in urine were substantially higher in patients than in controls (Zn: 0.592± 0.182 µg/dl vs. 0.213 ± 0.073 µg/dl, Cd: -0.460 ± 0.136 µg/dl, 0.148 ± 0.067 µg/dl). When serum Table (2) (Figs. 3 and 4) shows that the mean standard division values of zinc and cadmium in serum were not significantly different between patients and controls (Zn: 0.592± 0.182 µg/dl vs. 0.213 ± 0.073 µg/dl, Cd: -0.460 ± 0.136 µg/dl, 0.148 ± 0.067 µg/dl).

Table 2: Mean ± SD of Cd and Zn in the studies groups in serum and urine.

Trace element	Groups	Mean ± SD	p-value
Serum Cd mg/dl	Patients	0.447±0.202	0.3
	Healthy	0.383±0.097	NS
Serum Zn mg/dl	Patients	0.511 ± 0.210	0.3
	Healthy	0.440 ± 0.169	NS
Urine Cd mg/dl	Patients	0.460 ± 0.136	0.000***
	Healthy	0.148 ± 0.067	HS †
Urine Zn mg/dl	Patients	0.592 ± 0.182	0.000***
	Healthy	0.213 ± 0.073	HS †

NS = no significant HS = High significant

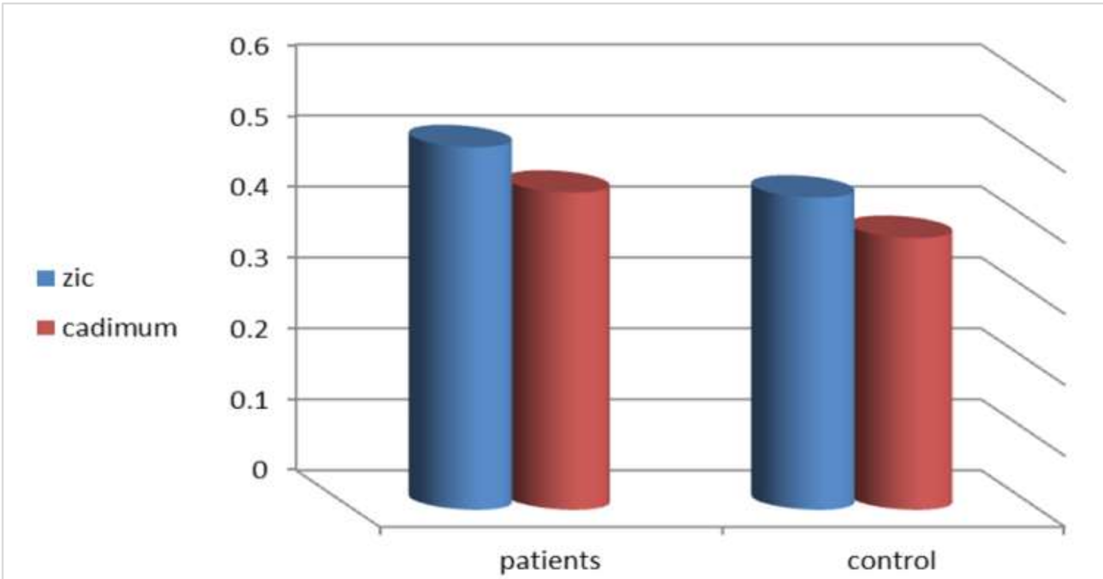

Figure 4: Serum zinc (Zn) and cadmium (Cd) concentrations in the lung cancer group compared with healthy controls.

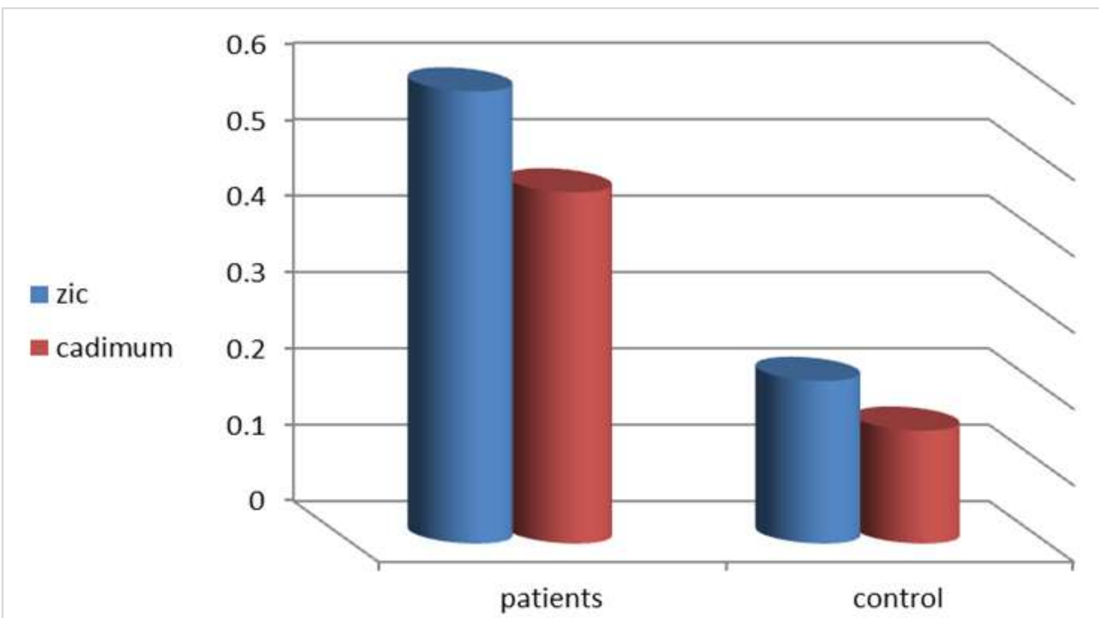

Figure 5: Urine zinc (Zn) and cadmium (Cd) concentrations in the lung cancer group compared with healthy controls.

5 Discussion

In this work, the distribution of specific trace minerals in relation to healthy individuals and their identification in the serum of Iraqi lung cancer patients were the main goals of using atomic absorption spectroscopy. Zinc has a major role in apoptosis, oxidative stress, and/or modifications to cell signaling (Gómez et al., 2016)[18]. According to Gómez et al.'s analysis of the relationship between zinc and lung cancer, there may be a way for zinc to prevent lung cancer. On the present results, there was no statistically significant difference seen in the serum zinc concentration between the control and patient groups. This investigation supported the findings of the other studies. (Wang et al., 2019)[19] examined the zinc concentration in lung cancer patients by doing a meta-analysis of 32 papers from the databases of CNKI, SinoMed, Wanfang, Cochrane, ScienceDirect, and PubMed. According to their findings, lung cancer patients' serum zinc levels were considerably lower than those of the control group. An further argument against (Cobanoglu et al., 2010)[20] is this: By testing serum levels of copper (Cu), lead (Pb), zinc (Zn), iron (Fe), cobalt (Co), cadmium (Cd), manganese (Mn), and magnesium (Mg), researchers were able to determine a correlation between particular mineral, trace element, and heavy metal levels in lung cancer patients. Comparing lung cancer patients to controls, Pb, Mn, and Co were greater, whereas Mg, Cu, and Zn were lower. Studies conducted by (Abbas et al., 2022)[21] revealed that there was a significant difference ($p<0.05$) in the serum concentrations of Pb, Cu, Cd, and Zn between healthy males with lung cancer and healthy females with lung cancer. However, there were not many differences between the cadmium metal concentrations in the patients' and control group.

The measurement of this study Urine samples from lung cancer patients had far higher levels of cadmium than those from healthy subjects. Greater air lead concentrations were correlated with comparatively greater urine Cd concentrations, according to a study (Lee et al., 2022)[22]. Tobacco use and air pollution were still considered possible sources of lead exposure even after controlling for behavioral and sociodemographic characteristics. The severely polluted zone showed a higher incidence of lung cancer. A 1 µg/g rise in urine Cd level was associated with a 1.25-fold increase in the probability of lung cancer incidence. Urinary Cd levels were noticeably higher in lung cancer patients. Urine Cd levels > 1.58 versus <1.58 µg/g-creatinine were associated with a significantly worse survival rate for lung cancer patients (survival, medium, 192.0 vs 342.5 days, $p < 0.001$). Those who had higher urine Cd levels at the longitudinal follow-up were more likely to develop lung cancer (urine Cd level ≥ 1.58 vs <1.58 µg/g-creatinine: 3.91% vs. 0.87%, hazard ratio: 4.65, $p < 0.001$). Furthermore, in line with a study (Mansouri et al., 2020)[23], smokers' urine included greater amounts of Cd (0.03 vs. 0.12 µg/L), Co (0.6 vs. 1.22 µg/L), and Cr (14.00 vs. 18.17 µg/L).
Zinc demonstrated to have the ability to neutralize free radicals protecting the body from harmful effects, immune disorders, and increased risk of cancer (Grigorescu et al, 2015)[24]; , the deficiency of zinc can increase oxidative stress (Gomes et al., 2006 and Song et al., 2009)[25], [26]. Importantly, an increase of oxidative and nitrosative stress and inflammation in rat lung, in a stage of marginal zinc deficiency, found (Biaggio et al., 2010)[27]. Zn microenvironment may play a key role in oxidative stress, apoptosis, and/or cell signaling alterations which influence the behavior of malignant cancer cells. In fact, the study of cancer biology has mainly focused on malignant epithelial cancer cells, although tumors also contain a stromal compartment, composed by different type of cells and also includes various types of macromolecules comprising the extracellular matrix. Following this rationale, several hundred zinc supplementation studies have been conducted, investigating the effects of zinc on cancer, often with contradictory results. The mechanisms responsible for Zn accumulation and the consequence of Zn dysregulation are poorly understood, and mostly dependent of the type of cell or tissue compromised. Cadmium can directly damage DNA (Filipic et al., 2006)[28] and inhibit its repair (Hartwig 1998)[29] and can affect methylation (Poirier et al., 2002) and Takiguchi et al., (2003)[30], [31]. Cadmium induces cancer through several mechanisms, including aberrant gene expression, inhibition of DNA damage repair, induction of oxidative stress and inhibition of apoptosis (Joseph et al., 2009)[32].the causes of that metal (Zn and Cd) in urine was significantly different compared with concentration in serum may be because of change in filtrate renal kidney or error in metabolism may be effect on the concentration of metal element in urine and secreted high.

6 Conclusion

In contrast to healthy persons, lung cancer patients had lower serum zinc and cadmium levels, but their urine samples showed greater zinc and cadmium levels. And that age group has higher infection rates than the other age groups.

Conflict of interests

The authors declare no competing interests.

References

[1] M. J. Thun, Early landmark studies of smoking and lung cancer. Lancet Oncol **11**, (12), 1200, doi:10.1016/S1470-2045(09)70401-2, (2010).

[2] P. Zhan, X. Q. Suo, Q. Q. Qian, Y. Q. Song, X. Y. Wang, J. L. Wang, Chlamydia pneumoniae infection and lung cancer risk: a meta-analysis. *Eur J Cancer* **47**, (5), 742–747, doi:10.1016/j.ejca.2010.11.007, (2011).

[3] Y. Wang, Z. Sun, A. Li, Y. Zhang, Association between serum zinc levels and lung cancer: a meta-analysis of observational studies. *World J Surg Oncol* **17**, (1), 1–8, doi:10.1186/s12957-019-1670-z, (2019)

[4] Y. Jin, Z. Wang, Z. Q. He, M. Yang, Y. Zhou, W. Liu, Combined effects of serum trace metals and polymorphisms of CYP1A1 or GSTM1 on non-small cell lung cancer: A hospital based case–control study in China. Cancer Epidemiol **35**, (2), 182–187, doi:10.1016/j.canep.2010.10.011, (2011).

[5] K. Zabłocka-Słowińska, J. Grajeta, A. M. Kwiatkowski, K. Wąsowicz, A. Słowińska, Serum and whole blood Zn, Cu and Mn profiles and their relation to redox status in lung cancer patients. *J Trace Elem Med Biol* **45**, 78–84, doi:10.1016/j.jtemb.2017.11.004, (2018).

[6] J. T. Juloski, S. Nikolić, I. Petrović, M. Ignjatović, Colorectal cancer and trace elements alteration. *J Trace Elem Med Biol* **59**, 126451, doi:10.1016/j.jtemb.2020.126451, (2020).

[7] Essa, H. O., Al-Attiyah, K. H. & Al-Hamzawi, A. A. Estimation of uranium concentration of cancer patients' blood in Babylon Province, Iraq. *Pollution* **10**, 236–247, doi: 10.22059/poll.2023.363196.2009, (2024).

[8] J. J. Muros, C. Cabrera-Vique, M. Briones, I. Seiquer, Assessing the dietary intake of calcium, magnesium, iron, zinc and copper in institutionalised children and adolescents from Guatemala. *J Trace Elem Med Biol* **53**, 91–97, doi:10.1016/j.jtemb.2018.10.004, (2019).

[9] T. Filippini, G. Ferrante, M. Piccinelli, C. Malagoli, S. Vescovi, J. Vinceti, Dietary intake of cadmium, chromium, copper, manganese, selenium and zinc in a Northern Italy community. *J Trace Elem Med Biol* **50**, 508–517, doi:10.1016/j.jtemb.2018.07.006, (2018).

[10] H. Sung, J. Ferlay, R. L. Siegel, M. Laversanne, I. Soerjomataram, A. Jemal, F. Bray, Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* **71**, (3), 209–249, doi:10.3322/caac.21660, (2021).

[11] E. B. Garon, R. Rizvi, R. Hui, N. Leighl, A. Balmanoukian, J. D. Eder, Five-year overall survival for patients with advanced non–small-cell lung cancer treated with pembrolizumab: results from the phase I KEYNOTE-001 study. *J Clin Oncol* **37**, (28), 2518–2527, doi:10.1200/JCO.19.00934, (2019).

[12] R. Ghosal, P. Kloer, K. E. Lewis, A review of novel biological tools used in screening for the early detection of lung cancer. *Postgrad Med J* **85**, 358–363, doi:10.1136/pgmj.2008.073817, (2009).

[13] J. Lubiński, M. Marciniak, W. Muszynska, J. Jaworska-Bieniek, P. Kaczmarek, A. Sukiennicki, Survival of laryngeal cancer patients depending on zinc serum level and oxidative stress genotypes. Biomolecules **11**, 865, doi:10.3390/biom11060865, (2021).

[14] G. M. Naja, B. Volesky, Toxicity and sources of Pb, Cd, Hg, Cr, As, and radionuclides in the environment. In: Handbook of Advanced Industrial and Hazardous Wastes Management 855–903, doi:10.1201/9781315117423, (2017).

[15] S. Satarug, S. H. Garrett, M. A. Sens, D. A. Sens, Cadmium, environmental exposure, and health outcomes. *Cien Saude Colet* **16**, 2587–2602, doi:10.1590/S1413-81232011000700033, (2011).

[16] M. N. Rashed, The role of trace elements on hepatitis virus infections: a review. *J Trace Elem Med Biol* **25**, 181–187, doi:10.1016/j.jtemb.2010.11.003, (2011).

[17] R. Garcia, A. P. Báez, Atomic absorption spectrometry (AAS). Tech, Ed 1–13, doi:10.5772/25925, (2012).

[18] N. N. Gomez, V. S. Biaggio, M. E. Ciminari, M. V. P. Chaca, S. M. Álvarez, Zinc: What Is Its Role in Lung Cancer? In: Nutritional Deficiency 789–800, doi:10.5772/63209, (2016).

[19] Naji, T. F. & Hassoon, S. O. Measuring of Radon Gas Concentrations in serum samples of lung-cancer patients in Babylon governorate, Iraq. *J. Phys.: Conf. Ser.* **1999**, 012054, doi: 10.1088/1742-6596/1999/1/012054, (2021).

[20] U. Cobanoglu, H. Demir, F. Sayir, M. Duran, D. Mergan, Some mineral, trace element and heavy metal concentrations in lung cancer. *Asian Pac J Cancer Prev* **11**, 1383–1388, doi:10.31557/APJCP.2010.11.5.1383, (2010).

[21] Ahmed, R. S., Mohammed, R. S., Mahdi, K. H., Mahdi, Q. A., Mostafa, M. Y. & Khalaf, H. N. Evaluation of uranium concentration in the blood of breast-cancer women using CR-39 detector. *Appl. Radiat. Isot.* **182**, 110120, https://doi.org/10.1016/j.apradiso.2022.110120, (2022).

[22] N.-W. Lee, J.-Y. Lee, H.-W. Kim, Y. J. Kim, M. Kim, Air-polluted environmental heavy metal exposure increase lung cancer incidence and mortality: A population-based longitudinal cohort study. *Sci Total Environ* **810**, 152186, doi:10.1016/j.scitotenv.2021.152186, (2022).

[23] B. Mansouri, S. M. Hamidian, A. R. Beigi Harchegani, Urinary metal levels with relation to age, occupation, and smoking habits of male inhabitants of eastern Iran. *Biol Trace Elem Res* **195**, 63–70, doi:10.1007/s12011-018-1553-0, (2020).

[24] Bolognesi, C., Migliore, L., Lista, F., Caroli, S., Patriarca, M., De Angelis, R., Capocaccia, R., Amadori, S., Pulliero, A., Balia, C. & Colognato, R. Biological monitoring of Italian soldiers deployed in Iraq. Results of the SIGNUM project. *Int. J. Hyg. Environ. Health* **219**, 24–32, https://doi.org/10.1016/j.ijheh.2015.08.001, (2016).

[25] N. N. Gomez, S. W. Leonard, M. G. Traber, E. Ho, Overexpression of inducible nitric oxide synthase and cyclooxygenase-2 in rat zinc-deficient lung: involvement of a NF-κB dependent pathway. Nitric Oxide **14**, 30–38, doi:10.1016/j.niox.2005.11.007, (2006).

[26] Y. Song, S. W. Leonard, M. G. Traber, E. Ho, Zinc deficiency affects DNA damage, oxidative stress, antioxidant defenses, and DNA repair in rats. *J Nutr* **139**, 1626–1631, doi:10.3945/jn.109.104216, (2009).

[27] V. S. Biaggio, M. V. Pérez Chaca, S. R. Valdéz, N. N. Gómez, M. S. Gimenez, Alteration in the expression of inflammatory parameters as a result of oxidative stress produced by moderate zinc deficiency in rat lung. *Exp Lung Res* **36**, 31–44, doi:10.3109/01902140903433804, (2010).

[28] M. Filipič, T. Fatur, M. Vudrag, Molecular mechanisms of cadmium induced mutagenicity. *Hum Exp Toxicol* **25**, 67–77, doi:10.1191/0960327106ht515oa, (2006).

[29] A. Hartwig, Carcinogenicity of metal compounds: possible role of DNA repair inhibition. *Toxicol Lett* **102**, 235–239, doi:10.1016/S0378-4274(98)00217-2, (1998).

[30] L. A. Poirier, T. I. Vlasova, The prospective role of abnormal methyl metabolism in cadmium toxicity. Environ Health Perspect **110**, (7), 793–795, doi:10.1289/ehp.02110793, (2002).

[31] M. Takiguchi, W. E. Achanzar, W. Qu, G. Li, M. P. Waalkes, Effects of cadmium on DNA-(Cytosine-5) methyltransferase activity and DNA methylation status during cadmium-induced cellular transformation. *Exp Cell Res* **286**, (2), 355–365, doi:10.1016/S0014-4827(03)00034-5, (2003).

[32] P. Joseph, Mechanisms of cadmium carcinogenesis. *Toxicol Appl Pharmacol* **238**, (3), 272–279, doi:10.1016/j.taap.2009.01.035, (2009).